UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from _to_

Commission File Number 001-36352

AKEBIA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**20-8756903**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
245 First Street, Cambridge, MA	**02142**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 871-2098

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	AKBA	The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒
If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐
Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐ Indicate by check mark whether registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the registrant's Common Stock on The Nasdaq Global Market on June 30, 2022, was $64,134,957.

The number of shares of registrant's Common Stock outstanding as of February 28, 2023 was 184,248,045.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2023 Annual Meeting of Stockholders within 120 days after the end of the registrant's fiscal year ended December 31, 2022. Portions of the proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that are being made pursuant to the provisions of the U.S. Private Securities Litigation Reform Act of 1995 with the intention of obtaining the benefits of the "safe harbor" provisions of that Act. All statements contained in this Annual Report on Form 10-K other than statements of historical fact are forward-looking statements. These forward-looking statements may be accompanied by words such as "anticipate," "believe," "build," "can," "contemplate," "continue," "could," "should," "designed," "estimate," "project," "expect," "forecast," "future," "goal," "intend," "likely," "may," "plan," "possible," "potential," "predict," "strategy," "seek," "target," "will," "would," and other words and terms of similar meaning, but the absence of these words does not necessarily mean that a statement is not forward-looking. These forward-looking statements include, but are not limited to, statements about:

- the potential therapeutic benefits, safety profile, and effectiveness of vadadustat;
- our expectations with respect to the development of vadadustat, if any, following our receipt of a complete response letter to our new drug application for vadadustat for the treatment of anemia due to chronic kidney disease in adult patients, including the timing of a potential response to the Formal Dispute Resolution Request from the U.S. Food and Drug Administration;
- that delivering value broadly to the kidney community, as well as others who may benefit from our medicines, will result in delivering value for stockholders;
- our pipeline and portfolio, including its potential, and our related research and development activities;
- the timing of or likelihood of regulatory filings and approvals, including with respect to labeling or other restrictions, the potential approval of vadadustat and our outlook related thereto, and potential indications for vadadustat;
- the timing, investment and associated activities involved in continued commercialization of Auryxia® (ferric citrate), its growth opportunities and our ability to execute thereon;
- the potential indications, demand and market opportunity, potential and acceptance of Auryxia and vadadustat, if approved, including the size of eligible patient populations;
- the potential therapeutic applications of the hypoxia inducible factor pathway;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations, projections and estimates regarding our capital requirements, need for additional capital, financing our future cash needs, costs, expenses, revenues, capital resources, cash flows, financial performance, profitability, tax obligations, liquidity, growth, contractual obligations, the period of time our cash resources and collaboration funding will fund our current operating plan, estimates with respect to our ability to operate as a going concern, our internal control over financial reporting and disclosure controls and procedures, and any future deficiencies or material weaknesses in our internal controls and procedures;
- the direct or indirect impacts of the COVID-19 pandemic on our business, operations and the markets and communities in which we and our partners, collaborators, vendors, and customers operate;
- our manufacturing, supply and quality matters and any recalls, write-downs, impairments or other related consequences or potential consequences;
- estimates, beliefs and judgments related to the valuation of intangible assets, goodwill, debt and other assets and liabilities, including our impairment analysis and our methodology and assumptions regarding fair value measurements;
- the timing of the availability and disclosure of clinical trial data and results;
- our and our collaborators' strategy, plans and expectations with respect to the development, manufacturing, supply, commercialization, launch, marketing and sale of Auryxia and vadadustat, if approved, and the associated timing thereof;
- the designs of our studies, and the type of information and data expected from our studies and the expected benefits thereof;
- our ability to maintain any marketing authorizations we currently hold or will obtain, including our marketing authorizations for Auryxia and our ability to complete post-marketing requirements with respect thereto;
- our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for Auryxia and vadadustat, if approved;
- the timing of initiation of our clinical trials and plans to conduct preclinical studies and clinical trials in the future;

- the timing and amounts of payments from or to our collaborators and licensees, and the anticipated arrangements and benefits under our collaboration and license agreements, including with respect to milestones and royalties;
- our intellectual property position, including obtaining and maintaining patents, and the timing, outcome and impact of administrative, regulatory, legal and other proceedings relating to our patents and other proprietary and intellectual property rights, patent infringement suits that we have filed or may file, or other actions that we may take against companies, and the timing and resolution thereof;
- expected ongoing reliance on third parties, including with respect to the development, manufacturing, supply and commercialization of Auryxia and vadadustat, if approved;
- accounting standards and estimates, their impact, and their expected timing of completion;
- estimated periods of performance of key contracts;
- our facilities, lease commitments, and future availability of facilities;
- cybersecurity;
- insurance coverage;
- management of personnel, including our management team, and our employees, including employee compensation, employee relations, and our ability to attract, train and retain high quality employees;
- the implementation of our business model, current operating plan, and strategic plans for our business, product candidates and technology, and business development opportunities including potential collaborations, alliances, mergers, acquisitions or licensing of assets;
- our workforce reductions, future charges expected to be incurred in connection therewith and estimated reductions in net cash required for operating activities in connection therewith; and
- the timing, outcome and impact of current and any future legal proceedings.

Any or all of these forward-looking statements in this Annual Report on Form 10-K may turn out to be inaccurate. These forward-looking statements involve risks and uncertainties, including those that are discussed below under the heading "Risk Factor Summary," and the risk factors detailed further in Part I, Item 1A. "Risk Factors" included in this Annual Report on Form 10-K and elsewhere in this Annual Report on Form 10-K and in our Securities and Exchange Commission reports filed after this report, that could cause our actual results, financial condition, performance or achievements to be materially different from those indicated in these forward-looking statements. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Except as required by law, we assume no obligation to publicly update or revise these forward-looking statements for any reason. Unless otherwise stated, our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

This Annual Report on Form 10-K also contains estimates and other information concerning our industry and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Unless otherwise expressly stated, we obtained this industry, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.
In this Annual Report on Form 10-K, unless otherwise stated or the context otherwise requires, references to “Akebia,” “we,” “us,” “our,” “the Company,” and similar references refer to Akebia Therapeutics, Inc. and, where appropriate, its subsidiaries, including Keryx Biopharmaceuticals, Inc., or Keryx.

AURYXIA®, AKEBIA Therapeutics®, Vafseo™ and their associated logos are trademarks of Akebia and/or its affiliates. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. All website addresses given in this Annual Report on Form 10-K are for information only and are not intended to be an active link or to incorporate any website information into this document.

RISK FACTORS SUMMARY

Investing in our common stock involves numerous risks, including the risks summarized below and described in further detail in "Part I, Item 1A. Risk Factors" of this Annual Report on Form 10-K, any one of which could materially adversely affect our business, financial condition, results of operations, and prospects. These risks include, but are not limited to, the risks noted below.

- We have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.
- We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.
- Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product and product candidates on unfavorable terms to us.
- If we fail to regain compliance with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.
- We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.
- We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.
- Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.
- Our obligations in connection with the loan agreement with Pharmakon and requirements and restrictions in the loan agreement could adversely affect our financial condition and restrict our operations.
- Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.
- Our business is substantially dependent on the commercial success of Auryxia. If we are unable to continue to successfully commercialize Auryxia, our results or operations and financial condition will be materially harmed.
- If we are unable to maintain or expand, or, if vadadustat is approved, initiate, sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, vadadustat, if approved, or any other product candidates that may be approved.
- Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, vadadustat, if approved, or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.
- We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.
- The commercialization of Riona™ and Vafseo™ in Japan and our current and potential future efforts with respect to the development and commercialization of our products and product candidates outside of the United States subject us to a variety of risks associated with international operations, which could materially adversely affect our business.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and, if approved, commercialization of vadadustat and any other product candidates.
- We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.
- Conducting clinical trials outside of the United States, as we have done historically and as we may decide to do in the future, presents additional risks and complexities and, if we decide to conduct a clinical trial outside of the United States in the future, we may not complete such trials successfully, in a timely manner, or at all, which could affect our ability to obtain regulatory approvals.
- Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.
- We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat or any other product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.
- Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved.
- We are subject to a complex regulatory scheme that requires significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

- We will incur significant liability if it is determined that we are promoting any “off-label” use of Auryxia or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.
- Disruptions in the FDA, regulatory authorities outside the U.S. and other government agencies caused by global health concerns or funding shortages could prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.
- Compliance with privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.
- Legislative and regulatory healthcare reform may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.
- We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona, Vafseo and vadadustat and if these collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia, Riona, Vafseo and vadadustat, and our business could be materially harmed.
- We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.
- We rely upon third parties to conduct all aspects of our product manufacturing, and in many instances only have a single supplier, and the loss of these manufacturers, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.
- We rely upon third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, vadadustat or any of our product candidates, and our business could be substantially harmed.
- If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.
- If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.
- We may not be able to protect our intellectual property rights throughout the world.
- The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.
- The market entry of one or more generic competitors or any third party’s attempt to challenge our intellectual property rights will likely limit Auryxia sales and have an adverse impact on our business and results of operation.
- Litigation and administrative proceedings, including third party claims of intellectual property infringement and opposition/invalidation proceedings against third party patents, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.
- We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.
- If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize vadadustat or commercialize Auryxia.
- Our cost savings plan and the associated workforce reductions implemented in April, May and November 2022 may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.
- We may encounter difficulties in managing our growth, including with respect to our employee base, and managing our operations successfully.
- We are currently subject to legal proceedings that could result in substantial costs and divert management's attention, and we could be subject to additional legal proceedings.
- Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors.

PART I

Item 1. Business

Overview

We are a fully integrated biopharmaceutical company committed to addressing patients' unmet needs. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative therapeutics that we believe serves as a foundation for future growth. Our purpose is to better the life of each person impacted by kidney disease, and we have established ourselves as a leader in the kidney community. We believe our demonstrated ability to deliver value broadly to the kidney community has enabled us to build a sustainable company. While our current focus centers on people living with kidney disease, we believe our continued commitment to our products and pipeline assets, focusing on all patients who can realize a meaningful benefit from our medicines, will result in delivering value for shareholders.

Our current portfolio includes:

- ***Auryxia® (ferric citrate)***, a medicine approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with dialysis dependent chronic kidney disease, or DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with non-dialysis-dependent chronic kidney disease, or NDD-CKD. The product is also available in Japan and Taiwan.
- ***Vafseo™ (vadadustat)***, an oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor, is approved in Japan for the treatment of anemia due to chronic kidney disease, or CKD, in adult patients. Vadadustat is under regulatory review for the treatment of anemia due to CKD in Europe, where it has received a positive opinion from the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, in adult patients on dialysis. Vadadustat is also under regulatory review for the treatment of anemia due to CKD in Australia, Korea, Taiwan and other countries. We continue to pursue a path to potentially gain approval for vadadustat in the U.S. Further, we have several lifecycle management and indication expansion opportunities currently under evaluation or in development for vadadustat.
- ***HIF-PH inhibitors*** in preclinical development. The discovery of hypoxia-inducible factor, or HIF, laid the foundation to explore the central role of oxygen sensing in many diseases. As we have seen through the development of vadadustat as a treatment for anemia due to CKD, when stabilized, HIF triggers wide-ranging adaptive, protective responses during hypoxic or ischemic conditions. Our clinical team and research scientists are eager to further develop HIF-PH inhibitors for various indications including acute kidney injury, or AKI, and retinopathy of prematurity, or ROP.

We continue to explore additional commercial and development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation to leverage our fully integrated team.

Auryxia

Today we market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Auryxia is a non-calcium, non-chewable, orally administered tablet that was approved for marketing by the U.S. Food and Drug Administration, or FDA, in September 2014 as a phosphate binder for the Hyperphosphatemia Indication and was commercially launched in the United States shortly thereafter. In November 2017, Auryxia received marketing approval from the FDA for a second indication, the treatment of iron deficiency anemia, and was commercially launched for this indication in the United States shortly thereafter. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize ferric citrate hydrate as Riona® in Japan. Averoa SAS, or Averoa, has an exclusive license to develop and commercialize ferric citrate in the European Economic Area, or EEA, Turkey, Switzerland and the United Kingdom.

In 2022, Auryxia product revenue increased approximately 24.5% over 2021 due to the company's focus on implementing a new contracting strategy in late 2021. Since 2018, Auryxia product revenue has grown at a compounded annual growth rate of approximately 17% due to market share gains and improved net price per pill, despite a 13% decline in total prescriptions for phosphate binders in the United States since 2018.

Vadadustat

We are seeking regulatory approval in the European Union and the United States for vadadustat as an oral treatment of anemia in adult DD-CKD patients. We and Mitsubishi Tanabe Pharma Corporation, or MTPC, are also seeking regulatory approval for vadadustat as a treatment for anemia in adult DD-CKD and NDD-CKD patients in the United Kingdom, Switzerland and Australia, and Korea and Taiwan, respectively.

Vadadustat is currently pending an European Commission, or EC, approval decision. On February 23, 2023, the CHMP of the EMA adopted a positive opinion recommending the EC approve Vafseo™ for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. We anticipate that the EC will grant marketing authorization for Vafseo in May 2023, which would be applicable to all 27 European Union member states and Iceland, Norway and Liechtenstein. Following the termination of our U.S. and international collaboration agreements with Otsuka in June 2022, we regained full rights to vadadustat in Europe, Australia, China, Canada, Latin America, the Middle East and Russia. As we do not have a commercial presence in Europe, we are seeking a partner in Europe and will support the partner's launch of vadadustat, if approved. We are seeking to identify and secure a partner that can effectively facilitate treatment of as many people as would benefit from vadadustat, if approved, thus maximizing the value of the asset.

We submitted a New Drug Application, or NDA, to the FDA for vadadustat in March of 2021. On March 29, 2022, the FDA issued a complete response letter, or CRL, to our NDA for vadadustat. The FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. The FDA expressed safety concerns noting failure to meet non-inferiority in MACE in the non-dialysis patient population, the increased risk of thromboembolic events, driven by vascular access thrombosis in dialysis patients, and the risk of drug-induced liver injury. We believe there are compelling data supporting a positive benefit-risk profile for the use of vadadustat broadly in patients with CKD, including non-dialysis patients though we have always remained cautious about receiving a broad label for vadadustat that would extend to non-dialysis patients with anemia due to CKD. As such, we began the process to dispute the FDA ruling, and in October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, with the FDA regarding the CRL, specifically related to DD-CKD adult patients. The appeal focused on the favorable balance of the benefits and risks of vadadustat for the treatment of adult DD-CKD patients in light of safety concerns expressed by the FDA in the CRL related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, which is still under consideration by the FDA at the time of this filing.

Following the termination of our collaboration agreement with Otsuka Pharmaceutical Co. Ltd., or Otsuka, we own full rights to vadadustat in the U.S., subject to our licensing agreement with Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor. If we obtain FDA approval of vadadustat for DD-CKD adult patients, we plan to commercialize vadadustat in the United States with CSL Vifor.

Leveraging our learnings from the research and development of vadadustat, and a breadth of scientific expertise on the HIF pathway, we believe there is potential to leverage HIFs to treat other hypoxic conditions and to explore the use of HIFs in acute settings. We believe this potential applies to vadadustat as well as other preclinical assets we are internally developing.

Regarding broader uses of vadadustat, in July 2020 we partially funded an investigator-sponsored clinical study conducted by The University of Texas Health Science Center at Houston, or UTHealth, in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and treat acute respiratory distress syndrome, or ARDS, in adult patients who have been hospitalized due to COVID-19 and hypoxemia (O2 saturation ≤94%). The study was a phase 2, randomized, double-blind, placebo-controlled trial that measured the proportion of patients who had scores of 6, 7, or 8 on the National Institute of Allergy and Infectious Disease Ordinal Scale, or NIAID-OS, at Day 7 and Day 14, with Day 14 being the primary endpoint. While the study missed the primary endpoint, the data, detailed in the Clinical Development Program section, were encouraging. For reference, subjects receiving vadadustat demonstrated 94% probability for conferring benefit on the NIAID-OS at Day 14, slightly below the primary superiority threshold of >95% probability. We believe vadadustat has the potential to prevent the worsening of ARDS more broadly since the mechanism underlying the benefits are not specific to COVID-19, and we will further explore vadadustat in an acute care setting.

Strategy

Our strategic focus and business operations are driven by our commitment to patients. We understand the unmet needs of kidney patients and others impacted by chronic and debilitating illness. Our strategy is to execute initiatives aligned with our three pillars to maximize value while advancing innovation to address patients' unmet needs.

- **Maximize the Value of Auryxia:** We continue to use our nephrology-focused commercial organization to increase awareness, demand for and adoption of Auryxia for its approved indications with key stakeholders including nephrologists, third-party payors, dialysis organizations and patients.

- **Support Vadadustat Globally:** We believe vadadustat as a treatment for anemia due to CKD represents a significant opportunity to drive shareholder value. We own full rights to vadadustat in Europe, China, Latin America and certain other territories and U.S. rights subject to our license agreement with CSL Vifor. We received a positive opinion from the CHMP for vadadustat for adult DD-CKD patients, and anticipate that the EC will grant marketing authorization for Vafseo in May 2023. In addition, we are engaged with regulatory bodies in the United Kingdom, Switzerland and Australia, which are part of the ACCESS Consortium, that could lead to approval of vadadustat in these countries. We continue to pursue a path for potential approval for vadadustat as a treatment for anemia in adult DD-CKD patients in the U.S. and remain actively engaged in a process to dispute the CRL issued for vadadustat. We believe in the benefits vadadustat can deliver to patients, if approved.

- **Invest in Pipeline and Explore Strategic Growth:** We aim to thoughtfully invest in our pipeline by developing internal assets and exploring other strategic growth opportunities.

    - ***Advance vadadustat clinical development for additional therapeutic indications***: We intend to advance development of vadadustat for the treatment of ARDS. We intend to work with UTHealth on an adequate, well-controlled study in a broad patient population, beyond COVID related ARDS.

    - ***Continue to drive our internal pipeline and portfolio of novel therapeutics*.** We aim to continue to add to our pipeline and portfolio of novel therapeutics through internal research, discovery and development. We plan to continue to develop early-stage assets and explore opportunities that align with our strategic vision. As a leader in HIF biology, we have invested resources to build out a preclinical portfolio of several potential development candidates which may enter the clinic in the next few years. Areas of interest for pursuit of clinical development include AKI, ARDS and ROP.

    - ***Explore opportunities for growth***: As a fully integrated biopharmaceutical company, we have an established commercial organization and expertise in research and development. We believe there may be opportunities to leverage our assets through strategic transactions, including establishing mutually beneficial relationships with other companies that are looking to advance assets potentially through regulatory processes or commercial launch.

We strive to execute our strategy from a strong financial position. We plan to continue to invest in prioritized drug research and development activities, funded by revenue from Auryxia and existing cash on hand. To do so, we are focused on maximizing Auryxia net product revenue, prioritizing the highest value development opportunities, and aggressively reducing discretionary spending.

Our management team has extensive experience in developing and commercializing innovation medications, a deep understanding of the renal space and biological pathways involved in kidney disease including HIF biology and iron metabolism, and broad business development expertise. We believe we are well positioned to execute on our strategy.

Background on Kidney Disease

Kidney disease is an area of major unmet need globally, driving massive healthcare costs and with a generally poor prognosis: eventually many patients will progress to a stage where they are dependent on dialysis, with high morbidity and a significant increase in mortality rate.

Kidney disease can be caused by a number of distinct and concomitant factors, including cardiometabolic disorders (primarily diabetes and hypertension), genetic diseases, autoimmune disorders, and aging. Given the prevalence and growth rates of these various underlying conditions, kidney disease prevalence is expected to continue to increase globally. In the United States, CKD significantly impacts the U.S. healthcare system, potentially affecting about 37 million patients and costing Medicare nearly $120 billion annually for treating Medicare beneficiaries with CKD of end-stage renal disease, or ESRD, or end-stage kidney disease, or ESKD, according to the Centers for Disease Control and Prevention. The U.S. Department of Health and Human Services has recognized this national pandemic and partnered with ASN to found the KidneyX Innovation Accelerator,

a public-private partnership to improve the lives of the 850 million people worldwide currently affected by kidney diseases by accelerating innovation in the prevention, diagnosis and treatment of kidney diseases.

Most of the conditions covered by the term “kidney disease” may lead to renal failure and dependence on dialysis or kidney transplant for survival. Dependence on dialysis is associated with a significant increase in mortality and hospitalizations, and a significant reduction in quality of life for patients. There is a clear need to improve the clinical and quality of life outcomes for people living with kidney disease. We are driven by our purpose, to provide or contribute to better alternatives that improve the lives of people impacted by kidney disease.

CKD is a condition in which the kidneys are progressively damaged to the point that they cannot properly filter the blood circulating in the body. This damage causes waste products to build up in the patient’s blood leading to other health problems, including anemia, cardiovascular disease and bone disease.

The prevalence and incidence of CKD is increasing in all segments of the United States population. Risk factors for the development of CKD include concomitant diseases such as hypertension, diabetes mellitus and cardiovascular disease, lifestyle factors such as tobacco use and inactivity, family history, aging and prenatal factors such as maternal diabetes mellitus, low birth weight and small-for-gestational-age status. The progression of CKD towards renal failure is complicated by multiple conditions which further deteriorate kidney function and the general health of patients if left untreated. Typically the prevalence of these conditions increases as CKD progresses. For instance, patients with CKD often experience high phosphorus and develop hyperphosphatemia, which can result in symptoms including nausea and muscle or bone pain. Additionally, anemia, characterized by low hemoglobin levels, is typically associated with a worsening quality of life, increased hospitalizations and increased mortality.

Anemia, or low hemoglobin/red blood count, in patients with CKD most commonly arises from two etiologies:

1. Anemia due to CKD: results from inadequate levels of EPO, a protein hormone synthesized by specialized cells in the kidney that stimulates red blood cell, or RBC, production in the bone marrow. As renal function declines, the body progressively loses the ability to produce endogenous EPO; and
2. IDA: results from low levels of iron due to abnormal iron absorption and utilization in patients with CKD.

Auryxia

Auryxia is a non-calcium, non-chewable, orally-administered tablet marketed in the United States, Japan and Taiwan for the Hyperphosphatemia Indication, and the treatment of IDA in adult NDD-CKD patients.

Market Opportunity – Hyperphosphatemia and Iron Deficiency Anemia

Hyperphosphatemia is a metabolic disorder characterized by elevated serum phosphorus levels. Phosphorus is a vital element required for most cellular processes and, in individuals with normal kidney function, excess dietary phosphorus is removed by the kidneys and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.5 to 4.5 mg/dL. In adults with DD-CKD, elevated phosphorus levels, or hyperphosphatemia, can be associated with adverse effects, including increased risk for cardiovascular disease, bone disease and death.

Phosphate binders are the only interventions marketed for the treatment of hyperphosphatemia. According to the U.S. Renal Data System, or USRDS, 2022 Annual Data Report, there were nearly 558,000 patients in the United States on dialysis in 2020, of which approximately 80% were treated with a phosphate binder. Phosphate binders need to be taken with meals and snacks, and it is not uncommon for DD-CKD patients to be prescribed as many as 12 or more phosphate binder pills per day, among other medications. Patients taking phosphate binders also experience gastrointestinal tolerability issues. As a result of the pill burden and tolerability issues associated phosphate binders, prescribed phosphate binders are often intolerable for many patients, leading to lack of treatment adherence and compliance.

In addition, in 2020 approximately 44% of patients treated with a phosphate binder were treated solely with a calcium-based binder, which can lead to side effects such as increased cardiovascular risk, hypercalcemia and gastrointestinal-related adverse events. Due to the risks associated with calcium-based binders, in 2017 Kidney Disease: Improving Global Outcomes, or KDIGO, recommended that clinicians limit the use of calcium-based binders.

Sevelamer and lanthanum-based phosphate binders are other alternatives. Lanthanum is a rare earth element and is minimally absorbed in the gastrointestinal tract. Lower level tissue deposition, particularly in bone and liver, has been observed in animals, however, the long-term, potentially harmful, effects due to the accumulation of lanthanum in these tissues have not been clearly

determined. Alternatively, sucroferric oxyhydroxide, sold under the brand name Velphoro, is a non-calcium, iron-based phosphate binder that is a chewable tablet used for the control of serum phosphorus levels.

Aluminum-type phosphate binders were widely used in the past. However, the systemic absorption of aluminum from these agents and the potential toxicity associated with their use no longer make this type of binder a viable long-term treatment option.

In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's Renazorb (lanthanum dioxycarbonate) or could otherwise enter the market, including Ardelyx, Inc.'s tenapanor (which is approved in the United States for the treatment of adults with irritable bowel syndrome with constipation, and for which the FDA granted an appeal in the fourth quarter of 2022 that will allow Ardelyx to resubmit a new drug application in 2023 with respect to the control of serum phosphorus in adult patients with CKD on dialysis), that may impact the market for Auryxia.

Anemia is a condition characterized by abnormally low levels of hemoglobin. Hemoglobin is contained within RBCs and carries oxygen to other parts of the body. If there are too few RBCs or if hemoglobin levels are low, the cells in the body will not get enough oxygen. IDA is a common form of anemia that is caused by patients not having enough iron to manufacture healthy RBCs. Although anyone can develop IDA, IDA is particularly common in patients with NDD-CKD. IDA is associated with fatigue, lethargy, decrease quality of life, cardiovascular complications, hospitalizations and increased mortality.

We estimate that there are more than 500,000 adult patients in the United States with NDD-CKD diagnosed with IDA and managed by a nephrologist. Currently, there are two forms of iron therapy used to treat IDA: oral iron supplements and iron delivered via intravenous infusion, or IV iron. Oral iron is currently the first-line iron replacement therapy for most physicians; however, oral iron supplements are poorly absorbed by many patients, which may adversely impact their effectiveness, and are associated with certain side effects, such as constipation, diarrhea and cramping, that may adversely affect patient compliance. IV iron is viewed as an effective treatment; however, like other intravenous medicines, it is logistically difficult to administer in an office setting, where NDD-CKD patients are more often treated.

Commercialization

We market Auryxia in the United States through our well-established, nephrology-focused sales force and commercial organization.

Auryxia, as an oral drug, is covered by Medicare only under Part D. We have gained access for Auryxia in the United States in both Medicare Part D and commercial channels. Auryxia is currently covered for the Hyperphosphatemia Indication in nine of the ten largest Medicare Part D plans, which provide coverage for approximately 35.8 million people, and the ten largest commercial plans and pharmacy benefit managers in the United States, which provide coverage for approximately 131.0 million people. In September 2018, the Centers for Medicare & Medicaid Services, or CMS, decided that Auryxia would no longer be covered by Medicare for the IDA Indication. While this decision does not impact CMS coverage of the Hyperphosphatemia Indication, it requires all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use in the Hyperphosphatemia Indication. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales of Auryxia for the Hyperphosphatemia Indication and the IDA Indication.

In recognition of the evolution of chronic kidney care to value-based reimbursement and care delivery, in late 2022 we shifted our commercial model to align to customer objectives. The team of key account managers are focused on high value individual prescribers that represent approximately 70% of Auryxia prescribing and 40% of the overall binder market potential. The team also focuses on large group practices that are part of the Comprehensive Kidney Care Contracting, or CKCC. These entities are focused on delivering coordinated, cost-effective care for advanced CKD patients, including those receiving dialysis. This customer group requires different clinical and economic rationale for supporting product use in protocols and formularies. Therefore, we have aligned key account managers to these high-volume, value-based care organizations. We believe this model will be more aligned to our customers' needs and recognition of our product's value proposition.

JT, and its subsidiary, Torii, market Riona in Japan. We receive tiered double-digit royalties from JT and Torii based on their sales in Japan.

Vadadustat

Market Opportunity

Anemia is common in patients with CKD, and its prevalence increases with disease progression. Anemia due to CKD results from inadequate EPO levels, which negatively affect RBC production. Left untreated, anemia accelerates overall deterioration of patient health with increased morbidity and mortality. Based on third party prevalence data and company estimates, approximately 5.7 million people in the United States with CKD suffer from anemia. According to the USRDS 2022 Annual Data Report, there were nearly 558,000 patients in the United States on dialysis in 2020, of which 86% were on in-center hemodialysis and the remainder on home dialysis, which includes both peritoneal dialysis and home hemodialysis.

The current standard of care for anemia due to CKD is treatment by injectable recombinant human erythropoiesis-stimulating agents, or ESAs, such as Epogen® (epoetin alfa), Aranesp® (darbepoetin alfa) and Mircera® (methoxy polyethylene glycol-epoetin beta), or blood transfusion. Based on publicly available information on ESA sales and market data compiled by a third-party vendor, global sales of injectable ESAs for all uses were estimated to be approximately $10 billion in 2022. The vast majority of these sales are believed to have been for the treatment of anemia due to CKD. In Europe, within the EU5, which refers to the five largest markets in Europe or France, Germany, Italy, Spain, and England, more than 200,000 dialysis patients are diagnosed with anemia due to CKD and are treated with ESAs.

When administered to a patient, injectable ESAs provide supraphysiological levels of exogenous EPO to stimulate production of RBCs. While injectable ESAs can be effective in raising hemoglobin levels, they have the potential to cause significant side effects, and need to be injected subcutaneously or intravenously. In particular, injectable ESAs may lead to thrombosis, stroke, myocardial infarction and death. Also, several randomized clinical trials have demonstrated that higher hemoglobin targets (≥13.0 g/dL) with ESA use are associated with increased cardiovascular risk, leading to changes in regulatory and clinical practice guidance. While these safety concerns, which became evident starting in 2006, have led to a significant reduction in the use of injectable ESAs, and an increase in the use of injectable iron, injectable ESAs remain the current standard of care for both DD-CKD and NDD-CKD patients with anemia.

We believe there is a significant opportunity for vadadustat to address limitations of injectable ESAs and become a new oral option for the treatment of anemia due to CKD in DD-CKD adult patients, if approved. In addition to clinical data from our Phase 3 INNO$_2$VATE program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (MACE) in DD-CKD adult patients, we believe the potential opportunity for vadadustat within the DD-CKD market is supported by a number of factors including vadadustat's convenient oral dosing and unique dialysis market dynamics. Further, in February 2023 the FDA approved daprodustat, an oral HIF-PH inhibitor marketed as Jesduvroq by GlaxoSmithKline plc, or GSK, as a once-a-day treatment of anemia due to CKD in adult patients who have been receiving dialysis for at least four months.

Injectable ESAs are administered by dialysis center staff to approximately 90% of in-center hemodialysis patients and 75% of home dialysis patients. Although the significant majority of dialysis patients are cared for in-center, recently, several factors including the COVID-19 pandemic, changing patient preferences, government initiatives, and reimbursement changes are supporting a shift toward home dialysis. We believe as an oral therapeutic, vadadustat has potential to be a convenient treatment alternative to injectable ESAs not only for in-center dialysis patients, but also for the growing number of home dialysis patients and patients transitioning to home dialysis.

Given the concentration of dialysis clinics in large networks, with DaVita, Inc., or DaVita, and Fresenius Kidney Care Group accounting for a vast majority of the dialysis population in the United States, treatment is usually driven by medical protocols that are implemented across the entire network of clinics. These protocols are informed by very large data sets and when updated, result in rapid change applicable to large segments of the patient population. This is particularly true of medications covered under the ESRD Prospective Payment System, or PPS, in Medicare, or the ESRD Bundle, a payment structure with a flat base rate per dialysis session adjusted for individual patient and facility characteristics. Dialysis-related drugs are included in the ESRD Bundle if they fall into functional categories such as anemia management and bone and mineral metabolism, except that oral-only drugs are exempted from inclusion until 2025. In a final ESRD PPS rule published in November 2018, CMS confirmed that it will expand the Transitional Drug Add-on Payment Adjustment, or TDAPA, to all new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA will provide separate payment for new drugs for two years based on the drug’s Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. Although there are several details that need further clarification, and the precise timing of when we could receive codes to allow for reimbursement under TDAPA is not known, the codes are assigned on a quarterly basis, and the rule provides support for our assumption that new anemia treatments, including those in the HIF-PH inhibitor class, will be included in the ESRD Bundle and will be eligible for separate payment initially under TDAPA.

Commercialization

We are supporting MTPC's commercialization of vadadustat in Japan and are preparing for a potential commercial launch of vadadustat in the United States, if approved. Our intention is to secure a partner to commercialize vadadustat in the EU and certain other countries.

If we obtain FDA approval of vadadustat for DD-CKD adult patients, we plan to commercialize vadadustat in the United States. In February 2022, we entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement, with CSL Vifor. Pursuant to the Vifor Second Amended Agreement, we granted CSL Vifor an exclusive license to sell vadadustat to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of group purchase organizations, and to certain non-retail specialty pharmacies in the United States, or the Territory. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the "Supply Group." During the term of the Vifor Second Amended Agreement, CSL Vifor is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group. We plan to commercialize vadadustat directly with organizations outside the Supply Group.

Clinical Development Program

Below is a summary of the clinical development work undertaken for vadadustat.

Vadadustat Global Phase 3 Clinical Program in Anemia Due To CKD

We conducted a global Phase 3 clinical development program for vadadustat, which included two programs, INNO$_2$VATE and PRO$_2$TECT. INNO$_2$VATE evaluated vadadustat in adult DD-CKD patients with anemia due to CKD in two studies, and PRO$_2$TECT evaluated vadadustat in adult NDD-CKD patients with anemia due to CKD in two studies. Combined, we enrolled approximately 7,500 patients in these studies and evaluated a once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa.

Both the INNO$_2$VATE and PRO$_2$TECT Phase 3 programs were global, multicenter, open-label, sponsor-blind, active-controlled non-inferiority programs. In both programs, patients were randomized 1:1 to receive either oral vadadustat or injectable darbepoetin alfa. The primary efficacy endpoint for each study in the INNO$_2$VATE and PRO$_2$TECT programs was the mean change in hemoglobin between baseline and the primary evaluation period. Non-inferiority, or NI, for the primary efficacy endpoint was achieved if the lower bound of the 95% confidence interval for the between-group difference of the mean hemoglobin change did not fall below the pre-specified NI margin. Both the INNO$_2$VATE and PRO$_2$TECT programs included the primary safety endpoint of the assessment of MACE, with a comparison of vadadustat to darbepoetin alfa. MACE is defined as the composite endpoint of all-cause mortality, non-fatal myocardial infarction, or non-fatal stroke. The primary safety analysis for each program was based on the combined MACE events from the two studies in each of INNO$_2$VATE and PRO$_2$TECT. NI for the primary safety analysis was achieved if the upper bound of the 95% confidence interval for the hazard ratio of vadadustat to darbepoetin alfa did not exceed the pre-specified NI margin. We prospectively defined and agreed to non-inferiority margins with the United States and European regulatory authorities and agreed with the United States regulatory authorities on the key components of our statistical analysis plan.

Top-line Results from Global Phase 3 INNO$_2$VATE Program within DD-CKD Adult Patients

The two INNO$_2$VATE studies (*Correction/Conversion* and *Conversion*), which collectively enrolled 3,923 patients, evaluated the efficacy and safety of vadadustat versus darbepoetin alfa for the treatment of anemia due to CKD in DD-CKD adult patients.

Vadadustat achieved the primary and key secondary efficacy endpoint in each of the two INNO$_2$VATE studies, demonstrating non-inferiority to darbepoetin alfa as measured by a mean change in hemoglobin, or Hb, between baseline and the primary evaluation period (weeks 24 to 36) and secondary evaluation period (weeks 40 to 52). Vadadustat also achieved the primary safety endpoint of the INNO$_2$VATE program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE across both INNO$_2$VATE studies.

Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the INNO$_2$VATE studies' primary efficacy endpoints of mean change in Hb between baseline and the primary evaluation period compared to darbepoetin alfa, in DD-CKD adult patients, demonstrating non-inferiority to darbepoetin alfa based on using a non-inferiority margin of -0.75 g/dL.

In INNO$_2$VATE's *Correction/Conversion* study of incident dialysis patients (n=369):

- ***Primary Efficacy Endpoint Result***: Vadadustat was *non-inferior* to darbepoetin alfa. The least square mean difference in Hb was -0.31 g/dL (95% CI: -0.53, -0.10), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.36 (1.13) g/dL for vadadustat-treated patients compared to 10.61 (0.94) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained the target Hb efficacy response at weeks 40 to 52 achieving non-inferiority compared to darbepoetin alfa. The least square mean difference in Hb was -0.07 g/dL (95% CI: -0.34, 0.19). The mean (SD) Hb level at week 40 to week 52 was 10.51 (1.19) g/dL for vadadustat treated-patients compared to 10.55 (1.14) g/dL for darbepoetin alfa-treated patients.

In INNO$_2$VATE's *Conversion* study of prevalent dialysis patients (n=3,554):

- ***Primary Efficacy Endpoint Result***: Vadadustat was *non-inferior* to darbepoetin alfa. The least square mean difference in Hb was -0.17 g/dL (95% CI: -0.23, -0.10), achieving the pre-specified non-inferiority criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.36 (1.01) g/dL for vadadustat-treated patients compared to 10.53 (0.96) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained efficacy in the *Conversion* study demonstrating non-inferiority to darbepoetin with a least square mean difference in Hb of -0.18 g/dL (95% CI: -0.25, -0.12). The mean (SD) Hb level at week 40 to week 52 was 10.40 (1.04) g/dL in the vadadustat-treated patients compared to 10.58 (0.98) g/dL for darbepoetin treated patients.

Primary Safety Major Adverse Cardiovascular Events (MACE) Endpoint Result

Vadadustat achieved the INNO$_2$VATE program's primary safety endpoint of non-inferiority for MACE. In the primary analysis of time to first MACE event, vadadustat demonstrated non-inferiority to darbepoetin alfa using a non-inferiority margin of 1.25 based on discussion with the FDA and a non-inferiority margin of 1.3 based on discussion with the EMA.

The INNO$_2$VATE program (*Correction/Conversion* and *Conversion* studies) of dialysis patients (n=3,902):

- Vadadustat was *non-inferior* to darbepoetin alfa. The upper bound of the 95% confidence interval (CI) of the Hazard Ratio (HR) was below the pre-specified non-inferiority margin of 1.25 for primary MACE analysis (HR 0.96, 95% CI: 0.83, 1.11.).

The incidence of treatment emergent adverse events during the *Correction/Conversion* study in vadadustat treated patients was 83.8% and 85.5 % in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were hypertension (16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious treatment emergent adverse events were lower in vadadustat treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of treatment emergent adverse events during the *Conversion* study in the vadadustat treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were diarrhea (13.0%/ 10.1%), pneumonia (11.0%/ 9.7%), hypertension (10.6%/ 13.8%), and hyperkalemia (9.0%/ 10.8%). Serious treatment emergent adverse events were slightly lower for vadadustat treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients. Patients with DD-CKD experienced an increased risk of thromboembolic events compared to darbepoetin alfa with a time to first event HR of 1.20 (95% CI 0.96 - 1.50) driven by thrombosis of vascular access.

INNO$_2$VATE results on key secondary safety endpoints showed that vadadustat also demonstrated non-inferiority to darbepoetin alfa in analyses of expanded MACE, cardiovascular MACE, cardiovascular mortality, and all-cause mortality.

Top-line Results from Global Phase 3 PRO$_2$TECT Program within NDD-CKD Adult Patients

The two PRO$_2$TECT studies (*Correction* and *Conversion*), which collectively enrolled 3,476 patients, evaluated the efficacy and safety of vadadustat for the treatment of anemia due to CKD in NDD-CKD adult patients.

Vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO$_2$TECT studies, demonstrating non-inferiority to darbepoetin alfa as measured by a mean change in Hb between baseline and the primary evaluation period (weeks 24 to 36) and secondary evaluation period (weeks 40 to 52). Vadadustat did not meet the primary safety endpoint of the PRO$_2$TECT program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE, across both PRO$_2$TECT studies.

Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the PRO_2TECT studies' primary efficacy endpoints of mean change in Hb between baseline and the primary evaluation period compared to darbepoetin alfa, in adult patients on dialysis, demonstrating non-inferiority to darbepoetin alfa using an NI margin of -0.75 g/dL.

In PRO_2TECT's *Correction* study (n=1,751):

- ***Primary Efficacy Endpoint Result***: Vadadustat was non-inferior to darbepoetin alfa. The least square mean difference in Hb was 0.05 g/dL (95% CI: -0.04, 0.15), achieving the pre-specified NI criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.39 (0.99) g/dL for vadadustat-treated patients compared to 10.35 (1.03) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained the target Hb efficacy response at weeks 40 to 52 achieving non-inferiority compared to darbepoetin alfa. The least square mean difference in Hb was 0.04 g/dL (95% CI: -0.06, 0.14). The mean (SD) Hb level at week 40 to week 52 was 10.48 (1.05) g/dL for vadadustat-treated patients compared to 10.45 (1.01) g/dL for darbepoetin alfa-treated patients.

In PRO_2TECT's *Conversion* study (n=1,725):

- ***Primary Efficacy Endpoint Result***: Vadadustat was non-inferior to darbepoetin alfa. The least square mean difference in Hb was -0.01 g/dL (95% CI: -0.09, 0.07), achieving the pre-specified NI criterion of -0.75 g/dL. The mean (SD) Hb level at week 24 to week 36 was 10.77 (0.98) g/dL for vadadustat-treated patients compared to 10.77 (0.99) g/dL for darbepoetin alfa-treated patients.
- ***Key Secondary Efficacy Endpoint Result***: Vadadustat sustained efficacy in the *Conversion* study demonstrating non-inferiority to darbepoetin with a least square mean difference in Hb of 0.00 g/dL (95% CI: -0.10, 0.09). The mean (SD) Hb level at week 40 to week 52 was 10.80 (1.04) g/dL in the vadadustat-treated patients compared to 10.79 (1.05) g/dL for darbepoetin alpha-treated patients.

Primary Safety Major Adverse Cardiovascular Events (MACE) Endpoint Result

The PRO_2TECT program (*Correction* and *Conversion* studies) (n=3,471):

- ***Primary Safety MACE Endpoint Result***: Vadadustat did not meet the PRO_2TECT program's primary safety endpoint of non-inferiority for MACE. The upper bound of the 95% confidence interval of the Hazard Ratio (HR) was above the pre-specified NI margin of 1.25 for primary MACE analysis (HR 1.17, 95% CI: 1.01, 1.36).

Analysis of MACE events conducted by Akebia in the PRO_2TECT program revealed that the greater number of MACE events observed among vadadustat patients as compared to the active comparator was primarily related to an excess of non-cardiovascular death and death-of-unknown-cause in regions outside of the United States where significant differences in treatment patterns for NDD-CKD patients were observed.

The PRO_2TECT analysis plan was prospectively designed to analyze the effect of regional differences, most notably, well-known differences in Hb treatment targets. Within PRO_2TECT, U.S. patients were treated to a target Hb range of 10 to 11 g/dL and non-U.S. patients were treated to a target Hb range of 10 to 12 g/dL. In October of 2020, we presented a pre-specified regional analysis that showed vadadustat was not associated with a clinically meaningful increase in cardiovascular risk compared to darbepoetin alfa in U.S. patients treated to a target Hb range of 10 to 11 g/dL, in an analysis of MACE (HR 1.06, 95% CI: 0.87, 1.29).

The incidence of treatment emergent adverse events during the *Correction* study in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious treatment emergent adverse events were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of treatment emergent adverse events during the *Conversion* study in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract infection (12.2%/ 14.5%), diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious treatment emergent adverse events were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

We are also conducting additional studies of vadadustat evaluating a modified approach to once-daily and three-times weekly dosing, including assessment of a vadadustat starting dose based on an individual's pre-conversion ESA dose prior to study entry and higher titration doses of vadadustat (up to 1200 mg). We expect to share topline data from these studies at an appropriate medical conference or in a peer-reviewed journal.

Hepatic Safety Profile of Vadadustat in Clinical Studies

During the conduct of our Phase 3 program our team and hepatic experts analyzed hepatic cases (unblinded to treatment) and, following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program, which included eight completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and two then-ongoing Phase 3b studies in DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review consisted of a blinded re-assessment of hepatic events conducted by a separate panel of hepatic experts. While hepatocellular injury attributed to vadadustat was reported in less than 1% of patients, there was one case of severe hepatocellular injury with jaundice, and we cannot guarantee that similar events will not happen in the future. Additionally, the FDA expressed safety concerns related to the risk of drug-induced liver injury in the CRL that it issued in March 2022.

Acute Respiratory Distress Syndrome

We have supported an investigator-sponsored study evaluating vadadustat for the prevention and treatment of ARDS in clinical trial subjects with COVID-19 and intend to develop vadadustat for the treatment of ARDS.

Market Opportunity

Acute respiratory distress syndrome, or ARDS, is a life-threatening acute form of lung disease characterized by acute bilateral pulmonary edema, severe hypoxia. Despite improvement in treatment strategies, a third-party study indicated high hospital mortality rates for patients with ARDS admitted to participating ICUs. The mortality rate among patients with ARDS was: 34.9% with mild ARDS; 40.3% with moderate ARDS and 46.1% with severe ARDS.

Clinical Development Program

Vadadustat for the Prevention and Treatment of ARDS in Hospitalized Patients with Coronavirus Disease 2019, or the VSTAT trial, was an investigator-sponsored clinical trial by UTHealth in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and treat ARDS in adult patients who have been hospitalized due to COVID-19 and hypoxemia (O2 saturation ≤94%). The VSTAT trial was a randomized, double-blind, placebo-controlled study, and patients were dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. In addition to funds provided by Akebia for the VSTAT trial, UTHealth was awarded $5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at UTHealth's facilities.

The VSTAT trial enrolled 449 adult subjects at five hospitals who were randomized 1:1 to vadadustat 900 mg or placebo once per day orally for up to 14 days while hospitalized. The VSTAT trial measured the proportion of subjects with either 6 (non-invasive ventilation or high flow oxygen devices), 7 (invasive mechanical ventilation or extracorporeal membrane oxygenation), or 8 (death) on the NIAID-OS at Day 7 and Day 14 (primary). While a smaller proportion of subjects in the vadadustat group had a score of 6, 7, or 8 on the NIAID-OS than in the placebo group at Day 14, the trial failed to meet its primary superiority threshold of >95% probability. Those receiving vadadustat, however, did demonstrate 94% probability of conferring benefit on the NIAID-OS at Day 14.

At Day 14, the proportions of subjects who had a 6, 7 or 8 on the NIAID-OS were 13.3% (9.6%, 17.7%; 2.5, 97.5 percentiles from Bayesian simulations) for vadadustat versus 16.9% (12.6%, 22.0%) for placebo with a relative risk of 0.79 and 94% probability that vadadustat was superior to placebo. In a pre-specified analysis at Day 7, the proportions of subjects who had a 6, 7 or 8 on the NIAID-OS were 25.4% (20.7%, 30.5%) for vadadustat versus 29.7% (24.5%, 35.3%) for placebo with a relative risk of 0.86 and 97% probability that vadadustat was superior to placebo.

The incidence of treatment emergent adverse events was 78.6% in the vadadustat group and 76.2% in the placebo group. The most common treatment emergent adverse events reported in vadadustat/placebo subjects were alanine aminotransferase increase (34.4%/28.7%), COVID-19 pneumonia (19.5%/27.4%), anemia (14.0%/17.0%), aspartate aminotransferase increase (14.0%/14.8%), hyponatremia (10.7%/15.7%), septic shock (11.6%/10.8%), hyperkalemia (10.2%/10.8%), and hypermagnesemia (7.0%/13.9%). The incidence of serious treatment emergent adverse events was 27.9% in the vadadustat

group and 32.7% in the placebo group. The most common serious treatment emergent adverse events reported in vadadustat/placebo subjects were COVID-19 pneumonia (19.5%/27.4%) and septic shock (11.6%/10.8%).

While the VSTAT trial missed the primary endpoint, we are encouraged by the data and believe the data supports further development of vadadustat as a potential treatment for ARDS due to COVID-19 or other causes.

Manufacturing and Supply

Overview

We neither own nor operate, and currently have no plans to own or operate, any manufacturing or distribution facilities. We currently rely on third-party contract manufacturing organizations, or CMOs, to produce all of our preclinical and clinical material and commercial supply and third-party distributors to distribute Auryxia. We expect to continue to rely on either existing or alternative distributors and CMOs to distribute our products and supply our ongoing and planned preclinical studies and clinical trials and for commercial production. Our CMOs have other clients and may have other priorities that could affect their ability to perform the work satisfactorily and/or on a timely basis. Both of these occurrences would be beyond our control.

We have established relationships with several CMOs under which the CMOs manufacture preclinical, clinical and commercial supply of vadadustat drug substance and drug product, and clinical and commercial supply of Auryxia drug substance and drug product. All clinical and commercial supplies are manufactured under current Good Manufacturing Practices, or cGMPs, which is a regulatory standard for the production of pharmaceuticals that will be used in humans.

Vadadustat

We currently rely on a single source supplier for our drug substance and drug product for preclinical, clinical and commercial supply of vadadustat. We have entered into a supply agreement with STA Pharmaceutical Hong Kong Limited, or STA, for the manufacture of vadadustat drug substance for commercial use and for the manufacture of vadadustat drug product for commercial use. We plan to mitigate potential commercial supply risks for vadadustat, if any, through inventory management and we may enter redundant manufacturing arrangements for both drug substance and drug product if vadadustat is approved in the United States.

Vadadustat is a small molecule. The synthesis of vadadustat is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale using no unusual manufacturing equipment. Vadadustat can be formulated into compressed tablets using proprietary processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

Auryxia

We currently rely on a single source supplier for our drug substance and drug product for preclinical, clinical and commercial supply of Auryxia. We have established CMO relationships for the supply of Auryxia to help ensure that we will have sufficient material for ongoing commercial sales and clinical trials. The drug substance for Auryxia is supplied by Siegfried Evionnaz SA, pursuant to a supply agreement, as amended, with pricing structured on a per-kilogram basis. Auryxia drug product is supplied by Patheon Manufacturing Services LLC (Thermo Fisher) pursuant to a Master Manufacturing Service Agreement with per-bottle pricing structured on a tiered basis, with the price reduced as the product volume increases. These agreements require that we satisfy certain minimum purchase requirements, but we are not obligated to use them as our sole suppliers. For more information about our manufacturing agreements for Auryxia, see Part II, Item 7. Management’s Discussion and Analysis and Note 15 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data.

The active pharmaceutical ingredient of Auryxia, ferric citrate, is a small molecule. The synthesis of ferric citrate is reliable and reproducible from starting materials available from multiple sources at commercially relevant scale. Ferric citrate can be formulated into compressed tablets using proprietary manufacturing processes. As with any supply program, obtaining raw materials and finished drug product of the required quality and quantity cannot be guaranteed, and we cannot ensure that we will be successful in this endeavor.

We utilize third parties for the commercial distribution of Auryxia, including wholesale distributors and certain specialty pharmacy providers. We have also engaged Cardinal Health as the exclusive third-party logistics distribution agent for commercial sales of Auryxia.

License, Collaboration and Other Strategic Agreements

Vadadustat

U.S. and International Collaboration with Otsuka Pharmaceutical Co. Ltd.

On December 18, 2016, we entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration was focused on the development and commercialization of vadadustat in the United States. We were responsible for leading the development of vadadustat, for which we submitted an NDA to the FDA in March 2021, and for which we received the CRL in March 2022. On April 25, 2017, we entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement, pursuant to which we granted Otsuka an exclusive license for the development and commercialization of vadadustat in certain territory outside the United States. The territory covered by the Otsuka International Agreement included the European Union, Russia, China, Australia, Canada, the Middle East and certain other countries, or the Otsuka International Territory, but excluded Latin America and previously licensed jurisdictions.

Under the terms of the Otsuka U.S. Agreement, Otsuka paid us an upfront payment of $125.0 million and additional funding of $353.0 million, based on the actual costs incurred, toward the vadadustat global Phase 3 development program. Under the terms of the Otsuka International Agreement, Otsuka paid us $289.9 million, comprised of $73.0 million that was paid upon execution of the Otsuka International Agreement and $216.9 million, based on actual costs incurred, of development funding.

On May 12, 2022, we received notice from Otsuka that it had elected to terminate the Otsuka U.S. Agreement and the Otsuka International Agreement (as defined below). On June 30, 2022, we and Otsuka entered into the Termination Agreement (as defined below), pursuant to which, among other things, we and Otsuka agreed to terminate, as of June 30, 2022, the Otsuka U.S. Agreement and the Otsuka International Agreement. In July 2022, we received a nonrefundable and non-creditable payment of $55.0 million in consideration for the covenants and agreements set forth in the Termination Agreement, including the settlement and release of all disputes and claims as provided therein. Also pursuant to the Termination Agreement, Otsuka has transferred the MAAs for vadadustat with the EMA, and in the United Kingdom, Switzerland and Australia to us.

Collaboration with Mitsubishi Tanabe Pharma Corporation

On December 11, 2015, we entered into a collaboration agreement with MTPC, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, or the MTPC Territory, which was amended effective as of December 2, 2022. In addition, we will supply vadadustat to MTPC for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product in the MTPC Territory. On July 15, 2020, we entered into a supply agreement with MTPC for the commercial supply of vadadustat for use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement, which was amended effective as of December 5, 2022.

We and MTPC agreed that, instead of including Japanese patients in our global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. MTPC reported top-line data for the two Phase 3 pivotal trials and data from the two supportive Phase 3 studies in March 2019 and 52-week data for the two Phase 3 pivotal trials in November 2019. In June 2020, vadadustat was approved in Japan for the treatment of anemia due to CKD by the Ministry of Health, Labor and Welfare. In August 2020, MTPC launched vadadustat commercially in Japan under the trade name, Vafseo™, as a treatment of anemia due to CKD for adult patients on dialysis and not on dialysis. MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan in January 2022 and in Korea in March 2022.

Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of the following: expiration of the last-to-expire patent covering vadadustat in such country in the MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of vadadustat in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

Under the terms of the MTPC Agreement, MTPC will make payments to us of up to approximately $225.0 million in the aggregate based on the achievement of certain development, regulatory and sales milestones, as well as tiered royalty payments ranging from 13% to 20% on annual net sales of vadadustat in the MTPC Territory, subject to reduction upon launch of a generic product on a country-by-country basis. MTPC was responsible for the costs of the Phase 3 program for vadadustat in Japan and other studies required in Japan and made no funding payments for our global Phase 3 program. Additionally, the development costs of approximately $20.5 million for our Phase 2 studies in Japan were reimbursed to us by MTPC. In February 2021, we entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or HCR, whereby we sold our right to receive royalties and sales milestones for vadadustat in Japan and certain other Asian countries in the MTPC territory under the MTPC Agreement. For more information on our royalty interest acquisition agreement with HCR, see Note 6 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

CSL Vifor License Agreement

On February 18, 2022, we entered into the Vifor Second Amended Agreement with CSL Vifor, which amended and restated the Vifor First Amended Agreement. Pursuant to the Vifor Second Amended Agreement, we granted CSL Vifor an exclusive license to sell vadadustat to the Supply Group in the Territory. We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. During the term of the Vifor Second Amended Agreement, CSL Vifor is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

Like the Vifor First Amended Agreement, the Vifor Second Amended Agreement is structured as a profit share arrangement between us and CSL Vifor in which we will receive approximately 66% of the profit, net of certain pre-specified costs. Under the Vifor First Amended Agreement, CSL Vifor made an upfront payment to us of $25 million in lieu of the previously disclosed milestone payment of $25 million that CSL Vifor was to pay to us following approval of vadadustat by the FDA. In addition, CSL Vifor made an equity investment in us, as further described below. We currently retain rights to commercialize vadadustat for use in the non-dialysis dependent CKD market and to sell to dialysis organizations outside of the Supply Group. As under the Vifor First Amended Agreement, during the term of the Vifor Second Amended Agreement, CSL Vifor is not permitted to sell any HIF product that competes with vadadustat in the Territory to the Supply Group.

As under the Vifor First Amended Agreement, the Vifor Second Amended Agreement provides that Akebia and CSL Vifor will enter into a commercial supply agreement for vadadustat pursuant to which we will supply all of CSL Vifor's requirements for vadadustat in the Territory. Under the Vifor Second Amended Agreement, CSL Vifor contributed $40 million to a working capital facility established to partially fund our costs of purchasing vadadustat from our contract manufacturers, which amount of funding will fluctuate, and which funding we are required to repay to CSL Vifor over time.

Unless earlier terminated, the Vifor Second Amended Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat or the expiration of marketing or regulatory exclusivity for vadadustat in the Territory. CSL Vifor may terminate the Vifor Second Amended Agreement in its entirety upon 30 months' prior written notice after the first anniversary of the receipt of regulatory approval, if approved, from the FDA for vadadustat for dialysis-dependent CKD patients. We may terminate the Vifor Second Amended Agreement in its entirety for convenience, following the earlier of a certain period of time elapsing or following certain specified regulatory events, and upon six months' prior written notice. If we so terminate for convenience, subject to a specified exception, we will pay a termination fee to CSL Vifor. In addition, either party may, subject to a cure period, terminate the Vifor Second Amended Agreement in the event of the other party's uncured material breach or bankruptcy. We may also terminate the Vifor Second Amended Agreement upon the occurrence of certain other events. The Vifor Second Amended Agreement also continues to include a standstill provision and customary representations and warranties.

Also in connection with entering into the Vifor Second Amended Agreement, on February 18, 2022, we and CSL Vifor entered into an Investment Agreement, or the Investment Agreement, pursuant to which we sold an aggregate of 4,000,000 shares of our common stock to CSL Vifor for a total of $20.0 million dollars.

Janssen Pharmaceutica NV Research and License Agreement

On February 9, 2017, we entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, pursuant to which Janssen granted us an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase targeted compounds.

Under the terms of the Janssen Agreement, we paid an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of our common stock, which expired on February 9, 2022. On August 1, 2022, we notified Janssen that we were exercising our right to terminate the Janssen Agreement in its entirety, and Janssen agreed to the termination which became effective on August 2, 2022.

Cyclerion Therapeutics License Agreement

On June 4, 2021, we entered into the Cyclerion Agreement with Cyclerion Therapeutics, Inc., or Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator.

Under the terms of the Cyclerion Agreement, we made an upfront payment of $3.0 million in cash to Cyclerion, which was paid during the second quarter of 2021. In addition, Cyclerion is eligible to receive up to an aggregate of $222.0 million from us in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a mid-single-digit to mid-teen percentage of

net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the territory. We recorded the upfront payment in the amount of $3.0 million to research and development expense in June 2021.

Unless earlier terminated, the Cyclerion Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longest of (i) the expiration of the patents licensed under the Cyclerion Agreement, (ii) the expiration of regulatory exclusivity for such product, and (iii) 10 years from first commercial sale of such product. We may terminate the Cyclerion Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Cyclerion. We and Cyclerion also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Cyclerion Agreement or in the event of certain additional circumstances.

Auryxia

License Agreement with Panion & BF Biotech, Inc.

Prior to the merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became our wholly owned subsidiary, Keryx entered into a license agreement, or the Panion License Agreement, which was amended from time to time, with Panion & BF Biotech, Inc., or Panion, under which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, or the Licensor Territory, for the development and commercialization of ferric citrate.

On April 17, 2019, we and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amends and restates in full the Panion License Agreement. The Panion Amended License Agreement provides Keryx with an exclusive license under Panion-owned know-how and patents covering the rights to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under Keryx-owned patents covering the rights to sublicense (with our written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Consistent with the Panion License Agreement, under the Panion Amended License Agreement, Panion is eligible to receive from us or any sublicensee royalty payments based on a mid-single digit percentage of sales of ferric citrate in our licensed territories. We are eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion's licensed territories.

The Panion Amended License Agreement terminates upon the expiration of each of our and Panion's obligations to pay royalties thereunder. In addition, we may terminate the Panion Amended License Agreement (i) in its entirety or (ii) with respect to one or more countries in our licensed territory, in either case upon 90 days' notice. We and Panion also each have the right to terminate the Panion Amended License Agreement upon the occurrence of a material breach of the Panion Amended License Agreement by the other party, subject to certain cure provisions, or certain insolvency events. The Panion Amended License Agreement also provides that, on a country-by-country basis, during the term and until the second anniversary of the expiration of our or Panion's obligation, as applicable, to pay royalties in a country in which such party has ferric citrate for sale on the date of such expiration, neither the other party nor its affiliates will, directly or indirectly, sell, distribute or otherwise commercialize or supply or cause to supply ferric citrate to a third party for sale or distribution in such country. In addition, the Panion Amended License Agreement provides that each of us and Panion has the right, but not the obligation, to conduct litigation against any infringer of certain patent rights under the Panion Amended License Agreement in certain territories.

During the year-ended December 31, 2022, Panion earned $13.8 million in royalty payments relating to the sales of Auryxia in the United States and JT and Torii net sales of Riona in Japan, as we are required to pay a mid-single digit percent of JT and Torii's net sales of Riona in Japan to Panion under the terms of the Panion Amended License Agreement.

Sublicense Agreement with Japan Tobacco Inc. and Torii Pharmaceutical Co., Ltd.

In September 2007, Keryx entered into a Sublicense Agreement with JT and Torii, under which JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate in Japan. Effective June 8, 2009, Keryx entered into an Amended and Restated Sublicense Agreement, which was amended in June 2013, or the Revised Agreement, with JT and Torii.

In January 2014, JT and Torii received manufacturing and marketing approval of ferric citrate from the Japanese Ministry of Health, Labour and Welfare. Ferric citrate hydrate, which launched in May 2014 and is being marketed in Japan by Torii under the brand name Riona, is indicated as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including NDD-CKD and DD-CKD. In July 2019, JT and Torii, reported positive top-line results from a pivotal Phase 3 comparative study evaluating Riona for the treatment of IDA in adult patients in Japan, which was approved in March 2021. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan. Under the terms

of the Revised Agreement with JT and Torii, we are eligible to receive royalty payments based on a tiered low double-digit percentage of net sales of Riona in Japan inclusive of amounts that we must pay to Panion on JT and Torii's net sales of Riona under the Panion Amended License Agreement, subject to certain reductions upon expiration or termination of the Panion Amended License Agreement, and may also receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones. We recorded $5.3 million in license revenue related to royalties earned on net sales of Riona in Japan during the twelve months ended December 31, 2022.

The sublicense under the Revised Agreement terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the Revised Agreement with or without cause upon at least six months prior written notice to us. Additionally, either party may terminate the Revised Agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the Revised Agreement, or after certain insolvency events.

Intellectual Property

The proprietary nature of, and protection for, our products, product candidates and our discovery programs, processes and know-how are important to our business. Our policy is to seek to protect our proprietary position by, among other methods, filing patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position. Additionally, we may benefit from a variety of statutory frameworks in the United States, Europe and other countries that provide periods of non-patent-based exclusivity for qualifying molecules. See "—Regulatory Matters."

Our commercial success will depend in part on obtaining and maintaining patent protection of our current products as well as current and future product candidates, methods of their use and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell or importing our products depends on the extent to which we have rights under valid and enforceable patents that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. Even once patents successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held not infringed or unenforceable. For this and more comprehensive risks related to our intellectual property, please see "Risk Factors—Risks Related to Our Intellectual Property" in Part I, Item 1A. Risk Factors.

Individual patents extend for varying periods of time depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, patents issued from applications filed in the United States are effective for 20 years from the earliest filing date of a United States non-provisional application or an international application filed under the Patent Cooperation Treaty. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, however, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest international filing date. Patent term recapture for loss of term as a result of the regulatory review period is available in some foreign jurisdictions. In the United States, a patent's term may also be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office, or USPTO, in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

Changes in either the patent laws or interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights. Accordingly, we cannot predict the breadth or enforceability of claims that may be granted in our patents or in third-party patents. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our drugs and technology will depend on our success in obtaining effective claims and enforcing those claims once granted. We do not know whether any of the patent applications that we may file or license from third parties will result in the issuance of any patents. The issued patents that we own or license or may receive or acquire in the future may be challenged, invalidated or circumvented, and the rights granted under any issued patents may not provide us with sufficient protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may be able to independently develop and commercialize similar drugs or duplicate our technology, business model or strategy without infringing our patents. Because of the extensive time required for clinical development and regulatory review of a drug we may develop, it is possible that, before any of our drugs can be commercialized, any related patent may

expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent. The patent positions for vadadustat and Auryxia are summarized below.

Vadadustat Patent Portfolio

We hold 12 issued patents covering the composition of matter, polymorph, method of treating anemia, pharmaceutical compositions of vadadustat, and processes for manufacturing vadadustat in the United States and additional patents issued or pending in many other major jurisdictions worldwide, including Europe, Japan, China, South Korea, Brazil, Mexico, Russia, Israel and India. The expected expiration dates for these patents are between 2027 and 2034 plus any extensions or adjustments of term available under national law.

We also hold patents and patent applications directed to starting materials and intermediates in the processes for manufacturing vadadustat, dosing regimens, formulations, and various other aspects relating to the treatment of anemia using vadadustat that are expected to expire between 2032 and 2042 exclusive of possible patent term extensions or adjustments.

We have ongoing opposition and invalidity proceedings relating to vadadustat. See Part I, Item 3. Legal Proceedings for further information relating to these matters.

Auryxia Patent Portfolio

Pursuant to Keryx's license with Panion, we have the exclusive rights under a series of patents and patent applications to commercialize Auryxia worldwide, excluding certain Asian-Pacific countries. These patents and patent applications include claims directed to compositions of matter, pharmaceutical compositions, methods of treatment, as well as methods for the manufacture of Auryxia.

Keryx's patent rights include 14 issued U.S. patents listed in the Orange Book covering the composition of matter, method of treating hyperphosphatemia, and pharmaceutical compositions of Auryxia. The expected expiration dates for these patents are between 2024 and 2030 plus any additional patent term extensions that may be available.

Pursuant to the sublicense with our Japanese partner, Japan Tobacco Inc., or JT, and its subsidiary, Torii Pharmaceutical Co. Ltd., or Torii, we have exclusively sublicensed certain Japanese patent rights to JT and Torii. These sublicensed rights include several Japanese patents and pending patent applications with composition of matter claims, methods of synthesizing claims, and methods of use claims covering Riona, the trade name under which JT and Torii market ferric citrate in Japan. The expected expiration dates for these patents and pending patent applications are between 2025 and 2027. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these Japanese patents.

Pursuant to the sublicense with our European partner, Averoa, we have exclusively sublicensed certain European patent rights to Averoa. These sublicensed rights include several European patents and pending patent applications with composition of matter claims and methods of use claims covering ferric citrate. The expected expiration dates for these patents and pending patent applications are between 2024 and 2036. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these European patents.

We received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA by third parties requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). In response we filed certain complaints for patent infringement against five third parties, and have entered into settlement and license agreements with each of the five ANDA filers. Each settlement agreement granted the defendants a license to market a generic version of Auryxia in the United States beginning on March 20, 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature.

Other Intellectual Property Rights

We depend upon trademarks, trade secrets, know-how and continuing technological advances to develop and maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators, upon commencement of a relationship with us, to execute confidentiality agreements and, in the case of parties other than our research and development collaborators, to agree to assign their inventions to us. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

In addition to patent protection, we may utilize orphan drug regulations, pediatric exclusivity or other provisions of the Food, Drug and Cosmetic Act of 1938, as amended, or FDCA, such as new chemical entity exclusivity or new formulation exclusivity, to provide market exclusivity for a drug candidate. In the United States, the FDA has the authority to grant additional data protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of data protection as well as to the term of a relevant patent, to the extent these protections have not already expired. We may also seek to utilize market exclusivities in other territories. We cannot assure you that our drug products or any drug candidates we may acquire or in-license, will obtain such orphan drug designation, pediatric exclusivity, new chemical entity exclusivity or any other market exclusivity in the United States, European Union or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any market exclusivity protection.

Know-How

In addition to patents, we rely upon unpatented know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment provisions in the confidentiality agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment provisions, to grant us ownership of technologies that are developed by our employees. These agreements may be breached, and we may not have adequate remedies for any breach.

To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

The Hatch-Waxman Act

Orange Book Listing

In seeking approval for a drug through an NDA, sponsors are required to list with the FDA each patent whose claims cover the sponsor's product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA sponsors are usually not required to conduct, or submit results of, nonclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA sponsor is required to make certain certifications to the FDA concerning any patents listed for the approved product in the FDA's Orange Book. Specifically, the sponsor must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA sponsor may also elect to submit a Section viii statement, certifying that its proposed ANDA label does not contain or carve out any language regarding the patented method-of-use, rather than certify to a listed method-of-use patent.

If the sponsor does not challenge the listed patents, the ANDA will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from receiving the Paragraph IV certification, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA sponsor. Also, the ANDA will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which time the FDA cannot accept any ANDA seeking approval of a generic version of that drug. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which the FDA cannot approve an ANDA for a generic drug that includes such changes.

An ANDA may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA may be filed before the expiration of the exclusivity period.

Patent Term Extension

After NDA approval, owners of relevant drug patents or their agents may apply for up to a five-year patent extension for delays caused by FDA regulatory review. The allowable patent term extension is calculated as half of the drug's testing phase which is the time between Investigational New Drug application, or IND submission and NDA submission, and all of the review phase, which is the time between NDA submission and approval, up to a maximum of five years. The time can be shortened if the FDA determines that the sponsor did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years from the date of approval by virtue of the patent term extension.

We have filed applications under the patent term extension provisions of 35 U.S.C. § 156 for U.S. Patent Nos. 8,299,298, 8,093,423, 7,767,851 and 8,338,642 each of which covers Auryxia for delays caused by FDA regulatory review. If granted, we can utilize the patent term extension on one of these patents, however, we cannot assure you that we can obtain any extension of the term of these patents. Upon expiration of these patents, competitors who obtain the requisite regulatory approval may potentially offer products with the same composition and/or method of use as our product, so long as the competitors do not infringe any other patents that we may own or license.

For patents that might expire before a determination regarding patent term extension, the patent owner or its agent may request an interim patent term extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely.

In addition, certain jurisdictions outside of the U.S., including Japan, have provisions that provide for patent term extension. In October 2014, following the regulatory approval of Riona in Japan, the Japan Patent office granted the patent term extensions filed by our sublicensee, JT, for Japanese Patents Nos. 4964585 and 4173553. As a result of the extension of patent term, Japanese Patent No. 4173553 expired in November 2022 and Japanese Patent No. 4964585 will expire in November 2025.

In the future, if and when our product candidates, including vadadustat, receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each product candidate and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

Competition

The pharmaceutical and biotechnology industries are highly competitive. Our competitors include pharmaceutical companies and biotechnology companies, as well as universities and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. To compete successfully in this industry, we must identify novel and unique drugs or methods of treatment and then complete the development of those drugs as treatments in advance of our competitors.

Vadadustat

Drugs that may compete with vadadustat, if approved, include Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by CSL Vifor in the United States and Roche Holding Ltd. outside of the United States.

In addition, in the United States, the FDA approved Jesduvroq (daprodustat), an oral HIF-PHI from GSK for the once-a-day treatment of anemia due to CKD in adults who have been receiving dialysis for at least four months. FibroGen filed an NDA for its product candidate, roxadustat, with the FDA, but the FDA issued a complete response letter indicating the FDA will not approve the NDA in its present form. In Europe however, roxadustat is approved for the treatment of anemia in patients with CKD.

We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PH inhibitor product candidates in various stages of development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by companies such as FibroGen Inc., or FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, JT, GSK, and Bayer HealthCare AG, or Bayer.

Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable ESA utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

In Japan, Vafseo, which is approved for patients with CKD, including both DD-CKD and NDD-CKD, competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of anemia due to CKD, including DD-CKD and NDD-CKD patients. In addition, daprodustat, GSK's product candidate, and enarodustat, JT's product candidate, are approved in Japan for the treatment of anemia due to CKD. In addition, Bayer HealthCare AG has submitted a new drug application for its product candidate for the treatment of renal anemia in Japan. In China, FibroGen launched roxadustat for the treatment of anemia due to CKD in DD-CKD patients and for the treatment of anemia due to CKD in NDD-CKD patients.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch vadadustat. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 and several biosimilar versions of injectable ESAs are available for sale in the EU.

Furthermore, vadadustat's commercial opportunities, if approved, may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than vadadustat.

Auryxia

Hyperphosphatemia Competition

Auryxia is competing in the hyperphosphatemia market in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Sanofi, PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's RENAZORB™ (lanthanum dioxycarbonate) or could otherwise enter the market, including Ardelyx, Inc.'s tenapanor (which is approved in the U.S. for the treatment of adults with irritable bowel syndrome with constipation, and which the FDA granted

Ardelyx's appeal to the FDA's CRL in December 2022 that will allow Ardelyx to resubmit a new drug application in 2023 with respect to the control of serum phosphorus in adult patients with CKD on dialysis), that may impact the market for Auryxia.

Iron Deficiency Anemia Competition

Auryxia is competing in the IDA market in the United States with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and intravenous iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate). In addition, other new therapies for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutic' plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA, and Accrufer® (ferric maltol), which was launched in the United States for the treatment of IDA in July 2021.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies have product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia. In addition, we entered into settlement agreements with each of our ANDA filers pursuant to which we granted licenses to market a generic version of Auryxia in the United States beginning in March 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature, which may impact our business and results of operation.

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, pricing, reimbursement, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory requirements, require the expenditure of substantial time and financial resources.

Review and Approval of Drug Products in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations.

Our product candidates must be approved by the FDA for therapeutic indications before we or our partners are able to market them in the United States. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products is referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations and consistent with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, or ICH, requirements;
- design of a clinical protocol and submission to the FDA of an IND, which must be reviewed and active by the FDA before human clinical trials may begin;
- approval by an independent local or central institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed product candidate for each indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product candidate, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity;

- satisfactory completion of FDA audits of clinical trial sites and records to assure compliance with GCPs and good practices, or GxPs, the integrity of the clinical data and that adequate controls and oversight are in place regarding manufacturing, clinical trials, pharmacovigilance, safety, data management, vendor oversight, collection and reporting of serious adverse events and other activities;
- payment of user fees and securing FDA approval of an NDA; and
- compliance with any post-approval requirements and/or commitments, including the potential requirement to implement a risk evaluation and mitigation strategy, or REMS, and potentially post-market requirement, or PMR, and post-market commitment, or PMC, studies.

Preclinical Tests

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND and are generally referred to as IND-enabling studies. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

Clinical trials involve the administration of the investigational product to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research patients provide their voluntary informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped through interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be obtained prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research patients will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold or require that the sponsor amend the clinical protocol to include additional safety measurements. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin (or resume if the clinical trial had been ongoing at the time a clinical hold was imposed).

In addition to the foregoing requirements related to the IND submission, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to study patients. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived by the FDA. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee and seeking and receiving informed consent from subjects. GCP requirements encompass both ethical and data integrity standards for clinical trials. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data.

Reporting Clinical Trial Results

Under the Public Health Service Act, or PHSA, sponsors of certain clinical trials of certain FDA-regulated products, including prescription drugs and biologics, are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are also obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017, and both NIH and the FDA have signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

Specifically, the PHSA grants the Secretary of the U.S. Department of Health and Human Services, or HHS, the authority to issue a notice of noncompliance to a responsible party for failure to submit clinical trial information as required. The responsible party, however, is allowed 30 days to correct the noncompliance and submit the required information. The failure to submit clinical trial information to clinicaltrials.gov, as required, is also a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. In addition to civil monetary penalties, violations may also result in other regulatory action, such as injunction and/or criminal prosecution or disqualification from federal grants. Although the FDA has historically not enforced these reporting requirements due to HHS's long delay in issuing final implementing regulations, those regulations have now been issued and the FDA has issued several Notices of Noncompliance to manufacturers since April 2021.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study for a covered investigational product; or 15 days after the investigational product receives designation from the FDA as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its product candidates available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product to human patients under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research patients provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- **Phase 1.** The product candidate is initially introduced into a small number of healthy human patients or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for

safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

- **Phase 2.** The product candidate is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- **Phase 3.** These clinical trials are commonly referred to as "pivotal" studies, which denote a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. The product candidate is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product candidate for approval, identify adverse effects, establish the overall risk-benefit profile of the product candidate and to provide adequate information for the labeling of the product candidate.
- **Phase 4.** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the study will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Moreover, as noted above, a pivotal trial is a clinical trial that is believed to satisfy FDA requirements for the evaluation of a product candidate's safety and efficacy such that it can be used, alone or with other pivotal or non-pivotal trials, to support regulatory approval. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans. Progress reports detailing the results of the clinical trials conducted under the IND must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA, IRB or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In response to the COVID-19 pandemic, the FDA issued guidance on March 18, 2020, and has updated it periodically since that time to address the conduct of clinical trials during the pandemic. The guidance sets out a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of COVID-19. On January 30, 2023, the Biden Administration announced that it will end the public health emergency declarations related to COVID-19 on May 11, 2023. On January 31, 2023, the FDA indicated that it would soon issue a Federal Register notice describing how the termination of the public health emergency will impact the agency's COVID-19 related guidance, including the clinical trial guidance and updates thereto. At this point, it is unclear how, if at all, these developments will impact our efforts to develop and commercialize our product candidates.

Pediatric Studies

Under the Pediatric Research Equity Act, or PREA, applications and certain types of supplements to applications must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor must submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The sponsor and the

FDA must reach agreement on a final plan. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical trials, early phase clinical trials, and/or other clinical development programs.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Pursuant to the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, the FDA must send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. FDASIA further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Acceptance and Review of an NDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things are submitted to the FDA as part of an NDA requesting approval to market the product candidate for one or more indications. The fee required for the submission and review of an application under the Prescription Drug User Fee Act, or PDUFA, is substantial (for example, for fiscal year 2023 this application fee is approximately $3.2 million), and the sponsor of an approved application is also subject to an annual program fee, currently more than $393,000 per eligible prescription product. These fees are typically adjusted annually, and exemptions and waivers may be available under certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the sponsor is a small business submitting its first human therapeutic application for review.

The FDA conducts a preliminary review of all applications within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. This is known as the filing decision. In the event that FDA determines that an application does not satisfy this standard, it will issue a Refuse to File determination to the sponsor. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. A product that has been designated as a breakthrough therapy may also be eligible for review within six months if supported by clinical data at the time of submission of the NDA. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing such as active pharmaceutical ingredients, finished drug product manufacturing, control testing laboratories, as well as packaging and labeling facilities. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The sponsor of the NDA may also have their records, processes, procedures, training, and other aspects reviewed during an inspection. The FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks.

Finally, the FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. The fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act. This law established a new regulatory scheme allowing for expedited review of products designated as “breakthrough therapies.” A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA’s review clock goal for taking action on a marketing application from ten months to six months.

Priority Review Vouchers

A PRV is a voucher that the FDA issues to a sponsor of a rare pediatric disease or tropical disease product application at the time of the marketing application approval. Vouchers are transferable to other sponsors that may apply it to their NDAs or BLAs. A PRV entitles the holder to designate a single human drug application submitted under Section 505(b)(1) of the U.S. Federal Food, Drug, and Cosmetic Act or Section 351 of the Public Health Service Act as qualifying for a priority review. An FDA priority review may expedite the review process of a marketing application reducing the review time from ten months after formal acceptance of the file to six months after formal acceptance of the file. Applying the PRV to a marketing application does not ensure the FDA’s approval of the marketing application and all requirements supporting the safety and efficacy of the product must be met. Our NDA submission for vadadustat did not include a PRV.

The FDA’s Decision on an NDA

The FDA reviews an application to determine, among other things, whether the product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The term “substantial evidence” is defined under the FDCA as “evidence consisting of adequate and well-controlled investigations, including clinical

investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the product involved, on the basis of which it could fairly and responsibly be concluded by such experts that the product will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. This approach was subsequently endorsed by Congress in 1998 with legislation providing, in pertinent part, that "If [FDA] determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, FDA may consider such data and evidence to constitute substantial evidence." This modification to the law recognized the potential for FDA to find that one adequate and well controlled clinical investigation with confirmatory evidence, including supportive data outside of a controlled trial, is sufficient to establish effectiveness. In December 2019, FDA issued draft guidance further explaining the studies that are needed to establish substantial evidence of effectiveness. It has not yet finalized that guidance.

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a CRL or an approval letter. To reach this determination, the FDA must determine that the drug is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA. This assessment is also informed by other factors, including: the severity of the underlying condition and how well patients' medical needs are addressed by currently available therapies; uncertainty about how the premarket clinical trial evidence will extrapolate to real-world use of the product in the post-market setting; and whether risk management tools are necessary to manage specific risks. In connection with this assessment, the FDA review team will assemble all individual reviews and other documents into an "action package," which becomes the record for FDA review. The review team then issues a recommendation, and a senior FDA official makes a decision.

A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. The CRL may require additional clinical or other data, additional pivotal Phase 3 clinical trial(s) and/or other significant and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. The FDA has committed to reviewing resubmissions in response to an issued CRL in either two or six months depending on the type of information included. Even with the submission of this additional information, however, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. The FDA has taken the position that a CRL is not final agency action making the determination subject to judicial review. Rather, for those seeking to challenge FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. That is, the approval will be limited to the conditions of use (e.g., patient population, indication) described in the FDA-approved labeling. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Under the Ensuring Innovation Act, which was signed into law in April 2021, the FDA must publish action packages summarizing its decisions to approve new drugs and biologics within 30 days of approval of such products. To date, CRLs are not publicly available documents.

Post-Approval Requirements and Commitments

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, conditions of NDA approval may include sponsor agreement to PMR or PMC studies, which are designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. These may include additional studies, registries, data collection, analyses, and/or information.

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a product candidate's safety or effectiveness are prohibited before the product candidate is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA or in a manner that is inconsistent with the product's prescribing information. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific conditions, for a manufacturer to engage in nonpromotional, truthful and non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. In addition, companies may also promote information that it consistent with the prescribing information and have the ability to proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug under some relatively recent guidance from the FDA. Moreover, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

However, if a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to a variety of federal and state laws, the most recent of which is still in the process of being phased into the U.S. supply chain and regulatory framework. The Prescription Drug Marketing Act, or PDMA, was the first federal law to set minimum standards for the registration and regulation of drug distributors by the states and to regulate the distribution of drug samples. Today, both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Congress more recently enacted the Drug Supply Chain Security Act, or DSCSA, which made significant amendments to the FDCA, including by replacing certain provisions from the PDMA pertaining to wholesale distribution of prescription drugs with a more comprehensive statutory scheme. The DSCSA now requires uniform national standards for wholesale distribution and, for the first time, for third-party logistics providers; it also provides for preemption of certain state laws in the areas of licensure and prescription drug traceability.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical trials which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the sponsor to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the sponsor for approval of the application "were not conducted by or for the sponsor and for which the sponsor has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the sponsor. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) sponsor can establish that reliance on the FDA's previous approval is scientifically appropriate, the sponsor may eliminate the need to conduct certain preclinical studies or clinical trials of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) sponsor. Products approved under Section 505(b)(2) are often referred to as follow-on products.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Under the Hatch-Waxman Act, the FDA may not approve an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a NCE. For the purposes of this provision, the FDA has consistently taken the position that an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, a

generic or follow-on drug application may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the sponsor and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs or 505(b)(2) applications seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight months for a drug that has three or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

As part of the submission of an NDA or certain supplemental applications, NDA sponsors are required to list with the FDA each patent with claims that cover the sponsor's product or an approved method of using the product. Upon approval of a new drug, each of the patents listed in the application for the drug is then published in the Orange Book. The FDA's regulations governing patent listings were largely codified into law with enactment of the Orange Book Modernization Act in January 2021. When an ANDA sponsor files its application with the FDA, the sponsor is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book. Specifically, the ANDA sponsor must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. Moreover, to the extent that the Section 505(b)(2) NDA sponsor is relying on studies conducted for an already approved product, the sponsor also is required to certify to the FDA concerning any patents listed for the NDA-approved product in the Orange Book to the same extent that an ANDA sponsor would.

If the generic drug or follow-on drug sponsor does not challenge the innovator's listed patents, FDA will not approve the ANDA or 505(b)(2) application until all the listed patents claiming the referenced product have expired. A certification that the new generic product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA sponsor has provided a Paragraph IV certification to the FDA, the sponsor must also send notice of the Paragraph IV certification to the NDA owner and patent holders once the ANDA has been accepted for filing by the FDA. The NDA owner and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earliest of 30 months after the receipt of the Paragraph IV notice, expiration of the patent or a decision in the infringement case that is favorable to the ANDA or 505(b)(2) NDA application.

Pediatric Studies and Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, for drug products, provides for the attachment of an additional six months of marketing protection to the term of any existing patent or regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product is effective in the pediatric population studied, rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to

any patents for which an ANDA or 505(b)(2) sponsor submitted a Paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities, in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, the HHS has issued regulations to protect the privacy and security of protected health information, or PHI, used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. While we are not a covered entity, as a business associate, we could be subject to penalties, including criminal penalties, and contractual damages if we knowingly obtain or further disclose PHI from a covered entity, such as a health care provider or clinical research site, and therefore we must ensure the proper authorizations are in place before we, or our vendors or business partners, obtain access to any PHI. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

At the state level, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act, or CCPA, it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA went into effect on January 1, 2020 and requires covered companies to provide new disclosures to California consumers, provide such consumers rights as it relates to their personal information, and allow for a new cause of action for data breaches. Additionally, starting on January 1, 2023, the California Privacy Rights Act, or CPRA, significantly modified the CCPA, including by expanding consumers' rights, particularly with respect to certain sensitive personal information and creating new principles, such as data minimization, purpose limitation, and storage limitation. The CPRA also created a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The CCPA and CPRA could impact our business activities depending on how it is interpreted and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and individually identifiable health information. These provisions may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah, and Connecticut already have passed state privacy laws. Virginia's privacy law also went into effect on January 1, 2023, and the laws in the other three states will go into effect later in 2023. Other states will be considering these laws in the future, and Congress has also been debating a proposed federal privacy law. These laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products, if and once approved.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under such laws, it is possible that some of our current or future business activities, including certain clinical research, sales and marketing practices and the provision of certain items and services to our customers, could be subject to challenge under one or more of such privacy and data security laws. The heightening compliance environment and the need to build and maintain robust and secure systems to comply with different privacy compliance and/or reporting requirements in multiple jurisdictions could increase the possibility that a healthcare company may fail to comply fully with one or more of these requirements. If our

operations are found to be in violation of any of the privacy or data security laws or regulations described above that are applicable to us, or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and administrative penalties, damages, fines, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a consent decree or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any product candidates we may develop, once approved, are sold in a foreign country, we may be subject to similar foreign laws.

Review and Approval of Drug Products Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the European Union

Before the new Clinical Trials Regulation, (EU) No 536/2014, or the Clinical Trials Regulation, came into application in January 2022, requirements for the conduct of clinical trials in the European Union including GCP were set forth in the Clinical Trials Directive 2001/20/EC, or the Clinical Trials Directive, and the GCP Directive 2005/28/EC, or the GCP Directive. Pursuant to the Clinical Trials Directive and the GCP Directive, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the EU member states. Under this system, approval must be obtained from the competent national authority of each EU member state in which a study is planned to be conducted. To this end, a clinical trial application, or CTA, is submitted to the local competent authority in each country, or Member State, where the clinical trial is being conducted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Clinical Trials Directive and the GCP Directive and other applicable guidance documents. These documents may be amended and/or updated by the European Commission at any time. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the Clinical Trials Regulation was adopted. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the “EU portal”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The Clinical Trials Regulation came into application on January 31, 2022, following confirmation of full functionality of the Clinical Trials Information System through an independent audit by the European Commission in mid-2020. The Clinical Trials Regulation came into application in all the EU Member States and repealed the previous Clinical Trials Directive. According to the transitional provisions, if a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation became applicable, the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the European Union

In March 2016, the EMA launched an initiative, the PRIority MEdicines, or PRIME, scheme, to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIME scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated agency contact and rapporteur from the Committee for Human Medicinal Products, or CHMP, or Committee for Advanced Therapies are appointed early in the PRIME scheme, facilitating increased understanding of the product at the EMA's committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Pediatric Studies

Prior to obtaining a marketing authorization in the EU, sponsors have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are set forth in Regulation (EC) No 1901/2006, which is referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine in children is not needed or is not appropriate because (a) the product is likely to be ineffective or unsafe in part or all of the pediatric population; (b) the disease or condition occurs only in adult population; or (c) the product does not represent a significant therapeutic benefit over existing treatments for pediatric population. Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Marketing Authorization

To obtain marketing approval of a product under EU regulatory systems, a sponsor must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the CHMP established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to sponsors who wish to market a product in various EU member states where such product has not received marketing approval in any EU member state before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the sponsor, known as the reference member state. Under this procedure, a sponsor submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

A marketing authorization may be granted only to a sponsor established in the European Union. Once the marketing authorization is obtained in all member states of the European Union and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

Conditional Approval

In particular circumstances, E.U. legislation (Article 14–a Regulation (EC) No 726/2004 (as amended by Regulation (EU) 2019/5) and Regulation (EC) No 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables sponsors to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for product candidates (including medicines designated as orphan medicinal products) if (1) the product candidate is intended for the treatment, prevention or medical diagnosis of seriously debilitating or life-threatening diseases; (2) the product candidate is intended to meet unmet medical needs of patients; (3) a marketing authorization may be granted prior to submission of comprehensive clinical data provided that the benefit of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required; (4) the risk-benefit balance of the product candidate is positive, and (5) it is likely that the sponsor will be in a position to provide the required comprehensive clinical trial data. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new clinical studies and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization, but sponsors can also request EMA to conduct an accelerated assessment, for instance in cases of unmet medical needs.

Periods of Authorization and Renewals in the European Union

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU member state. To that end, the marketing authorization holder must provide the EMA or the relevant competent authority of the EU member state with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU member state decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU member state which delivered the marketing authorization within three years after authorization ceases to be valid.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the European Union on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, sponsors for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to a total of ten years' market exclusivity. During this ten-year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a NCE so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Pediatric Exclusivity

If a sponsor obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC, or alternatively a one year extension of the regulatory market exclusivity from ten to eleven years, as selected by the marketing authorization holder.

Brexit and the Regulatory Framework in the United Kingdom

The U.K.'s withdrawal from the EU took place on January 31, 2020. The EU and the U.K. reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the U.K. will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the U.K. is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law, the body of EU law instruments governing medicinal products that pre-existed prior to the U.K.'s withdrawal from the EU. Since a significant proportion of the regulatory framework for pharmaceutical products in the U.K. covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the U.K. For example, the U.K. is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market our product candidates, including vadadustat, in the U.K.

Access Consortium

In October 2020, the MHRA joined the Access Consortium along with the Australian Therapeutic Goods Administration of Australia, Health Canada, Health Sciences Authority of Singapore and Swissmedic. The consortium is a coalition of these regulatory authorities that work together to promote greater regulatory collaboration and alignment of regulatory requirements. The consortium's goal is to maximize international co-operation between partners in the consortium, reduce duplication, and increase each agency's capacity to ensure patients have timely access to high quality, safe and effective therapeutic products. The MHRA commenced work-sharing applications with Access partners on January 1, 2021. Access Consortium working group members have regular meetings to exchange information on regulatory issues and challenges faced by the participating regulatory agencies, including issues on clinical trials, marketing authorizations, product manufacturing site inspections, post-marketing surveillance, joint development of technical guidelines or regulatory standards, and collaboration on information platforms. The Access consortium has developed three authorization procedures: the New Active Substance and Biosimilar Work Sharing Initiatives and the Generic Medicine Work Sharing Initiative.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the EEA, and the processing of personal data that takes place in the EEA, is subject to the European Union General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain

compensation for damages resulting from violations of the GDPR. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

There are ongoing concerns about the ability of companies to transfer personal data from the EU to other countries. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. This CJEU decision may lead to increased scrutiny on data transfers from the EU to the U.S. generally and increase our costs of compliance with data privacy legislation as well as our costs of negotiating appropriate privacy and security agreements with our vendors and business partners.

Additionally, in October 2022, U.S. President Biden signed an executive order to implement a new EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-U.S. Privacy Shield. The EU initiated the process to adopt the EU-U.S. Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU.

As with other issues related to Brexit, there are open questions about how personal data will be protected in the U.K. and whether personal information can transfer from the EU to the U.K. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR. While the Data Protection Act 2018 in the U.K. that "implements" and complements the GDPR has achieved Royal Assent on May 23, 2018 and is now effective in the U.K., it is still unclear whether transfer of data from the EEA to the U.K. will remain lawful under GDPR. The U.K. government has already determined that it considers all European Union and EEA member states to be adequate for the purposes of data protection, ensuring that data flows from the U.K. to the European Union/EEA remain unaffected. In addition, a recent decision from the European Commission appears to deem the U.K. as being "essentially adequate" for purposes of data transfer from the EU to the U.K., although this decision may be re-evaluated in the future.

Beyond GDPR, there are privacy and data security laws in a growing number of countries around the world. While many loosely follow GDPR as a model, other laws contain different or conflicting provisions. These laws will impact our ability to conduct our business activities, including both our clinical trials and any eventual sale and distribution of commercial products.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication. In addition, third-party payors may impose prior authorization or step edit requirements requiring patients to have tried other therapies prior to our products for coverage. Payors may also decline to include our products or product candidates on their formulary, which means that unless healthcare providers seek a medical exception for coverage, the payors will not pay for the product.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

Dialysis-related drugs are included in the ESRD prospective payment system (PPS) bundled payment and are grouped into functional categories such as anemia management and bone and mineral metabolism, except that oral-only drugs are exempted from inclusion until 2025. In a final ESRD PPS rule published in October 2019, CMS confirmed that it will expand the TDAPA to most new dialysis drugs approved by the FDA after January 1, 2020. The TDAPA provides separate payment for eligible new drugs for two years based on the drug's Average Sales Price, or ASP, that will be in addition to the base rate in order to facilitate the adoption of innovative therapies. Although there are several details that need further clarification, including precise timing related to receiving codes to allow for reimbursement under TDAPA, which are assigned on a quarterly basis, the rule provides support for our assumption that new anemia treatments, including those in the HIF-PH inhibitor class, will be included in the ESRD PPS bundle and will be eligible for separate payment initially under TDAPA.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Dialysis Organizations Protocols

Dialysis organizations have their own formularies that list primary or preferred therapeutic options based on contracting status with drug manufacturers. While a prescriber may make their own independent decision to prescribe what they determine most appropriate for a given patient, any non-formulary therapeutic options are only available through an exception process based on clinical need. Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, resulting in that product not being on that organization's formulary. Additionally, dialysis organizations typically assess a product's efficacy before adding it to their formulary. Their process for assessing a product may differ among organizations and the timing of such assessment could delay adding such treatment to formulary, further affecting product sales.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians, teaching hospitals and other healthcare providers, patient privacy laws and regulations, and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government
- HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;
- the federal transparency requirements, known as the federal Physician Payments Sunshine Act (renamed the Open Payments Act), under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- the PDMA and its implementation regulations, as well as the DSCSA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the regulation of drug distributors by the states; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by third-party payors, including private insurers, and state gift ban and disclosure law requirements that differ from the federal Physician Payments Sunshine Act in terms of the nature and type of transfers of value that are reportable and the types of covered recipients.

Violations of these laws are punishable by criminal and/or civil sanctions, including, in some instances, exclusion from participation in federal and state health care programs, such as Medicare and Medicaid. Ensuring compliance is time consuming and costly. Similar healthcare laws and regulations exist in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing the privacy and security of personal information.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. State and foreign laws also govern the privacy and security of health information in

some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare.

In March 2010, the United States Congress enacted the ACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 203. Pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions were suspended and reduced through the end of June 2022 but the full 2% cut has resumed as of July 2022. Under current legislation, the actual reductions in Medicare payments may vary up to 4%.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the Tax Act, which was signed by the prior administration on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The prior administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden rescinded those orders and issued a new executive order that directs federal agencies to reconsider rules and other policies that limit access to healthcare, and consider actions that will protect and strengthen that access. Under this order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and under the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, the prior administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this

rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current safe harbor drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager service fees. It originally was set to go into effect on January 1, 2022, but with passage Inflation Reduction Act has been delayed by Congress to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Laws Relating to Foreign Trade

We are subject to various federal and foreign laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their representatives from paying, offering to pay, promising, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate for the purposes of obtaining or retaining business, or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the health care professionals we regularly interact with may meet the FCPA's definition of a foreign government official. Additionally, interactions with or on the part of our partners, collaborators, contract research organizations, vendors or other agents may also implicate the FCPA. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls. Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents unique challenges in the pharmaceutical industry because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments made by pharmaceutical companies to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Our international operations could also be subject to compliance with national laws of other countries, such as the United Kingdom Bribery Act. of 2010, or U.K. Bribery Act. The U.K. Bribery Act applies to any company "carrying on business" in the U.K., irrespective of where the offending conduct occurs. The U.K. Bribery Act applies to bribery activities both in the public and private sector and prohibits the provision of an "advantage" intended to induce or reward "improper performance" of the recipient's function. The failure by a company to prevent third parties from providing a bribe on its behalf could also constitute an offense. Penalties under the U.K. Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances.

There are local antibribery and anticorruption laws in countries where we are conducting clinical trials, such as Brazil and Russia, and many of these also carry the risk of significant financial or criminal penalties. Our clinical trial operations could also result in enforcement actions by U.S., U.K., or other governmental authorities. There are also trade laws within the United States and in other regions that regulate the sale, purchase, import, export, reexport, transfer and shipment of goods, currency, products, materials, services and technology. Violations of these laws can lead to serious consequences, including substantial fines.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees and Human Capital Resources

As of December 31, 2022, we had 205 employees, all but one of whom were full-time. None of our employees are represented by any collective bargaining unit. We believe that we maintain good relations with our employees.

Retention, growth, training and development of our employees are integral to our success. We offer competitive compensation (including base salary, incentive bonus, and long-term equity awards tied to the value of our stock price) as well as benefits packages designed to attract, motivate and reward talented individuals who possess the skills necessary to support our business objectives, assist in the achievement of our strategic goals and create value for our stockholders. Our compensation program is designed to differentiate us from our competition and incentivize achievement of corporate goals, individual performance and demonstrate our corporate values. In addition, we provide development and leadership opportunities to our employees to cultivate talent throughout the Company.

We are committed to our employees' health, safety and well-being. In March 2020, in response to the COVID-19 pandemic, we adjusted our workplace policies to allow employees to work from home and in 2021 we remodeled our work paradigm to one that is flexible and designed to accommodate a range of work profiles from office based, to hybrid to fully remote, to field-based, allowing us to maximize productivity and performance. Recognizing the pandemic had an impact on well-being as well as the availability of support services, we launched Modern Health, a platform focused on services to support employees' and their dependents in areas such as mental, physical, financial, social and professional health, making it easier for them to get personalized care faster.

We are also committed to diversity, equality and inclusion, and this is reflected in Akebia's leadership. Two members of our Board of Directors, Cynthia Smith and LeAnne M. Zumwalt, are women, and women comprise approximately 45% of our senior management team. In addition, Ron Frieson has served on our Board of Directors since November 2021, increasing the diversity of our Board of Directors.

With the goal of ensuring every employee is included, supported, and treated equitably, we developed a team (IDEA – Inclusion, Diversity & Equity Alliance) to support and guide Akebia as a diverse, inclusive, and culturally intelligent workplace. Over the past two and a half years this team has worked with executive leadership to identify areas for growth and education and move forward several initiatives that will enable us to continue to build an inclusive workplace and a diverse workforce. We also provide access to LinkedIn Learning, an online learning platform that recommends expert-led courses for relevant skill development for all of our employees.

In addition, we support kidney patient communities where we live and work. In the United States, we have a patient services program, Akebia Cares, designed to provide one-on-one support to help communicate individual benefits and available resources for patients today facing financial obstacles that keep them from accessing important medications. In 2022, we provided over $5.3 million worth of Auryxia for free to approximately 14,000 patients needing assistance. We also support and work closely with multiple kidney patient advocacy organizations, including the National Kidney Foundation, the American Kidney Fund, the Renal Support Network, Dialysis Patient Citizens and American Association of Kidney Patients. We believe our involvement with these organizations shows our commitment to our purpose of bettering the life of each person impacted by kidney disease.

Available Information

Our principal executive offices are located at 245 First Street, Cambridge, Massachusetts 02142. Our telephone number is (617) 871-2098. Our website address is www.akebia.com. The information on our website or that may be accessed by links on our website is not incorporated by reference into this Form 10-K. We make available, free of charge and through our website, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any amendments to any such reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as soon as reasonably practicable after they are electronically filed with or furnished to the U.S. Securities and Exchange Commission.

Item 1A. Risk Factors.

We face a variety of risks and uncertainties in our business. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also become important factors that affect our business. If any of the following risks occurs, our business, financial condition, financial statements, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy

We have incurred significant losses since our inception, and anticipate that we will continue to incur significant losses and cannot guarantee when, if ever, we will become profitable or attain positive cash flows.

Investment in pharmaceutical product development and commercialization is highly speculative because it requires upfront capital expenditures and there is significant risk that a product candidate will fail to gain marketing approval or that an approved product will not be commercially viable. Since our inception, we have devoted most of our resources to research and development, including our preclinical and clinical development activities and commercialization of Auryxia. We have financed our operations primarily through sales of equity securities, our strategic collaborations and product revenues, a royalty monetization transaction and debt. Prior to the merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became our wholly owned subsidiary, we had no products approved for commercial sale and had not generated any revenue from the sale of products. We are not currently profitable, and we have incurred net losses each year since our inception, including a net loss of $92.6 million for the year ended December 31, 2022. As of December 31, 2022, we had an accumulated deficit of $1.6 billion. We cannot guarantee when, if ever, we will become profitable.

In March 2022, we received a complete response letter, or CRL, from the FDA regarding our NDA for vadadustat, our lead investigational product candidate, for the treatment of anemia associated with CKD. The FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. In October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, to the FDA. The FDRR focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, and there can be no assurances that we will be successful in our appeal and obtain approval for vadadustat in a timely manner, on favorable terms, or at all. As a result, the regulatory approval process for vadadustat in the U.S. is highly uncertain. We may not obtain approval at all, and if we are able to obtain approval, the expense and time to do so could adversely impact our ability to successfully commercialize vadadustat or conduct our other business operations, and our financial condition could be materially harmed.

Our ability to generate product revenue and achieve profitability depends on the overall success of Auryxia(R), vadadustat, if approved, and any current or future product candidates, including those that may be in-licensed or acquired, which depends on several factors, including:

- obtaining adequate or favorable pricing and reimbursement from private and governmental payors for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- obtaining and maintaining market acceptance of Auryxia, vadadustat, if approved, and any other product candidate, including those that may be in-licensed or acquired;
- the size of any market in which Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, receives approval and obtaining adequate market share in those markets;
- addressing the issues identified in the CRL for vadadustat that we received from the FDA and the outcome of our appeal;
- the timing and scope of marketing approvals for vadadustat, if approved, and any other product candidate, if approved, including those that may be in-licensed or acquired; maintaining marketing approvals for Auryxia, vadadustat, if approved, and any other product, including those that may be in-licensed or acquired;
- actual or perceived advantages or disadvantages of our products or product candidates as compared to alternative treatments, including their respective safety, tolerability and efficacy profiles, the potential convenience and ease of administration and cost;
- maintaining an acceptable safety and tolerability profile of our approved products, including the frequency and severity of any side effects;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies, based, in part, on their perception of our clinical trial data and/or the actual or perceived safety, tolerability and efficacy profile;

- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate supplies of products that are compliant with good manufacturing practices, or GMPs, to support the clinical development and the market demand for Auryxia, vadadustat, if approved, and any other product and product candidate, including those that may be in-licensed or acquired;
- current and future restrictions or limitations on our approved or future indications and patient populations or other adverse regulatory actions or in the event that the FDA requires Risk Evaluation and Mitigation Strategies, or REMS, or risk management plans that use restrictive risk minimization strategies;
- the effectiveness of our sales, marketing, manufacturing and distribution strategies and operations;
- competing effectively with any products for the same or similar indications as our products;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and trade secrets; and
- the impact of the COVID-19 pandemic on the above factors, including the disproportionate impact of the COVID-19 pandemic on CKD patients, the adverse impact on the phosphate binder market in which we compete, and the limitation of our sales professionals to meet in person with healthcare professionals as the result of travel restrictions or limitations on access for non-patients.

Our ability to achieve profitability also depends on our ability to manage our expenses. Following receipt of the CRL, in April and May 2022, we implemented a reduction of our workforce, by approximately 42% across all areas of the Company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. We recorded a restructuring charge of $15.9 million in the aggregate primarily related to contractual termination benefits including severance, non-cash stock-based compensation expense, healthcare and related benefits in the year ended December 31, 2022. However, we may incur additional costs not currently contemplated due to events associated with or resulting from the workforce reductions. Additionally, the reductions in workforce could impact our operations, including our commercialization of Auryxia, which could affect our ability to generate revenue.

We expect to continue to incur additional operating expenses, including additional research and development expenses to our pipeline, additional costs related to vadadustat, and research and development and selling, general and administrative expenses for ongoing development and commercialization of Auryxia, which could lead to operating losses for the foreseeable future. In addition to any additional costs not currently contemplated due to events associated with or resulting from the workforce reductions noted above, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, on product revenue, collaboration revenue, and our ability to obtain additional funding. On June 30, 2022, we entered into a Termination and Settlement Agreement, or the Termination Agreement, with Otsuka Pharmaceutical Co. Ltd., or Otsuka, pursuant to which we agreed to the immediate termination of the December 18, 2016 collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement, and the April 25, 2017 collaboration and license agreement with Otsuka, or the Otsuka International Agreement, in exchange for the payment of $55.0 million to us and the agreement between the parties with respect to the conduct of certain activities. Unless and until we are able to find a new partner for vadadustat in Europe and other countries previously licensed to Otsuka, we will incur additional expenses in connection with the development of vadadustat and will receive less collaboration revenue and, if approved, product revenue than originally anticipated. In addition, we expect to continue to incur significant expenses if and as we:

- continue our commercialization activities for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product or product candidate, including those that may be in-licensed or acquired;
- address the issues identified in the CRL for vadadustat that we received from the FDA and pursue our appeal of the CRL for vadadustat with the FDA;
- conduct and enroll patients in any clinical trials, including post-marketing studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired;
- maintain marketing approvals for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product, including those that may be in-licensed or acquired;
- manufacture Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, for commercial sale and clinical trials;
- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop and commercialize other product candidates and technologies;

- continue to repay, and pay any associated pre-payment penalties, if applicable, the senior secured term loans in an aggregate principal amount of $67.0 million as of December 31, 2022, or the Term Loans, that were made available to us pursuant to the Loan Agreement;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- make decisions with respect to our personnel, including the retention of key employees;
- make decisions with respect to our infrastructure, including to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any additional delays or encounter issues with any of the above.

We have and will continue to expend significant resources on our legal proceedings, as described below under Part I, Item 3. Legal Proceedings, or any other legal proceedings brought by or against us in the future.

Because of the numerous risks and uncertainties associated with pharmaceutical product development and commercialization, we are unable to accurately predict the timing or amount of increased expenses. The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter, the progress of our clinical development and our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We will continue to incur substantial expenditures relating to continued commercialization and post-marketing requirements for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other products, including those that may be in-licensed or acquired, as well as costs relating to the research and development of any other product candidate, including those that may be in-licensed or acquired. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency, or the EMA, or other regulatory authorities, or if we otherwise believe it is necessary, to change our manufacturing processes or assays, to amend or replace our study protocols, to conduct any additional clinical trials, whether in order to obtain approval or as a post-approval study, including any additional clinical trial that we decide to conduct for vadadustat, to perform studies in addition to, different from or larger than those currently planned, if there are any delays in completing our clinical trials or if there are further delays in or issues with obtaining marketing approval for vadadustat in the United States, the European Union, or EU, or other jurisdictions. In addition, our ability to generate revenue would be negatively affected if the size of our addressable patient population is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we sought or the patient population for treatment is narrowed by competition, physician choice, coverage or reimbursement, or payor or treatment guidelines. Even though we generate product revenue from Auryxia and royalties from Riona™ and Vafseo™ in Japan and may generate revenue and royalties from the sale of any products that may be approved in the future, including those that may be in-licensed or acquired, we may never generate revenue and royalties that are significant enough for us to become and remain profitable, and we will need to obtain additional funding to continue to fund our operating plan beyond Auryxia and certain development activities, and achieve strategic growth.

We will require substantial additional financing to achieve our goals. A failure to obtain this necessary capital when needed, or on acceptable terms, could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of December 31, 2022, our cash and cash equivalents were $90.5 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Auryxia; pursue our appeal for vadadustat in the U.S. with the FDA; support the regulatory process with respect to vadadustat with the EMA and ACCESS Consortium; and develop and commercialize any other product or product candidate, including those that may be in-licensed or acquired. These expenditures will include costs associated with research and development, manufacturing, potentially obtaining marketing approvals and marketing products approved for sale. In addition, other unanticipated costs may arise. Because the outcomes of our current and anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete clinical development for any current or future product candidates, including vadadustat depending on what is required to address the issues identified in the CRL for vadadustat, including the outcome of our appeal and if additional clinical trials are required in order to obtain marketing approval, or to complete post-marketing studies for Auryxia and vadadustat, if approved. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of conducting clinical trials or any post-marketing requirements or any other clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;

- the cost and timing of commercialization activities, including product manufacturing, marketing, sales and distribution costs, for Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- the results of our meetings with the FDA, the EMA and other regulatory authorities and any consequential effects, including on timing of and ability to obtain and maintain marketing approval, study design, study size and resulting operating costs;
- any difficulties or delays in conducting our clinical trials, or enrolling patients in our clinical trials, for Auryxia, vadadustat or any other product candidates;
- the outcome of our efforts to obtain marketing approval for vadadustat in the United States, Europe and in other jurisdictions and any other product candidates, including those that may be in-licensed or acquired, including any additional clinical trials or post-approval commitments imposed by regulatory authorities;
- the timing of, and the costs involved in obtaining, marketing approvals for vadadustat, including in the United States, Europe and certain other markets, and any other product candidate, including those that may be in-licensed or acquired, including to fund the preparation, filing and prosecution of regulatory submissions;
- the costs of maintaining marketing approvals for Auryxia or any other product, including those that may be in-licensed or acquired;
- the number of generic versions of Auryxia that enter the market following loss of exclusivity for Auryxia in March 2025, and the timing of, and the magnitude of, the impact on the price of Auryxia;
- the cost of securing and validating commercial manufacturing for any of our product candidates, including those that may be in-licensed or acquired, and maintaining our manufacturing arrangements for Auryxia and vadadustat or any other product, including those that may be in-licensed or acquired, or securing and validating additional arrangements;
- the costs involved in preparing, filing and prosecuting patent applications and maintaining, defending and enforcing our intellectual property rights, including litigation costs, and the outcome of such litigation;
- the costs involved in any legal proceedings to which we are a party;
- our status as a publicly traded company on the Nasdaq Capital Market;
- our decisions with respect to personnel;
- our decisions with respect to infrastructure; and
- the extent to which we engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we could develop and market commercial products, or develop other product candidates and technologies.

We will need to obtain substantial additional funding to fund our operating plan beyond Auryxia and certain development activities, and achieve strategic growth. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We expect our cash resources to fund our current operating plan through at least the next twelve months from the filing of this Annual Report on Form 10-K. However, if our operating performance deteriorates significantly from the levels achieved in 2022, it could have an effect on our liquidity and our ability to continue as a going concern in the future. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. We have based this estimate on assumptions that may be substantially different than actual results, and we could utilize our available capital resources sooner than we currently expect. In addition, if we fail to satisfy any of the covenants under our Loan Agreement with Pharmakon, including the covenant that our Annual Report on Form 10-K for the fiscal year ending December 31, 2023 not be qualified as to going concern, and the loan is accelerated, we may not have sufficient resources to fund our operating plan through the next twelve months. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources will fund our operating plan for the period anticipated by us, or that additional funding will be available on terms acceptable to us, or at all.

Any additional fundraising efforts may divert our management’s attention away from their day-to-day activities, which may adversely affect our ability to develop and commercialize Auryxia and any other products or product candidates, including those that may be in-licensed or acquired, or to continue to seek regulatory approval for vadadustat. Also, additional funds may not be available to us in sufficient amounts or on acceptable terms or at all. If we are unable to raise additional capital in sufficient amounts when needed or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development and/or commercialization of Auryxia and any other products or product candidates, including those that may be in-licensed or acquired, or to take any actions with respect to vadadustat depending on future decisions with respect to vadadustat in the U.S. Any of these events could significantly harm our business, financial condition and prospects.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product and product candidates on unfavorable terms to us.

We expect to finance future cash needs through product revenue, royalty transactions, strategic transactions, public or private equity or debt transactions, or a combination of these approaches. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, our fixed payment

obligations may increase, any such securities may have rights senior to those of our common stock, and the terms may include liquidation or other preferences and anti-dilution protections that adversely affect the rights of our common stockholders. Additional debt financing, if available, may involve agreements that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, make capital expenditures, declare dividends, acquire, sell or license intellectual property rights, and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through royalty transactions, we may have to relinquish valuable rights to our portfolio and future revenue streams, and enter into agreements that would restrict our operations and strategic flexibility. If we raise additional funds through strategic transactions with third parties, we may have to do so at an earlier stage than otherwise would be desirable. In connection with any such strategic transactions, we may be required to relinquish valuable rights to our product and product candidates, future revenue streams or research programs or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds when needed, we may not be able to pursue planned development and commercialization activities and we may need to grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

If we fail to regain compliance with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

On May 12, 2022, we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market, referred to as the minimum bid price rule. In accordance with Nasdaq Listing Rules, we were provided an initial period of 180 calendar days, or until November 8, 2022, to regain compliance with the minimum bid price rule. We did not regain compliance with the minimum bid price rule by the initial compliance date.

On November 9, 2022, Nasdaq notified us that we were eligible for an additional 180 calendar day period, or until May 8, 2023, to regain compliance with the minimum bid price rule. Nasdaq's determination was based on our meeting the continued listing requirement for market value of publicly held shares and all other applicable requirements for initial listing on the Nasdaq Capital Market with the exception of bid price requirement, and our written notice of our intention to cure the deficiency during the second compliance period by effecting a reverse stock split, if necessary. On November 9, 2022, Nasdaq approved our transfer from the Nasdaq Global Market to the Nasdaq Capital Market, a continuous trading market that operates in substantially the same manner as the Nasdaq Global Market. The transfer became effective at the opening of business on November 11, 2022.

To date, we have not regained compliance with the minimum bid price rule. If, at any time during the additional compliance period the bid price for our common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, the Nasdaq Listing Qualifications Department staff will provide written notification to us that we are in compliance with the minimum bid price rule, unless the staff exercises its discretion to extend this 10-day period pursuant to the Nasdaq Listing Rules.

If we do not regain compliance with the minimum bid price rule by the required date and we are not eligible for any additional compliance period at that time, the Nasdaq Listing Qualifications Department staff will provide us written notification that our common stock may be delisted. At that time, we may appeal the staff's delisting determination to a Nasdaq Listing Qualifications Panel. We expect that our common stock would remain listed pending the panel's decision. However, there can be no assurance that, even if we appeal the staff's delisting determination to the Nasdaq Listing Qualifications Panel, such appeal would be successful.

On March 1, 2023, we filed a definitive proxy statement for a Special Meeting of Stockholders to be held on April 11, 2023 at which meeting we are seeking stockholder approval of a reverse stock split with the primary intent of increasing the price of our common stock to meet the price criteria for continued listing on Nasdaq. We intend to continue to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the minimum bid price rule, which could include seeking to effect a reverse stock split. However, there can be no assurance that our stockholders will approve a reverse stock split or that we will be able to regain compliance with the minimum bid price rule.

There are many factors that may adversely affect our minimum bid price, including those described throughout this section titled "Risk Factors." Many of these factors are outside of our control. As a result, we may not be able to sustain compliance with the minimum bid price rule in the long term. Any potential delisting of our common stock from the Nasdaq Capital Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Capital Market would also make it more difficult for our stockholders to sell our common stock in the public market.

We may not be successful in our efforts to identify, acquire, in-license, discover, develop and commercialize additional products or product candidates or our decisions to prioritize the development of certain product candidates over others may not be successful, which could impair our ability to grow.

Although we continue to focus a substantial amount of our efforts on the commercialization of Auryxia and to pursue our appeal for vadadustat in the U.S. with the FDA and to seek regulatory approval for vadadustat in Europe and other territories, a key element of our long-term growth strategy is to develop additional product candidates and acquire, in-license, develop and/or market additional products and product candidates.

Research programs to identify product candidates require substantial technical, financial and human resources, regardless of whether product candidates are ultimately identified. Our research and development programs may initially show promise, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- the research methodology used may not be successful in identifying potential indications and/or product candidates;
- we may not be able or willing to assemble sufficient resources to acquire or discover additional product candidates;
- a product candidate may be shown to have harmful side effects, a lack of efficacy or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance;
- a product candidate we develop and seek regulatory approval for, including vadadustat, may not be approved by the FDA on a timely basis, or at all;
- product candidates we develop may nevertheless be covered by third party patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer commercially reasonable;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted as safe and effective by patients, the medical community, or third party payors, if applicable.

If any of these events occur, we may be forced to abandon our research and development efforts for one or more of our programs, or we may not be able to identify, discover, develop or commercialize additional product candidates, which may have a material adverse effect on our business.

Because we have limited financial and managerial resources, especially as a result of the CRL for vadadustat that we received in March 2022 and the reductions in workforce that we implemented in 2022, we focus on products, research programs and product candidates for specific indications. As a result, we may forgo or delay pursuit of opportunities with other product candidates or for other indications, or out license rights to product candidates, that later prove to have greater commercial potential. For example, as a result of receipt of the CRL and implementation of the reductions in workforce, we delayed certain research activities. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities on a timely basis, or at all. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists and institutions, and other researchers to sell or license product candidates, products or technology to us. The success of this strategy depends partly upon our ability to identify, select, and acquire promising product candidates and products. The process of identifying, selecting, negotiating and implementing a license or acquisition of a product candidate or an approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of a product candidate or an approved product. We have limited resources to identify and execute the acquisition or in-licensing of third party products, businesses, and technologies and integrate them into our current infrastructure.

Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. Any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA, the EMA, the Japanese Pharmaceuticals and Medical Devices Agency, or PMDA, or other regulatory authorities, or post-approval testing or other requirements if approved. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot provide assurance that any of our products will be manufactured in a cost effective manner, achieve market acceptance or not require substantial post-marketing clinical trials.

Accordingly, there can be no assurance that we will ever be able to identify, acquire, in-license or develop suitable additional products or product candidates, which could materially adversely affect our future growth and prospects. We may focus our efforts and resources on potential products, product candidates or other programs that ultimately prove to be unsuccessful.

We may engage in strategic transactions to acquire assets, businesses, or rights to products, product candidates or technologies or form collaborations or make investments in other companies or technologies that could harm our operating results, dilute our stockholders' ownership, increase our debt, or cause us to incur significant expense.

As part of our business strategy, we may engage in additional strategic transactions to expand and diversify our portfolio, including through the merger, acquisition or in-license of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our existing and prior collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, on favorable terms, on a cost-effective basis, or at all. Moreover, we may devote resources to potential opportunities that are never completed or we may incorrectly judge the value or worth of such opportunities. Even if we successfully execute a strategic transaction, we may not be able to realize the anticipated benefits of such transaction and may experience losses related to our investments in such transactions. Integration of an acquired company or assets into our existing business may not be successful and may disrupt ongoing operations, require the hiring of additional personnel and the implementation and integration of additional internal systems and infrastructure, and require management resources that would otherwise focus on developing our existing business. Even if we are able to achieve the long-term benefits of a strategic transaction, our expenses and short-term costs may increase materially and adversely affect our liquidity. Any of the foregoing could have a detrimental effect on our business, results of operations and financial condition. For example, on June 4, 2021, we entered into a license agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted us an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase, or sGC, stimulator. Although we have progressed preclinical studies for praliciguat, we need to do additional work to manufacture product for clinical trials before we can initiate the trials, and when started, we may be unsuccessful in developing praliciguat. If any of the assumptions that we made in valuing the transaction, including the costs or timing of development of, or the potential benefits of, praliciguat, were incorrect, we may not recognize the anticipated benefits of the transaction and our business could be harmed.

In addition, future transactions may entail numerous operational, financial and legal risks, including:

- incurring substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;
- exposure to known and unknown liabilities, including contingent liabilities, possible intellectual property infringement claims, violations of laws, tax liabilities and commercial disputes;
- higher than expected acquisition and integration costs;
- difficulty in integrating operations, processes, systems and personnel of any acquired business;
- increased amortization expenses or, in the case of a write-down of the value of acquired assets, impairment losses, such as the Auryxia intangible asset impairment in the second quarter of 2020 and corresponding adjustments to the estimated useful life of the developed product rights for Auryxia;
- impairment of relationships with key suppliers or customers of any acquired business due to changes in management and ownership;
- inability to retain personnel, customers, distributors, vendors and other business partners integral to an in-licensed or acquired product, product candidate or technology;
- potential failure of the due diligence processes to identify significant problems, liabilities or other shortcomings or challenges;
- entry into indications or markets in which we have no or limited development or commercial experience and where competitors in such markets have stronger market positions; and
- other challenges associated with managing an increasingly diversified business.

If we are unable to successfully manage any transaction in which we may engage, our ability to develop new products and continue to expand and diversify our portfolio may be limited.

Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic.

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and continues to affect our patients, healthcare providers with whom we interact, customers, our contract manufacturing organizations, or CMOs, and other vendors. The full extent to which the COVID-19 pandemic and the lasting effects of the pandemic will directly or indirectly impact our business, results of operations and financial condition continues to depend on future developments that are highly uncertain and cannot be accurately predicted, including any resurgences or variants of COVID-19, the actions taken to contain it or treat its impact and the economic and other impacts on local, regional, national and international markets where the healthcare providers with whom we interact, our CMOs, and our other vendors operate. On January 30, 2023, the Biden Administration announced that it will end the public health emergency declarations related to

COVID-19 on May 11, 2023. On January 31, 2023, the FDA indicated that it would soon issue a Federal Register notice describing how the termination of the public health emergency will impact the agency's COVID-19 related guidance, including the clinical trial guidance and updates thereto. At this point, it is unclear how, if at all, these developments will impact our efforts to develop and commercialize our product candidates.

We believe our revenue growth was negatively impacted by the COVID-19 pandemic in 2021 and 2022 primarily as the CKD patient populations that we serve experienced both high hospitalization and mortality rates due to COVID-19, and the pandemic had an adverse impact on the phosphate binder market in which Auryxia competes. Labor shortages and costs have adversely impacted dialysis providers. These impacts have refocused clinical efforts in addressing bone and mineral disorders like hyperphosphatemia to more acute operational issues to ensure patients receive dialysis treatments and still some patients have been rescheduled or missed treatments due to labor shortages. We believe, this and potentially other factors, has led to the reduction in the phosphate binder market, which has not experienced growth since early 2020. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, the COVID-19 pandemic and the ongoing impacts from the COVID-19 pandemic continue to adversely and disproportionately impact CKD patients and the phosphate binder market; therefore, we expect the ongoing impacts from the pandemic to continue to have a negative impact on our revenue growth for the foreseeable future.

In addition, several healthcare facilities have previously restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have previously restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers have, and could continue to, negatively impact our access to healthcare providers and, ultimately, our sales, including with respect to vadadustat, if approved. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, some restrictions remain, and more restrictions may be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of COVID-19, which may be more contagious and more severe than prior strains of the virus. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand in the United States for Auryxia and will be for vadadustat, if approved, including the potential for further declines or changes in prescription trends and customer orders, which could have a material adverse effect on our business, results of operations, and financial condition.

In addition, the direct and indirect impacts of the pandemic or the response efforts to the pandemic, including, among others, competition for labor and resources and increases in labor, sourcing, manufacturing and shipping costs, may cause disruptions to, closures of or other impacts on our CMOs and other vendors in our supply chain on which we rely for the supply of our products and product candidates. For example, areas of China have recently continued to implement lockdowns for COVID-19, which could impact the global supply chain. At this time, our CMOs continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturers' ability to manufacture and deliver Auryxia and vadadustat (if approved in the United States or EMA and which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in increased costs and delays, or disruptions to the manufacturing and supply of our products. These impacts could have a negative effect on our inventory reserves, which could result in an increase in inventory write-offs due to expiry.

If we or any of the third parties with whom we engage, including our collaboration partners, vendors, or any of our customers were to experience further shutdowns, delays or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned, and our revenue expectations, could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results.

While we are working to mitigate the impacts on our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control. The COVID-19 pandemic has, and may continue to, significantly impact the phosphate binder market in which we compete and economies and financial markets worldwide, which could result in adverse effects on our business and operations, impact our ability to raise additional funds and impact the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has been contained or mitigated, we may continue to experience adverse impacts to our business as a result of the adverse impact on the patient population for Auryxia, the decline in the phosphate binder market and any economic recession or depression that has occurred or may occur in the future.

Risks Related to our Financial Arrangements

Our obligations in connection with the loan agreement with Pharmakon and requirements and restrictions in the loan agreement could adversely affect our financial condition and restrict our operations.

We entered into the Loan Agreement with Pharmakon, pursuant to which the Term Loans were made available to us in two tranches. The first tranche of $80.0 million closed on November 25, 2019, and the second tranche of $20.0 million closed on December 10, 2020. See Note 11 to our audited consolidated financial statements in Part II, Item 8. Financial Statements of this Annual Report on Form 10-K for additional information regarding our obligations under the Loan Agreement.

The Loan Agreement contains affirmative and negative covenants applicable to us and our subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold, which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia, which started in the fourth quarter of 2020. In addition, the Loan Agreement contains covenants that our Annual Reports on Form 10-K, must not be subject to any qualification as to going concern. Failure to maintain compliance with these or other covenants would result in an event of default under the Loan Agreement, which could result in enforcement action, including acceleration of amounts due under the Loan Agreement. Additionally, the liabilities under the Loan Agreement will be accelerated, subject to certain exceptions, if we are required to repay to CSL Vifor all or a part of the working capital facility established in connection with the Second Amended and Restated License Agreement that we entered into with CSL Vifor, in February 2022, or the Vifor Second Amended Agreement, as a result of certain terminations of the Vifor Second Amended Agreement or due to a reduction in the balance of the working capital facility by more than a prespecified amount.

In the event there is an acceleration of our and certain of our subsidiaries' liabilities under the Loan Agreement as a result of an event of default or otherwise, we may not have sufficient funds or may be unable to arrange for additional financing to repay the liabilities or to make any accelerated payments, and Pharmakon could seek to enforce security interests in the collateral securing the Loan Agreement and our guarantee of the Term Loans, which would have a material adverse effect on our business, financial condition and results of operations.

The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to prepayment premiums and make-whole premiums prior to certain dates. We made a voluntary prepayment of $25.0 million, including $0.5 million of prepayment penalties on July 15, 2022, pursuant to the Second Amendment and Waiver. This represented the repayment of $5.0 million of the first tranche and the full $20.0 million of the second tranche. Upon a change of control, mandatory prepayment provisions require us to prepay the principal amount outstanding, the applicable prepayment premium and make-whole premium and accrued and unpaid interest. In addition, our obligations in connection with the Loan Agreement could have additional significant adverse consequences, including, among other things:

- restricting our activities, including limitations on transferring certain of our assets, engaging in certain transactions, terminating certain agreements, including the Vifor Second Amended Agreement, incurring certain additional indebtedness, creating certain liens, paying dividends or making certain other distributions and investments;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a possible competitive disadvantage compared to our competitors who have a smaller amount of debt or competitors with comparable debt at more favorable interest rates; and
- limiting our ability to borrow additional amounts for working capital, capital expenditures, research and development efforts, acquisitions, debt service requirements, execution of our business strategy and other purposes.

Any of these factors could materially and adversely affect our business, financial condition and results of operations.

Our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P. contains various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.

On February 25, 2021, we entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which we sold to HCR our right to the to receive royalties and sales milestones for vadadustat, collectively the Royalty Interest Payments, in each case, payable to us under our Collaboration Agreement dated December 11, 2015, or the MTPC Agreement, with Mitsubishi Tanabe Pharma Corporation, or MTPC, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. Under the Royalty Agreement, we are required to comply with various covenants, including obligations to take certain actions, such as actions with respect to the Royalty Interest Payments, the MTPC Agreement, our agreement with MTPC for the commercial supply of vadadustat drug product, and our intellectual property. In addition, the Royalty Agreement includes customary events of default upon the occurrence of enumerated events, including failure to perform certain covenants and the occurrence of insolvency events. In the event we violate certain covenants and other provisions, we may not receive sales milestones from HCR even if the applicable sales thresholds are met. Upon the occurrence of an event of default, HCR would have the ability to exercise all available remedies in law and equity, which could have a material adverse effect on our financial condition.

Risks Related to Commercialization

Our business is substantially dependent on the commercial success of Auryxia. If we are unable to continue to successfully commercialize Auryxia, our results or operations and financial condition will be materially harmed.

Our business and our ability to generate product revenue largely depend on our, and our collaborators', ability to successfully commercialize Auryxia. Our ability to generate revenue depends on our ability to execute on our commercialization plans, and the size of the market for, and the level of market acceptance of, Auryxia and any other product or product candidate, including those that may be in-licensed or acquired. If the size of any market for which a product or product candidate is approved decreases or is smaller than we anticipate, our revenue and results of operations could be materially adversely affected. For example, the phosphate binder market has declined since 2020, which we believe was partially a result of the COVID-19 pandemic. If the phosphate market does not recover or continues to decline, our revenue from Auryxia could be materially adversely affected.

Market acceptance is also critical to our ability to generate significant product revenue. Any product may achieve only limited market acceptance or none at all. If Auryxia, or any of our product candidates that is approved, is not accepted by the market to the extent that we expect or market acceptance decreases, we may not be able to generate significant product revenue and our business would be materially harmed. Market acceptance of Auryxia or any other approved product depends on a number of factors, including:

- the availability of adequate coverage and reimbursement by and the availability of discounts, rebates and price concessions from third party payors, pharmacy benefit managers, or PBMs, and governmental authorities;
- the safety and efficacy of the product, as demonstrated in clinical trials and in the post-marketing setting;
- the prevalence and complications of the disease treated by the product;
- the clinical indications for which the product is approved and the product label approved by regulatory authorities, including any warnings or limitations that may be required on the label as a consequence of potential safety risks associated with the product;
- the countries in which marketing approvals are obtained;
- the claims we and our collaborators are able to make regarding the safety and efficacy of the product;
- the success of our physician and patient communications and education programs;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety and efficacy of the product in relation to alternative treatments;
- the timing of receipt of marketing approvals and product launch relative to competing products and potential generic entrants;
- relative convenience and ease of administration;
- the frequency and severity of adverse side effects;
- favorable or adverse publicity about our products or favorable or adverse publicity about competing products;
- the effectiveness of our and our collaborators' sales, marketing and distribution efforts; and
- the restrictions on the use of the product together with other medications, if any.

If we are unable to maintain or expand, or, if vadadustat is approved, initiate, sales and marketing capabilities or enter into additional agreements with third parties, we may not be successful in commercializing Auryxia, vadadustat, if approved, or any other product candidates that may be approved.

In order to market Auryxia and any other approved product, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We have built a commercial infrastructure and sales force in the United States for Auryxia, our only commercial product. However, following receipt of the CRL, in April and May 2022, we implemented a reduction of our workforce by approximately 42% across all areas of the Company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. If the remaining sales and marketing team cannot successfully commercialize Auryxia, or if additional sales and marketing employees decide to leave as a result of the reduction in workforce or otherwise, it could have a material adverse effect on Auryxia revenue and our financial condition.

If we obtain regulatory approval to market vadadustat in the U.S., we believe that we can leverage the current commercial foundation for vadadustat in the U.S., but if we are unable to do so successfully this would materially harm our business. Additionally, training a sales force to successfully sell and market a new commercial product is expensive and time-consuming

and could delay any commercial launch of such product candidate or distract the sales force from promoting Auryxia. We may underestimate the size of the sales force required for a successful product launch and we may need to expand our sales force earlier and at a higher cost than we anticipated. In 2021 and early 2022, we incurred commercialization expenses for vadadustat that were premature or unnecessary as a result of the receipt of the CRL for vadadustat, and may in the future incur additional commercialization expenses prematurely or unnecessarily if we do not receive marketing approval in the timeframe we expect, or at all.

We devote significant effort, in particular, to recruiting individuals with experience in the sales and marketing of pharmaceutical products. Competition for personnel with these skills is significant and retaining qualified personnel with experience in our industry is difficult. Further, our recent reductions in workforce may further exacerbate these conditions and interfere with our ability to find and retain qualified personnel. As a result, we may not be able to retain our existing employees or hire new employees quickly enough to meet our needs. At the same time, we may face high turnover, requiring us to expend time and resources to source, train and integrate new employees.

There are risks involved with maintaining our own sales and marketing capabilities, including the following:

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- potential lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines, especially as a result of the receipt of the CRL for vadadustat; and
- costs and expenses associated with maintaining our own sales and marketing organization.

If we are unable to maintain our own sales and marketing capabilities, we will not be successful in commercializing Auryxia, vadadustat, if approved, and any other product candidate that may be approved.

Furthermore, if we are unable to maintain our arrangements with third parties with respect to sales and marketing, if we are unsuccessful in entering into additional arrangements with third parties to sell and market our products or we are unable to do so on terms that are favorable to us, or if such third parties are unable to carry out their obligations under such arrangements, it will be difficult to successfully commercialize our product and product candidates, including vadadustat, if approved. For example, if in connection with the Vifor Second Amended Agreement, we experience difficulties with CSL Vifor, or if CSL Vifor experiences difficulties with other parties to whom it expects to sell vadadustat, if approved, our ability to commercialize vadadustat, if approved, will be severely hindered and our business operations will be materially harmed.

Our, or our partners', failure to obtain or maintain adequate coverage, pricing and reimbursement for Auryxia, vadadustat, if approved, or any other future approved products, could have a material adverse effect on our or our collaboration partners' ability to sell such approved products profitably and otherwise have a material adverse impact on our business.

Market acceptance and sales of any approved products, including Auryxia and, if approved, vadadustat, depends significantly on the availability of adequate coverage and reimbursement from third party payors and may be affected by existing and future healthcare reform measures. Governmental authorities, third party payors, and PBMs decide which drugs they will cover, as well as establish formularies or implement other mechanisms to manage utilization of products and determine reimbursement levels. We cannot be sure that coverage or adequate reimbursement will be available for Auryxia, vadadustat, if approved, or any of our potential future products. Even if we obtain coverage for an approved product, third party payors may not establish adequate reimbursement amounts, which may reduce the demand for our product and prompt us to have to reduce pricing for the product. If reimbursement is not available or is limited, we may not be able to commercialize certain of our products. Coverage and reimbursement by a governmental authority, third-party payor or PBM may depend upon a number of factors, including the determination that use of a product is:

- a covered benefit under the health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient; and
- cost effective.

Obtaining coverage and reimbursement approval for a product from a governmental authority, PBM or a third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. In the United States, there are multiple governmental authorities, PBMs and third-party payors with varying coverage and reimbursement levels for pharmaceutical products, and the timing of commencement of reimbursement by a governmental payor can be dependent on the assignment of codes via the Healthcare Common Procedural Coding System, which codes are assigned on a quarterly basis. Within Medicare, for oral drugs dispensed by pharmacies and also administered in facilities, coverage and reimbursement may vary depending on the setting. CMS, local Medicare

administrative contractors, Medicare Part D plans and/or PBMs operating on behalf of Medicare Part D plans, may have some responsibility for determining the medical necessity of such drugs, and therefore coverage, for different patients. Different reimbursement methodologies may apply, and CMS may have some discretion in interpreting their application in certain settings.

As an oral drug, Auryxia is covered by Medicare under Part D. However, in September 2018, CMS decided that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the CMS Decision. While this decision does not impact CMS coverage for the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, it requires Part D plan sponsors to impose prior authorization or other steps to ensure that Auryxia is reimbursed only for the Hyperphosphatemia Indication. While we believe that the vast majority of the Medicare prescriptions written for Auryxia today are for the Hyperphosphatemia Indication and therefore will continue to be covered by Medicare with prior authorization, the CMS Decision has had and will continue to have an adverse impact on the sales and future growth of Auryxia for the Hyperphosphatemia Indication and the IDA Indication. For example, in the second quarter of 2020, we reduced our short-term and long-term Auryxia revenue forecast, primarily driven by the compounding impact of the CMS Decision. As a result, we recorded an impairment charge of $115.5 million to the Auryxia intangible asset associated with the developed product rights for Auryxia during the three months ended June 30, 2020.

Medicaid reimbursement of drugs varies by state. Private third-party payor reimbursement policies also vary and may or may not be consistent with Medicare reimbursement methodologies. Manufacturers of outpatient prescription drugs may be required to provide discounts or rebates under government healthcare programs or to certain third-party payors in order to obtain coverage of such products.

Additionally, we may be required to enter into contracts with third party payors and/or PBMs offering rebates or discounts on our products in order to obtain favorable formulary status and we may not be able to agree upon commercially reasonable terms with such third party payors or PBMs, or provide data sufficient to obtain favorable coverage and reimbursement for many reasons, including that we may be at a competitive disadvantage relative to companies with more extensive product lines. In addition, third party payors, PBMs and other entities that purchase our products may impose restrictions on our ability to raise prices for our products over time without incurring additional costs. Four distributors, Fresenius Medical Care Rx, McKesson Corporation, Cardinal Health, Inc. and Amerisource Bergen Drug Corporation, in the aggregate, accounted for a significant percentage of our gross revenue during 2022. If we are not able to maintain our arrangements with these key distributors on favorable terms, on a timely basis or at all, or if there is any adverse change in one or more of these distributors' business practices or financial condition, it would adversely impact the market opportunity for Auryxia, our product revenues and operating results.

Furthermore, vadadustat was approved in Japan for the treatment of adult patients with anemia due to CKD and is being marketed by MTPC in Japan under the trade name Vafseo™. Pricing and reimbursement strategy is a key component of MTPC's commercialization plans for Vafseo in Japan. If coverage and reimbursement terms change, MTPC may not be able to, or may decide not to, continue commercialization of Vafseo in Japan.

We currently believe it is likely that vadadustat, if approved, will be reimbursed using the Transitional Drug Add-on Payment Adjustment, or TDAPA, followed by inclusion in the bundled reimbursement model for Medicare beneficiaries. For those that obtain dialysis through commercial insurance during the 30-month coordination period or through Medicaid prior to Medicare becoming primary payer after 90 days, patients may access vadadustat through contracts we negotiate with third party payors for reimbursement of vadadustat, which would be subject to the risks and uncertainties described above. Additionally, applying for and obtaining reimbursement under the TDAPA is expected to take at least six months following approval, which will affect adoption, uptake and product revenue for vadadustat during that time, and if there are updates to the TDAPA rule that decrease the basis for reimbursement or eligibility criteria during the transition period or if the TDAPA is eliminated, then our profitability may be adversely affected. For example, the Medicare Payment Advisory Commission, or MedPAC, an independent legislative branch advisory body to Congress on issues related to the Medicare program, has recommended that TDAPA not be provided to newly approved drug products considered to fall within "functional categories" for which costs are already accounted for in the bundled reimbursement model, such as for anemia management drugs.

Further, if vadadustat is approved in the United States and included in the fixed reimbursement model for a bundle of dialysis services, or the bundle, we would be required to enter into contracts to supply vadadustat to specific dialysis providers, instead of through distributors, which we believe could be challenging. The dialysis market is unique and is dominated by two providers: DaVita and Fresenius, which account for a vast majority of the dialysis population in the United States. Under the Vifor Second Amended Agreement, we granted CSL Vifor an exclusive license to sell vadadustat to Fresenius Medical Care North America and its affiliates, including Fresenius Kidney Care Group LLC, to certain third-party dialysis organizations approved by us, to independent dialysis organizations that are members of group purchase organizations, and to certain non-retail specialty pharmacies in the United States. We refer to Fresenius Medical Care North America and its affiliates, these organizations and specialty pharmacies collectively as the "Supply Group". See Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for additional information

regarding the Vifor Second Amended Agreement. If vadadustat is approved and we are not able to maintain the Vifor Second Amended Agreement or enter into a supply agreement with DaVita or other dialysis clinics, our business may be materially harmed.

Similar to how payor coverage may affect the sales of a product, formulary status within dialysis organizations may affect what products are prescribed within that specific organization. Therefore, if a product is not on a formulary, the prescribers within that organization may be less likely to prescribe that product or may have a difficult time prescribing that product, resulting in less sales. Further, one dialysis organization's determination to add a product to their formulary does not assure that other dialysis organizations will also add the product to theirs. There is always a risk a dialysis organization will not contract with a drug manufacturer for a specific product, resulting in that product not being on that organization's formulary. If any dialysis organization does not add vadadustat, if approved, to the formulary, our business may be materially harmed.

In addition, we may be unable to sell Auryxia or vadadustat, if approved, to dialysis providers on a profitable basis if CMS significantly reduces the level of reimbursement for dialysis services and providers choose to use alternative therapies or look to re-negotiate their contracts with us. Our profitability may also be affected if our costs of production increase faster than increases in reimbursement levels. Adequate coverage and reimbursement of our products by government and private insurance plans are central to patient and provider acceptance of any products for which we receive marketing approval.

Further, in many countries outside the United States, a drug must be approved for reimbursement before it can be marketed or sold in that country. In some cases, the prices that we intend to charge for our products are also subject to approval. Approval by the EMA or another regulatory authority does not ensure approval by reimbursement authorities in that jurisdiction, and approval by one reimbursement authority outside the United States does not ensure approval by any other reimbursement authorities. However, the failure to obtain reimbursement in one jurisdiction may negatively impact our ability to obtain reimbursement in another jurisdiction. We may not be able to obtain such reimbursement approvals on a timely basis, if at all, and favorable pricing in certain countries depends on a number of factors, some of which are outside of our control. In addition, if vadadustat is approved outside of the United States, we plan to rely on a partner to obtain approval by reimbursement authorities outside the United States. If we are unsuccessful or delayed in entering into an agreement with a new partner, the launch of vadadustat following approval outside the United States may be delayed, which could have an adverse effect on our results of operations.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.

The development and commercialization of new drugs is highly competitive and subject to rapid and significant technological change. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the development and commercialization of Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired. Our objective is to continue to commercialize Auryxia and develop and commercialize new products with clinically proven efficacy, convenience, tolerability and/or safety. In many cases, any approved products that we commercialize will compete with existing, market-leading products.

Auryxia is competing in the hyperphosphatemia market in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Sanofi, PhosLo® and Phoslyra® (calcium acetate), marketed by Fresenius Medical Care North America, Fosrenol® (lanthanum carbonate), marketed by Shire Pharmaceuticals Group plc, and Velphoro® (sucroferric oxyhydroxide), marketed by Fresenius Medical Care North America, as well as over-the-counter calcium carbonate products such as TUMS® and metal-based options such as aluminum, lanthanum and magnesium. Most of the phosphate binders listed above are now also available in generic forms. In addition, other agents are in development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Unicycive's Renazorb (lanthanum dioxycarbonate) or could otherwise enter the market, including Ardelyx, Inc.'s tenapanor (which is approved in the United States for the treatment of adults with irritable bowel syndrome with constipation, and for which the FDA granted an appeal in the fourth quarter of 2022 that will allow Ardelyx to resubmit a new drug application in 2023 with respect to the control of serum phosphorus in adult patients with CKD on dialysis), that may impact the market for Auryxia.

Auryxia is competing in the IDA market in the United States with over-the-counter oral iron, ferrous sulfate, other prescription oral iron formulations, including ferrous gluconate, ferrous fumerate, and polysaccharide iron complex, and intravenous iron formulations, including Feraheme® (ferumoxytol injection), Venofer® (iron sucrose injection), Ferrlicit® (sodium ferric gluconate complex in sucrose injection), Injectafer® (ferric carboxymaltose injection), and Triferic® (ferric pyrophosphate citrate). In addition, other new therapies for the treatment of IDA may impact the market for Auryxia, such as Shield Therapeutics plc's Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA and Accrufer® (ferric maltol), which was launched in the United States for the treatment of IDA in July 2021.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective, safer or offer greater patient convenience than Auryxia. Other companies have

product candidates in various stages of preclinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia. In addition, we and Keryx's licensors, Panion & BF Biotech, Inc., or Panion, and, as applicable, Dr. Hsu, entered into settlement agreements with each of the third parties who submitted Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA, pursuant to which we granted licenses to market a generic version of Auryxia in the United States beginning in March 2025 (subject to FDA approval), or earlier under certain circumstances customary for settlement agreements of this nature, which may impact our business and results of operation.

Drugs that may compete with vadadustat include Epogen® (epoetin alfa) and Aranesp® (darbepoetin alfa), both commercialized by Amgen, Procrit® (epoetin alfa) and Eprex® (epoetin alfa), commercialized by Johnson & Johnson in the United States and Europe, respectively, and Mircera® (methoxy PEG-epoetin beta), commercialized by CSL Vifor in the United States and Roche Holding Ltd. outside of the United States.

We and our partners may also face competition from potential new anemia therapies. There are several other hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor product candidates in various stages of development for anemia indications that may be in direct competition with vadadustat if and when they are approved and launched commercially. These candidates are being developed by companies such as FibroGen Inc., or FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, Japan Tobacco International, or JT, GlaxoSmithKline plc, or GSK, and Bayer HealthCare AG, or Bayer.

Furthermore, certain companies are developing potential new therapies for renal-related diseases that could potentially reduce injectable erythropoiesis stimulating agent, or ESA, utilization and thus limit the market potential for vadadustat if they are approved and launched commercially. Other new therapies are in development for the treatment of conditions inclusive of renal anemia that may impact the market for anemia-targeted treatment.

In addition, in the United States, FibroGen filed an NDA for its product candidate, roxadustat, with the FDA, but the FDA issued a complete response letter indicating the FDA will not approve the NDA in its present form and requested that an additional clinical trial for roxadustat be conducted prior to resubmission of the NDA or additional response to the FDA's complete response letter. In Europe however, roxadustat is approved for the treatment of anemia in patients with CKD. Further, in February 2023 the FDA approved daprodustat, an oral HIF-PH inhibitor marketed as Jesduvroq by GSK, as a once-a-day treatment of anemia due to CKD in adult patients who have been receiving dialysis for at least four months. If we obtain approval for vadadustat in the U.S., and roxadustat is also approved by the FDA, then both daprodustat and roxadustat will compete with vadadustat.

In Japan, Vafseo, which is approved for both the DD and NDD indications, competes with roxadustat, daprodustat and enarodustat. Roxadustat is approved for the treatment of anemia due to CKD in patients on dialysis, or DD-CKD, and patients not on dialysis, or NDD-CKD. In addition, daprodustat, GSK's product, and enarodustat, JT's product candidate, are approved in Japan for the treatment of anemia due to CKD. In addition. Bayer HealthCare AG has submitted an NDA for its product candidate for the treatment of renal anemia in Japan. In China, roxadustat has launched for the treatment of anemia of DD-CKD and for the treatment of anemia due to CKD in NDD-CKD patients.

A biosimilar is a biologic product that is approved based on demonstrating that it is highly similar to an existing, FDA-approved branded biologic product. The patents for the existing, branded biologic product must expire in a given market before biosimilars may enter that market without risk of being sued for patent infringement. In addition, an application for a biosimilar product cannot be approved by the FDA until 12 years after the existing, branded product was approved under a Biologics License Application, or BLA. The patents for epoetin alfa, an injectable ESA, expired in 2004 in the EU, and the remaining patents expired between 2012 and 2016 in the United States. Because injectable ESAs are biologic products, the introduction of biosimilars into the injectable ESA market in the United States will constitute additional competition for vadadustat if we are able to obtain approval for and commercially launch vadadustat. In the United States, Pfizer's biosimilar version of injectable ESAs, Retacrit® (epoetin alfa-epbx), was approved by the FDA in May 2018 and launched in November 2018 and several biosimilar versions of injectable ESAs are available for sale in the EU.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products. Large and established companies such as Amgen, Roche and GSK, among others, compete in the market for drug products to treat kidney disease. In particular, these companies have greater experience and expertise in conducting preclinical testing and clinical trials, obtaining marketing approvals, manufacturing such products on a broad scale and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we are developing obsolete.

Smaller and other early-stage companies may also prove to be significant competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or marketing approval, or discovering, developing and commercializing competitive products, before, or more effectively than, we do. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

The commercialization of Riona™ and Vafseo™ in Japan and our current and potential future efforts with respect to the development and commercialization of our products and product candidates outside of the United States subject us to a variety of risks associated with international operations, which could materially adversely affect our business.

Our Japanese sublicensee, JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona, the trade name for ferric citrate hydrate in Japan, as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and for the treatment of adult patients with IDA in Japan. In Japan and certain other countries in Asia, we granted MTPC exclusive rights to commercialize vadadustat, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo™. We also granted Averoa SAS, or Averoa, an exclusive license to develop and commercialize ferric citrate in the EEA, Turkey, Switzerland and the United Kingdom.

Pursuant to the terms of the Termination Agreement with Otsuka, Otsuka has transferred to us the marketing authorization application, or MAA, for vadadustat with the EMA, and in the United Kingdom, Switzerland and Australia. In addition, we have conducted and in the future plan to conduct clinical trials outside of the United States for Auryxia, vadadustat and any other product or product candidate that may be in-licensed or acquired. As a result of these and other activities, we are or may become subject to additional risks in developing and commercializing Auryxia and vadadustat outside the United States, including, among others:

- political, regulatory, compliance and economic developments, weakness or instability that could restrict our ability to manufacture, market and sell our products;
- changes in international medical reimbursement policies and programs;
- changes in healthcare policies of foreign jurisdictions;
- trade protection measures, including import or export licensing requirements and tariffs and our compliance therewith;
- our ability to develop or manage relationships with qualified local distributors and trading companies;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;
- compliance with laws, including the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation, the EU General Data Protection Regulation, or GDPR, and similar data protection laws, and tax, employment, immigration and labor laws;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad, including as a result of the COVID-19 pandemic; and
- business interruptions resulting from geopolitical actions, including war and terrorism, global pandemics, or natural disasters including earthquakes, typhoons, floods and fires.

In addition, we receive revenues from royalty payments converted to U.S. dollars based on net sales of Riona and Vafseo™ in Japanese yen. The exchange rates between the Japanese yen on the one hand, and the U.S. dollar, on the other hand, have changed substantially in recent years and may fluctuate substantially in the future. Our results of operations could be adversely affected over time by certain movements in exchange rates, particularly if the Japanese yen depreciates against the U.S. dollar.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations. As and if we continue to expand our commercialization efforts, we may encounter new risks.

Risks Related to Product Development

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and, if approved, commercialization of vadadustat and any other product candidates.

The risk of failure in drug development is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and conduct extensive clinical trials to demonstrate the safety

and efficacy of our product candidates in humans. Preclinical studies and clinical trials are expensive, difficult to design and implement, can take several years to complete, and their outcomes are inherently uncertain. Failure can occur at any time during the process. For example, we are currently conducting a clinical trial to evaluate three times per week oral dosing of vadadustat for dialysis dependent patients with anemia due to chronic kidney disease, or CKD. If we experience delays in the conduct of this clinical trial or the results are not positive, it could affect the market potential of vadadustat, if approved.

We may be unable to successfully complete clinical trials of Auryxia, vadadustat and other product candidates or to successfully obtain approval of vadadustat or other product candidates, if the results of those trials and studies are not positive or are only modestly positive, or if there are concerns with the profile due to efficacy or safety. Further, the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, interim results of a clinical trial do not necessarily predict final results, and results of Phase 3 clinical trials for one indication may not be predictive of results of Phase 3 clinical trials for another indication. For example, we announced positive top-line results from $INNO_2VATE$ and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO_2TECT studies, but the PRO_2TECT program did not meet the primary major adverse cardiovascular event, or MACE, safety endpoint. Many companies in the biopharmaceutical industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their product candidates. In addition, in March 2022, we received the CRL for vadadustat indicating that the FDA had determined that it could not approve the NDA in its present form, thus delaying any potential approval of vadadustat. In October 2022, we submitted the FDRR to the FDA and in February 2023, we received a second interim response from the FDA to our FDRR. However, it is impossible to predict when or if vadadustat or any of our other product candidates will prove effective or safe in humans or will receive marketing approval or on what terms. In February 2023, the Committee for Medicinal Products for Human Use, or CHMP, of the EMA adopted a positive opinion recommending the European Commission, or EC, to approve Vafseo™ (vadadustat), an oral HIF-PH inhibitor for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. However, before we can market and sell vadadustat in Europe, the EC must approve vadadustat, and there can be no assurances that we will receive such approval in a timely manner, or at all.

We may experience numerous unforeseen events during, or as a result of, preclinical development or clinical trials that could delay, prevent or make more challenging our ability to receive or maintain marketing approval or commercialize our product candidates. We may be required to complete additional clinical trials for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, in order to obtain or maintain required regulatory approvals. Our preclinical studies and clinical trials may take longer to complete than currently anticipated, or may be delayed, suspended, required to be repeated, prematurely terminated or may not successfully demonstrate safety and/or efficacy needed to obtain or maintain regulatory approval for a variety of other reasons, such as:

- the costs may be greater than we anticipate;
- the number of patients required for clinical trials may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third party contractors, such as our CROs, may fail to comply with regulatory requirements, perform effectively, or meet their contractual obligations to us in a timely manner, or at all, or we may fail to communicate effectively or provide the appropriate level of oversight of such third party contractors;
- the supply or quality of our starting materials, drug substance and drug product necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- regulators, independent data monitoring committees, or IDMCs, institutional review boards, or IRBs, safety committees, or ethics committees, may require that we suspend or terminate our clinical trials for various reasons, including noncompliance with regulatory requirements, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using our product candidate, or a finding that the participants are being exposed to unacceptable health risks;
- clinical trials of our product candidates may produce negative or inconclusive results or results that may be interpreted in a manner different than we interpret them, and we may decide, or regulators may require us, to conduct additional clinical trials, repeat a clinical trial or abandon product development programs;
- lack of adequate funding to continue a clinical trial, including unforeseen costs due to enrollment delays, requirements to conduct additional clinical trials or repeat a clinical trial and increased expenses associated with the services of our CROs and other third parties;
- we may fail to initiate, delay of or failure to complete a clinical trial as a result of an Investigational New Drug application, or IND, being placed on clinical hold by the FDA, the EMA, the PMDA, or other regulatory authorities, or for other reasons, such as failure to recruit or enroll suitable patients or patients' failure to return for post-treatment follow up;
- we may determine to change or expand a clinical trial, including after it has begun;

- clinical trial sites and investigators deviating from the clinical protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial, or failure by us or our CROs to communicate effectively or provide the appropriate level of oversight of such clinical sites and investigators;
- there may be an inability, delay, or failure in identifying and maintaining a sufficient number of clinical trial sites, many of which may already be engaged in other clinical programs;
- there may be a delay or failure in reaching agreement with the FDA, the EMA, the PMDA or other regulatory authorities on a clinical trial design upon which we are able to execute;
- there may be a delay or failure in obtaining authorization to commence a clinical trial or inability to comply with conditions imposed by a regulatory authority regarding the scope or design of a clinical trial;
- there may be delays in reaching, or failure to reach, agreement on acceptable terms with prospective clinical trial sites and prospective CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- the FDA, the EMA, the PMDA or other regulatory authorities may require us to submit additional data or impose further requirements before permitting us to initiate a clinical trial or during an ongoing clinical trial;
- the FDA, the EMA, the PMDA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;
- third parties with which we work may fail to comply with good practice quality guidelines and regulations, or GXP, including good laboratory practice, good clinical practice, or GCP, and current good manufacturing practice, or cGMP; or
- there may be changes in governmental regulations or administrative actions.

If any of the foregoing occurs, the following may occur:

- regulators may require that we conduct additional clinical trials, repeat clinical trials or conduct other studies beyond those that we currently contemplate;
- we may be delayed in obtaining marketing approval for vadadustat or other product candidates;
- we may not obtain marketing approval for vadadustat or other product candidates at all;
- we may obtain approval for indications or patient populations that are not as broad as intended or desired;
- we may obtain approval with labeling that includes significant use or distribution restrictions or safety warnings that would reduce the potential market for any approved product or inhibit our ability to successfully commercialize any approved product;
- a REMS or FDA-imposed risk management plan that use risk minimization strategies to ensure that the benefits of certain prescription drugs outweigh their risks, may be required;
- we may be subject to additional post-marketing restrictions and/or requirements; or
- the product may be removed from the market after obtaining marketing approval.

Our product development costs may also increase if we experience development delays or delays in receiving the requisite marketing approvals. Our preclinical studies or clinical trials may need to be restructured or may not be completed on schedule, or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize vadadustat, if approved, or any other product candidate, including those that may be in-licensed or acquired, or allow our competitors to bring products to market before we do. This could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

Identifying and qualifying patients to participate in clinical trials is critical to our success. The timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our clinical trials. Patients may be unwilling to participate in our clinical trials because of concerns about investigational research studies, the time and commitment needed to participate in a study, adverse events observed with the product candidate under study, the current standard of care, competitor products and/or other investigational agents, in each case for the same indications and/or similar patient populations. In addition, in the case of clinical trials of any product candidate, patients currently receiving treatment with the current standard of care or a competitor product may be reluctant to participate in a clinical trial with an investigational drug. Additionally, it is often more difficult to enroll special or particular subpopulations of patients, such as pediatric or elderly patients, due to a number of factors including parental or other caregiver considerations, concerns and burdens. For example, we enrolled sites in a post-approval pediatric study for the Hypophosphatemia Indication of Auryxia in the second quarter of 2022, which began patient recruitment in the third quarter of 2022, but study sites have not yet enrolled any eligible pediatric patients despite efforts to do so. Furthermore, the COVID-19 pandemic resulted in temporary closures of, and may continue to impact, clinical

trial sites on which we rely for the conduct of clinical trials and COVID-19 pandemic precautions and staffing shortages have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials.

Finally, competition for clinical study sites may limit our access to patients appropriate for our clinical trials. As a result, the timeline for recruiting patients and conducting studies may be delayed. These delays could result in increased costs, delays in advancing our development of any product or product candidate, or termination of the clinical trial altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment is affected by many factors, including:

- severity of the disease under investigation;
- design of the study protocol;
- size and nature of the patient population;
- eligibility criteria for, and design of, the study in question, including study complexity;
- perceived risks and benefits of the product or product candidate under study, including as a result of adverse effects observed in similar or competing therapies;
- proximity and availability of clinical study sites for prospective patients;
- availability of competing therapies and clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product or product candidate being studied in relation to available therapies or other product candidates in development;
- efforts to facilitate timely enrollment in clinical trials;
- participation length and demands on patients and caregivers;
- site staffing shortages and turnover;
- clinical trial sites and investigators failing to perform effectively; and
- patient referral practices of physicians.

We may not be able to initiate or complete clinical trials in a timely manner, or at all, if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which may delay approval, or result in failure to maintain or obtain approval, of our products or product candidates, which would have a material adverse effect on our business.

Conducting clinical trials outside of the United States, as we have done historically and as we may decide to do in the future, presents additional risks and complexities and, if we decide to conduct a clinical trial outside of the United States in the future, we may not complete such trials successfully, in a timely manner, or at all, which could affect our ability to obtain regulatory approvals.

Our ability to successfully initiate, enroll and complete a clinical study in any country outside of the United States is subject to numerous additional risks unique to conducting business in jurisdictions outside the United States, including:

- difficulty in establishing or managing relationships with qualified CROs, physicians and clinical trial sites;
- difficulty in complying with different local standards for the conduct of clinical trials;
- difficulty in complying with various and complex import laws and regulations when shipping drug to certain countries; and
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments.

Data obtained from studies conducted in the United States may not be accepted by the EMA, the PMDA and other regulatory authorities outside of the United States. Also, certain jurisdictions require data from studies conducted in their country in order to obtain approval in that country. Further, when a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, the studies must be conducted in accordance with GCP, including undergoing review and receiving approval by an independent ethics committee, and seeking and receiving informed consent from subjects. Thus, to the extent that we rely on data from foreign clinical studies that are not the subject of an IND but are used to support of an NDA, there is a risk that FDA may not review such data in connection with its review of the NDA.

If we or our collaboration partners have difficulty conducting future clinical trials in jurisdictions outside the United States as planned, we may need to delay, limit or terminate such clinical trials, any of which could have an adverse effect on our business.

Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that may delay or prevent marketing approval or limit their commercial potential.

Undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, or competing commercial products or product candidates in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials, could result in a more restrictive label or the delay, denial or withdrawal of marketing approval by the FDA or other regulatory authorities, and could lead to potential product liability claims. In addition, results of our clinical trials could reveal a high frequency of undesirable effects or unexpected characteristics. For example, in March 2022, we received the CRL from the FDA for our NDA for vadadustat in which the FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. The FDA expressed safety concerns noting failure to meet non-inferiority in MACE in the non-dialysis patient population, the increased risk of thromboembolic events, driven by vascular access thrombosis in dialysis patients, and the risk of drug-induced liver injury. In October 2022, we submitted the FDRR to the FDA. The FDRR focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, and there can be no assurances that we will be successful in our appeal. If we are unable to overcome these concerns, vadadustat may not be approved by the FDA on favorable terms, or at all, and our financial condition could be materially harmed. In February 2023, the CHMP of the EMA adopted a positive opinion recommending the EC to approve Vafseo™ for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. However, before we can market and sell vadadustat in Europe, the EC must approve vadadustat, and there can be no assurances that we will receive such approval in a timely manner, or at all.

If we or others identify undesirable effects caused by, or other undesirable properties of, Auryxia, vadadustat, or any other product or product candidate, including those that may be in-licensed or acquired, or if known undesirable effects are more frequent or severe than in the past, or if any of the foregoing are perceived to have occurred, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our product candidates may not be approved by regulatory authorities;
- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- regulatory authorities may require warnings on the label, such as the warning on Auryxia's label regarding iron overload;
- REMS or FDA-imposed risk management plans that use restrictive risk minimization strategies may be required;
- we may decide to, or be required to, send drug warnings or safety alerts to physicians, pharmacists and hospitals (or the FDA or other regulatory authorities may choose to issue such alerts), or we may decide to conduct a product recall or be requested to do so by the FDA or other regulatory authority;
- reformulation of the product, additional non-clinical or clinical trials, restrictive changes in labeling or changes to or re-approvals of manufacturing facilities may be required;
- we may be precluded from pursuing additional development opportunities to enhance the clinical profile of a product within its indicated populations, or studying the product or product candidate in additional indications and populations or in new formulations; and
- we could be investigated by the government or sued and held liable for harm caused to patients, including in class action lawsuits; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining, whether on a restricted basis or at all, marketing approval and, ultimately, market acceptance or penetration of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired. In addition, any of these events could substantially increase our costs, and could significantly impact our ability to successfully commercialize Auryxia, vadadustat or any other product and product candidate, including those that may be in-licensed or acquired, and generate product revenue.

The patient populations treated with Auryxia and potential patient populations for vadadustat, if approved, have CKD, a serious disease that increases the risk of cardiovascular disease including heart attacks and stroke and, in its most severe form, results in, kidney failure and the need for dialysis or kidney transplant. Many patients with CKD are elderly with comorbidities making them susceptible to significant health risks. Therefore, the likelihood of these patients having adverse events, including serious adverse events is high.

With respect to the global INNO$_2$VATE Phase 3 program, the incidence of treatment emergent adverse events during the *Correction and Conversion* study in vadadustat treated patients was 83.8% and 85.5% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were hypertension (16.2%/ 12.9%) and diarrhea (10.1%/ 9.7%). Serious treatment emergent adverse events were lower in vadadustat treated patients at 49.7% compared to 56.5% for darbepoetin alfa treated patients. The incidence of treatment emergent adverse events during the prevalent dialysis patient study (*Conversion*) in the vadadustat treated patients was 88.3%, and 89.3% in darbepoetin alfa treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa treated patients were diarrhea (13.0%/ 10.1%), pneumonia (11.0%/ 9.7%), hypertension (10.6%/ 13.8%), and hyperkalemia (9.0%/ 10.8%). Serious treatment emergent adverse events were slightly lower for vadadustat treated patients at 55.0% and 58.3% for darbepoetin alfa-treated patients. Patients with DD-CKD experienced an increased risk of thromboembolic events compared to darbepoetin alfa with a time to first event HR of 1.20 (95% CI 0.96 - 1.50) driven by thrombosis of vascular access.

With respect to the global PRO$_2$TECT Phase 3 program, the incidence of treatment emergent adverse events during the ESA untreated patients study (*Correction*) in the vadadustat-treated patients was 90.9%, and 91.6% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (34.7%/ 35.2%), hypertension (17.7%/ 22.1.%), hyperkalemia (12.3.%/ 15.6%), urinary tract infection (12.9%/ 12.0%), diarrhea (13.9%/ 10.0%), peripheral oedema (12.5%/ 10.5%), fall (9.6%/ 10%) and nausea (10%/ 8.2%). Serious treatment emergent adverse events were 65.3% for vadadustat-treated patients and 64.5% for darbepoetin alfa-treated patients. The incidence of treatment emergent adverse events during the ESA-treated patients study (*Conversion*) in vadadustat treated patients was 89.1% and 87.7% in darbepoetin alfa-treated patients. During the study, the most common treatment emergent adverse events reported in vadadustat/darbepoetin alfa-treated patients were end-stage renal disease (27.5%/ 28.4%), hypertension (14.4%/ 14.8%), urinary tract infection (12.2%/ 14.5%), diarrhea (13.8.%/ 8.8.%), peripheral oedema (9.9%/ 10.1%) and pneumonia (10.0%/ 9.7%). Serious treatment emergent adverse events were 58.5% for vadadustat-treated patients and 56.6% for darbepoetin alfa-treated patients.

For example, during the conduct of our Phase 3 program our team and hepatic experts analyzed hepatic cases (unblinded to treatment) and, following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program, which included eight completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and two then-ongoing Phase 3b studies in DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). This review consisted of a blinded re-assessment of hepatic events conducted by a separate panel of hepatic experts. While hepatocellular injury attributed to vadadustat was reported in less than 1% of patients, there was one case of severe hepatocellular injury with jaundice, and we cannot guarantee that similar events will not happen in the future. Additionally, the FDA expressed safety concerns related to the risk of drug-induced liver injury in the CRL that it issued in March 2022.

Serious adverse events considered related to vadadustat, including those noted in the CRL, and any other product candidates could have material adverse consequences on the development and potential approval of vadadustat or our other product candidates and our business as a whole. Our understanding of adverse events in prior clinical trials of our product candidates may change as we gather more information, the FDA may not agree with our assessment of adverse events and additional unexpected adverse events may be observed in future clinical trials or in the market.

Any of the above safety data or other occurrences could delay or prevent us from achieving or maintaining marketing approval, harm or prevent sales of Auryxia or, if approved, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, increase our expenses and impair or prevent our ability to successfully commercialize Auryxia, vadadustat or any other products or product candidates.

In addition, any post-marketing clinical trials conducted, if successful, may expand the patient populations treated with Auryxia, vadadustat or any other product we acquire or for which we receive marketing approval, within or outside of their current indications or patient populations, which could result in the identification of previously unknown undesirable effects, increased frequency or severity of known undesirable effects, or result in the identification of unexpected safety signals. In addition, as vadadustat, if approved, and any other products are commercialized, they will be used in significantly larger patient populations, in less rigorously controlled environments and, in some cases, by less experienced and less expert treating practitioners, than in clinical trials, which could result in increased or more serious adverse effects being reported. As a result, regulatory authorities, healthcare practitioners, third party payors or patients may perceive or conclude that the use of Auryxia,

vadadustat, if approved, or any other products are associated with serious adverse effects, undermining our commercialization efforts.

Risks Related to Regulatory Approval

We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat or any other product candidate, or we may experience significant delays in doing so, any of which would materially harm our business.

Clinical trials, manufacturing and marketing of any product or product candidate are subject to extensive and rigorous review and regulation by numerous governmental authorities in the United States and other jurisdictions. Before obtaining marketing approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing and clinical trials that the product candidate is safe and effective for use in each target indication. This process can take many years and marketing approval may never be achieved. Of the large number of drugs in development in the United States and in other jurisdictions, only a small percentage successfully complete the FDA's and other jurisdictions' marketing approval processes and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development and commercialization efforts, we may be unable to successfully obtain regulatory approval for or commercialize vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

We are not permitted to market vadadustat in the United States until we receive approval from the FDA, in the EU until we receive approval from the EMA, or in any other jurisdiction until the requisite approval from regulatory authorities in such jurisdiction is received. As a condition to receiving marketing approval for vadadustat, we may be required by the FDA, the EMA or other regulatory authorities to conduct additional preclinical studies or clinical trials.

In March 2022, we received the CRL from the FDA regarding our NDA for vadadustat for the treatment of anemia due to CKD. The FDA concluded that the data in the NDA do not support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. In October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, to the FDA. The FDRR focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, and there can be no assurances that we will be successful in our appeal and obtain approval for vadadustat in a timely manner, on favorable terms, or at all. As a result, the regulatory approval process for vadadustat in the U.S. is highly uncertain. We may not obtain approval at all, and if we are able to obtain approval, it may only be for patients with DD-CKD and, in any event, the expense and time to do so could adversely impact our ability to successfully commercialize vadadustat, and our financial condition could be materially harmed.

Further, vadadustat and any other product candidate may not receive marketing approval in the United States or the EU even if it is approved in other countries. For example, although vadadustat is approved in Japan for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients, such approval does not guarantee approval in the United States by the FDA or in the EU by the EMA for these indications or at all. In addition, while each regulatory authority makes their own assessment as to the safety and efficacy of a drug, FDA's concern about the safety or efficacy of vadadustat or any other product candidate could impact the regulatory authority's decision in another country.

Obtaining marketing approval in the United States and other jurisdictions for any product candidate depends upon numerous factors, many of which are subject to the substantial discretion of the regulatory authorities, including that regulatory agencies may not complete their review processes in a timely manner and, following completion of the review process, may not grant marketing approval or such marketing approval may be limited. Furthermore, approval of a drug does not ensure successful commercialization. For example, on September 23, 2015, the European Commission, or EC, approved Fexeric for the control of hyperphosphatemia in adult patients with CKD. Pursuant to the sunset clause under EU law, the EC's approval of Fexeric in the EU was contingent on, among other things, our commencing marketing of Fexeric within three years; although we successfully negotiated an extension to December 23, 2019, we did not commence marketing Fexeric by such date and therefore the Fexeric approval in the EU has ceased to be valid.

We could face heightened risks with respect to seeking marketing approval in the United Kingdom, or UK, as a result of the recent withdrawal of the UK from the EU, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK withdrew from the EU, effective December 31, 2020. On December 24, 2020, the UK and the EU entered into a Trade and Cooperation Agreement. The agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement would prevent us from commercializing vadadustat or any other product candidate, including those that may be in-licensed or acquired, in the UK and/or the EU and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to

seek regulatory approval in the UK and/or the EU for vadadustat or any other product candidate, which could significantly and materially harm our business. As of January 1, 2021, the Medicines and Healthcare Products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended) as the basis for regulating medicines.

In addition, the safety concerns associated with the current standard of care for the indications for which we are seeking marketing approval for vadadustat may affect the FDA's, the EMA's or other regulatory authorities' review of the safety results of vadadustat. Additionally, these regulatory authorities may not agree with our assessment of adverse events. Further, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. It is possible that vadadustat will never obtain marketing approval in the United States or certain other jurisdictions or for some or all of the indications for which we seek approval. The FDA, the EMA or other regulatory authorities may delay, limit or deny approval of vadadustat for many reasons including, among others:

- we may not be able to demonstrate that vadadustat is safe and effective in treating adult patients with anemia due to CKD to the satisfaction of the relevant regulatory authority;
- the results of our clinical trials may only be modestly positive, or there may be concerns with the profile due to efficacy or safety;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the relevant regulatory authority for review and/or marketing approval;
- the relevant regulatory authority may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the relevant regulatory authority may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the relevant regulatory authority may not approve the formulation, labeling or specifications we request for vadadustat;
- the relevant regulatory authority may approve vadadustat or any other product candidate for use only in a small patient population or for fewer or more limited indications than we request;
- the relevant regulatory authority may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA or other relevant regulatory authority may require development of a REMS as a condition of approval or post-approval;
- the relevant regulatory authority may grant approval contingent on the performance of costly post-marketing clinical trials;
- the relevant regulatory authority's onsite inspections may be delayed due to the COVID-19 pandemic or otherwise;
- we, or our CROs or other vendors, may fail to comply with GXP or fail to pass any regulatory inspections or audits;
- we or our third party manufacturers may fail to perform in accordance with the FDA's or other relevant regulatory authority's cGMP requirements and guidance;
- the FDA may disagree with inclusion of data obtained from certain regions outside the United States to support the NDA for potential reasons such as differences in clinical practice from United States standards;
- the relevant regulatory authority could deem that our financial relationships with certain principal investigators constitute a conflict of interest, such that the data from those principal investigators may not be used to support our applications;
- as part of any future regulatory process, the FDA may ask an Advisory Committee to review portions of the NDA, the FDA may have difficulty scheduling an Advisory Committee meeting in a timely manner or, if convened, an FDA Advisory Committee could recommend non-approval, conditions of approval or restrictions on approval, and the FDA may ultimately agree with the recommendations;
- the relevant regulatory authority's review process and decision-making regarding vadadustat and any other product candidate may be impacted by the results of our and our competitors' clinical trials and safety concerns of marketed products used to treat the same indications as the indications for which vadadustat and any other product candidate are being developed;
- the relevant regulatory authority may not approve the manufacturing processes or facilities of third party manufacturers with whom we contract; or
- the policies or regulations of the relevant regulatory authority may significantly change in a manner that renders our clinical data insufficient for approval or requires us to amend or submit new clinical protocols.

If we experience further delays in obtaining approval, or if we fail to obtain approval of vadadustat for some or all of the indications for which we have sought approval, the commercial prospects for vadadustat may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business. For example, the FDRR we submitted to the FDA in October 2022 focuses on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult patients on dialysis.

Products approved for marketing are subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and we may be subject to penalties, including withdrawal of marketing approval, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, or product candidates, when and if any of them is approved.

Marketing approvals may be subject to limitations on the approved indicated uses for which the product may be marketed or other conditions of approval, or contain requirements or commitments for potentially costly post-marketing studies and surveillance to monitor the safety and efficacy of the product, including REMS, or registries or observational studies. For example, in connection with the FDA approvals of Auryxia, we initially committed to the FDA to conduct certain post-approval pediatric studies of Auryxia under the Pediatric Research Equity Act of 2003, or PREA. With regard to the Hyperphosphatemia Indication for Auryxia, we committed to completing the post-approval pediatric study and submitting a final report to the FDA by December 31, 2019. However, we did not complete the study and therefore did not submit the post-marketing requirement pediatric clinical study report by December 31, 2019. Consequently, we received a notification of noncompliance with PREA. Our request to extend this deadline was denied, and the study is considered delayed although we have initiated sites in the study and are recruiting for one patient cohort. Recruitment of the other patients is pending receipt of further data regarding the manufacturing of the smaller size tablets and the FDA's concurrence before proceeding with the use of such formulation. With regard to our IDA Indication, we initially committed to completing the post-approval pediatric study and submitting a final report to the FDA by January 2023. We did not meet a milestone relating to this post-approval pediatric study of Auryxia in a timely manner and received a notification from the FDA. Subsequently, the FDA agreed to extend the pediatric clinical study timelines for the IDA Indication. We subsequently communicated to the FDA that we would be delaying the start of the clinical trial in the IDA Indication while we work to produce smaller size tablets. In response, the FDA issued a partial clinical hold until we manufacture the smaller tablets and provide the FDA with relevant information regarding the smaller sized tablets for review. The FDA lifted the partial clinical hold in June 2022, however, we have not commenced start up of this study pending resolution of the manufacturing of the smaller size tablets. If we are unable to complete these studies successfully, or have further delays in completing these studies, we will need to inform the FDA, have further discussions and, if the FDA finds that we failed to comply with pediatric study requirements, in violation of applicable law, it could institute enforcement proceedings to seize or enjoin the sale of Auryxia or seek civil penalties, which would have a material adverse impact on our ability to commercialize Auryxia and our ability to generate revenues from Auryxia.

In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for Auryxia, vadadustat, if approved, and any other product for which we receive regulatory approval will be subject to extensive and ongoing regulatory requirements and guidance. These requirements and guidance include manufacturing processes and procedures (including record keeping), the implementation and operation of quality systems to control and assure the quality of the product, submissions of safety and other post-marketing information and reports, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. If we, our CMOs or other third parties we engage fail to adhere to such regulatory requirements and guidance, we could suffer significant consequences, including product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, loss of customer confidence, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs, and our development or commercialization efforts may be materially harmed.

Moreover, the FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on companies' communications regarding use of their products, and if we promote any approved product beyond its approved indications or inconsistent with the approved label, we may be subject to enforcement actions or prosecution arising from such activities. Violations of the U.S. Federal Food, Drug, and Cosmetic Act, or the FDCA, relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws, insurance fraud laws, third party payor actions, stockholder actions and other lawsuits.

Post-approval discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency or relating to manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing, distribution, use or manufacturing of the product;
- withdrawal of the product from the market, or product recalls;

- restrictions on the labeling or marketing of a product;
- fines, restitution or disgorgement of profits or revenues;
- warning or untitled letters or clinical holds;
- refusal by the FDA or other regulatory authorities to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- REMS; and
- injunctions or the imposition of civil or criminal penalties.

For example, we previously had three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia, Vafseo™, in Japan or vadadustat, if approved, for commercial and clinical use.

Non-compliance with the FDA, the EMA, the PMDA and other regulatory authorities' requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties.

The FDA's policies and those of other regulatory authorities may change, and additional government regulations may be enacted. We cannot predict the likelihood, nature or extent of government regulations that may arise from future legislation or administrative action, either in the United States or in other jurisdictions. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially adversely affect our business.

Risks Related to Governmental Regulation and Compliance

We are subject to a complex regulatory scheme that requires significant resources to ensure compliance and our failure to comply with applicable laws could subject us to government scrutiny or enforcement, potentially resulting in costly investigations, fines, penalties or sanctions, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

In general, a variety of laws apply to us or may otherwise restrict our activities, including the following:

- laws and regulations governing the conduct of preclinical studies and clinical trials in the United States and other countries in which we are conducting such studies;
- anti-corruption and anti-bribery laws, including the FCPA, the UK Bribery Act and various other anti-corruption laws in countries outside of the United States;
- data privacy laws existing in the United States, the EU, the UK and other countries in which we operate, including the U.S. Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, state privacy and data protection laws, such as the California Consumer Privacy Act, or CCPA, and the California Privacy Rights Act of 2020, or CPRA, as well as state consumer protection laws, GDPR, any additional applicable EU member state data protection laws in force from time to time, the retained EU law version of the General Data Protection Regulation as saved into United Kingdom law by virtue of section 3 of the United Kingdom's European Union (Withdrawal) Act 2018, or the EU GDPR;
- federal and state laws requiring the submission of accurate product prices and notifications of price increases;
- federal and state securities laws;
- environmental, health and safety laws and regulations; and
- international trade laws, which are laws that regulate the sale, purchase, import, export, re-export, transfer and shipment of goods, products, materials, services and technology.

In addition, our relationships with healthcare providers, physicians and third party payors expose us to broadly applicable fraud and abuse laws that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Auryxia and vadadustat, if approved, and any other products for which we may obtain marketing approval. As such, these arrangements are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations at federal, state and international levels. These restrictions include, but are not limited to, the following:

- the FDCA which among other things, strictly regulates drug product marketing and promotion and prohibits manufacturers from marketing such products for off-label use;
- federal laws that require pharmaceutical manufacturers to report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under government healthcare programs, and laws requiring notification of price increases;
- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act, which imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, and violations of the FDCA, the federal government pricing laws, and the federal Anti-Kickback Statute trigger liability under the federal False Claims Act;
- HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the HITECH, and their respective implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act (renamed the Open Payments Act) requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by state Medicaid or other programs, or non-governmental third party payors, including private insurers, and which are not preempted by federal laws and often differ from state to state, thus complicating compliance efforts; and
- U.S. state laws restricting interactions with healthcare providers and other members of the healthcare community or requiring pharmaceutical manufacturers to implement certain compliance standards, which vary from state to state.

Because of the breadth of these U.S. laws, and their non-U.S. equivalents, and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reforms have strengthened these laws. For example, the Health Care Reform Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate the law. The Health Care Reform Act also amended the False Claims Act, such that violations of the Anti-Kickback Statute are now deemed violations of the False Claims Act.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines, such as the Pharmaceutical Research and Manufacturers of America Code on Interactions with Health Care Professionals, known as the PhRMA Code. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA.

Efforts to ensure that our business complies with applicable healthcare laws and regulations involves substantial costs and requires us to expend significant resources. One of the potential areas for governmental scrutiny involves federal and state requirements for pharmaceutical manufacturers to submit accurate price reports to the government. Because our processes for calculating applicable government prices and the judgments involved in making these calculations involve subjective decisions and complex methodologies, these calculations are subject to risk of errors and differing interpretations. In addition, they are subject to review and challenge by the applicable governmental agencies, or potential qui tam complaints, and it is possible that such reviews could result in changes, recalculations, or defense costs that may have adverse legal or financial consequences. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could materially adversely affect our business and would result in increased costs and diversion of management attention and could negatively impact the development, regulatory approval and commercialization of Auryxia or vadadustat, any of which could have a material adverse effect on our business. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they

may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government funded healthcare programs.

We will incur significant liability if it is determined that we are promoting any "off-label" use of Auryxia or any other product we may develop, in-license or acquire or if it is determined that any of our activities violates the federal Anti-Kickback Statute.

Physicians are permitted to prescribe drug products for uses that differ from those approved by the FDA or other applicable regulatory agencies. Although the FDA and other regulatory agencies do not regulate a physician's choice of treatments, the FDA and other regulatory agencies do restrict manufacturer communications regarding unapproved uses of an approved drug. Companies are not permitted to promote drugs for unapproved uses or in a manner that is inconsistent with the FDA-approved labeling. There are also restrictions about making comparative or superiority claims based on safety or efficacy that are not supported by substantial evidence. Accordingly, we may not promote Auryxia in the United States for use in any indications other than the Hyperphosphatemia Indication and the IDA Indication, and all promotional claims must be consistent with the FDA-approved labeling for Auryxia.

Promoting a drug off-label is a violation of the FDCA and can give rise to liability under the federal False Claims Act, as well as under additional federal and state laws and insurance statutes. The FDA, the Department of Justice and other regulatory and enforcement authorities enforce laws and regulations prohibiting promotion of off-label uses and the promotion of products for which marketing approval has not been obtained, as well as the false advertising or misleading promotion of drugs. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. In addition, laws and regulations govern the distribution and tracing of prescription drugs and prescription drug samples, including the Prescription Drug Marketing Act of 1976 and the Drug Supply Chain Security Act, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level and set minimum standards for the regulation of drug distributors by the states. A company that is found to have improperly promoted off-label uses or to have otherwise engaged in false or misleading promotion or improper distribution of drugs will be subject to significant liability, potentially including civil and administrative remedies as well as criminal sanctions. It may also be subject to exclusion and debarment from federal healthcare reimbursement programs.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. In addition, under some relatively recent guidance from the FDA, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We intend to engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. Although we believe we have put in place a robust compliance program and processes designed to ensure that all such activities are performed in a legal and compliant manner, such program and processes may not be sufficient to deter or detect all violations.

In addition, if a company's activities are determined to have violated the federal Anti-Kickback Statute, this can also give rise to liability under the federal False Claims Act and such violations can result in significant fines, criminal and civil remedies, and exclusion from Medicare and Medicaid. There is increased government focus on relationships between the pharmaceutical industry and physicians, pharmacies (especially specialty pharmacies), and other sources of referrals. Common industry activities, such as speaker programs, insurance assistance and support, relationships with foundations providing copayment assistance, and relationships with patient organizations and patients are receiving increased governmental attention. If any of our relationships or activities is determined to violate applicable federal and state anti-kickback laws, false claims laws, or other laws or regulations, the company and/or company executives, employees, and other representatives could be subject to significant fines and criminal sanctions, imprisonment, and potential exclusion from Medicare and Medicaid, and could harm our reputation or result in significant legal expenses and distraction of management.

Disruptions in the FDA, regulatory authorities outside the U.S. and other government agencies caused by global health concerns or funding shortages could prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA and regulatory authorities outside the U.S. to review and approve new products can be affected by a variety of factors, including global health concerns, government budget and funding levels, staffing shortages, statutory, regulatory, and policy changes and other events that may otherwise affect the FDA's or other regulatory authorities' ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result of certain of these factors. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may increase the time necessary for new drugs to be reviewed or approved by necessary government agencies, which would adversely affect our

business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our, or our collaboration partners', regulatory submissions, which could have a material adverse effect on our business.

In response to the COVID-19 pandemic, a number of companies in 2020 and 2021 announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Following a period of false starts, and temporary suspensions due to the omicron variant, the FDA announced on February 2, 2022 that it would resume domestic inspections beginning on February 7, 2022, and indicated that it would conduct foreign inspections beginning in April 2022 on a prioritized basis. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and/or any travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the United States may also impose similar restrictions or other policy measures in response to the COVID-19 pandemic or other travel restrictions. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Compliance with privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which took effect across all member states of the EEA, in May 2018. Following the withdrawal of the U.K. from the EU, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the U.K. and includes parallel obligations to those set forth by GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data when required, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, when required, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third party processors. The GDPR increases our obligations as a sponsor in clinical trials in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial patients and investigators. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data and permits EU member states to adopt further penalties for violations that are not subject to the administrative fines outlined in the GDPR.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that we should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. There is ongoing uncertainty about the transfer mechanisms that companies rely upon to enable the legal transfer of personal data from the EU to other countries. For example, in July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the U.S. As court decisions and regulatory guidance evolves, challenges remain with respect to GDPR compliance. Companies must continue to monitor the regulatory landscape and implement necessary changes, all of which may be costly and may put the company out of compliance while any changes are being implemented.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private

litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the CCPA, which went into effect on January 1, 2020, and the CPRA, which amends CCPA by expanding the scope and applicability, while also introducing new privacy protections, is creating similar risks and obligations as those created by GDPR. The CPRA also creates a new agency that is specifically responsible for enforcing the new law. Because of this, we may need to engage in additional activities (e.g., data mapping) to identify the personal information we are collecting and the purposes for which such information is collected. In addition, we will need to ensure that our policies recognize the rights granted to consumers (as that phrase is broadly defined in the CCPA and can include business contact information). Other states have also passed privacy laws that are similar to the CCPA/CPRA, including Virginia, Colorado, Connecticut, and Utah. The laws in the various states vary in terms of their exact requirements, but they all provide regulators in these states with enforcement authority. Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of potential consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Legislative and regulatory healthcare reform may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of vadadustat, or any other product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and vadadustat, if approved. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by legislative initiatives. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any FDA approved product, such as Auryxia or vadadustat, if approved, or any reimbursement that physicians receive for administering any approved product.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for Auryxia and any other approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the ACA. In addition, other legislative changes and regulatory have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2031. However, pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, and subsequent legislation, these Medicare sequester reductions were suspended and reduced through the end of June 2022 but with the full 2% cut resuming as of July 1, 2022. The American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, other legislative and regulatory changes have been proposed, but not yet adopted. For example, in July 2019, HHS proposed regulatory changes in kidney health policy and reimbursement. Any new legislative or regulatory changes may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for Auryxia or vadadustat, if approved, or the frequency with which Auryxia and vadadustat, if approved, is prescribed or used.

The costs and prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement

methodologies for drug products. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

For example, the former administration issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

At the same time, the administration may seek to limit Medicare Part D and public option drug prices through a tax penalty on manufacturers for increases in the cost of drugs and biologics above the general inflation rate. The American Rescue Plan Act of 2021, comprehensive COVID-19 pandemic relief legislation recently enacted under the current administration, includes a number of healthcare-related provisions, such as support to rural health care providers, increased tax subsidies for health insurance purchased through insurance exchange marketplaces, financial incentives to states to expand Medicaid programs and elimination of the Medicaid drug rebate cap effective in 2024.

Further, on July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs HHS to create a plan within 45 days to combat “excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging.” On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated “maximum fair price” under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products or put pressure on our product pricing.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for Auryxia and any product candidates for which we receive marketing approval or additional pricing pressures. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for Auryxia and any products candidates for which we receive marketing approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain and maintain coverage and reimbursement approval for Auryxia or any other approved product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

In addition, in some countries, including member states of the EU the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take a significant amount of time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices, and in certain instances render commercialization in certain markets infeasible or disadvantageous from a financial perspective. In some countries, we or our collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product and/or our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or government authorities may lead to further pressure on the prices or reimbursement levels. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, the commercial launch of our product and/or product candidates could be delayed, possibly for lengthy periods of time, we or our collaborators may not launch at all in a particular country, we may not be able to recoup our investment in one or more product candidates, and there could be a material adverse effect on our business.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the use and disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from the use of hazardous materials by our employees, contractors or consultants, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to our Reliance on Third Parties

We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona, Vafseo and vadadustat and if these collaborations are not successful or if our collaborators terminate their agreements with us, we may not be able to capitalize on the market potential of Auryxia, Riona, Vafseo and vadadustat, and our business could be materially harmed.

We sublicensed the rights to commercialize Riona to JT and Torii in Japan. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. In addition, we entered into the Vifor Second Amended Agreement pursuant to which we granted CSL Vifor an exclusive license to sell vadadustat to the Supply Group in the United States. We also granted to Averoa an exclusive license to develop and commercialize ferric citrate

in the EEA, Turkey, Switzerland and the United Kingdom. We may form or seek other strategic alliances, joint ventures, or collaborations, or enter into additional licensing arrangements with third parties that we believe will complement or augment our and our partners' commercialization efforts with respect to Auryxia, Riona, Vafseo and our and our partners' development and, if approved, commercialization efforts with respect to vadadustat and any other product candidates. We may not be able to maintain our collaborations for development and commercialization. For example, on May 13, 2022, Otsuka elected to terminate our collaboration agreements with them, and we subsequently negotiated the Termination Agreement with Otsuka. This termination by Otsuka may delay the approval or launch of vadadustat in Europe or other territories or adversely affect how we are perceived in scientific and financial communities. In addition, our current and any future collaborations may not be successful due to a number of important factors, including the following:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborations may be terminated in accordance with the terms of the collaboration agreements and, if terminated, may make it difficult for us to attract new collaborators or adversely affect how we are perceived in scientific and financial communities, and may result in a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable products and product candidates;
- if permitted by the terms of the collaboration agreements, collaborators may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus, availability of funding or other external factors such as a business combination that diverts resources or creates competing priorities;
- if permitted by the terms of the collaboration agreements, collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- a collaborator with marketing and distribution rights to our products may not commit sufficient resources to their marketing and distribution;
- if permitted by the terms of the collaboration agreements, we and our collaborator may have a difference of opinion regarding the development or commercialization strategy for a particular product or product candidate, and our collaborator may have ultimate decision making authority;
- disputes may arise between a collaborator and us that cause the delay or termination of activities related to research, development, supply or commercialization of Auryxia, Riona, Vafseo or vadadustat and any other product candidate, or that result in costly litigation or arbitration that diverts management attention and resources;
- collaborations may not lead to development or commercialization of products and product candidates, if approved, in the most efficient manner or at all;
- a significant change in the senior management team, a change in the financial condition or a change in the business operations, including a change in control or internal corporate restructuring, of any of our collaborators, could result in delayed timelines, re-prioritization of our programs, decreasing resources or funding allocated to support our programs, or termination of the collaborations; and
- collaborators may not comply with all applicable regulatory and legal requirements.

If any of these events occurs, the market potential of Auryxia, Riona, Vafseo or vadadustat, if and where approved, and any other products or product candidates, could be reduced, and our business could be materially harmed. Collaborations may also divert resources, including the attention of management and other employees, from other parts of our business, which could have an adverse effect on other parts of our business, and we cannot be certain that the benefits of the collaboration will outweigh the potential risks.

We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

We will require substantial additional cash to fund the continued commercialization of Auryxia and the development and potential commercialization of any of our product candidates, including vadadustat, if approved, especially following the termination of our collaboration agreements with Otsuka. We may decide to enter into additional collaborations for the development and commercialization of vadadustat or Auryxia, both within and outside of the United States. For example, we plan to pursue a new partner to develop and commercialize vadadustat in Europe and other territories previously licensed to Otsuka. If we are unsuccessful in entering into a new agreement for the development and commercialization of vadadustat in Europe and other territories in a timely manner, or at all, it may result in a delay in the approval or launch of vadadustat in Europe or other territories, a need for additional capital and expansion of our internal capabilities to pursue further development or commercialization of the applicable products and product candidates, particularly the development and commercialization of vadadustat in Europe and other territories, and could have an adverse effect on our results of operations. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders, divert management’s attention, or disrupt our business.

We may not be successful in entering into additional collaborations as a result of many factors, including the following:

- competition in seeking appropriate collaborators;
- a reduced number of potential collaborators due to recent business combinations in the pharmaceutical industry;
- an inability to negotiate collaborations on acceptable terms, on a timely basis or at all;
- any international rules, regulations, guidance, laws, risks or uncertainties with respect to potential partners outside of the United States;
- a potential collaborator's evaluation of Auryxia, vadadustat or any other product or product candidate may differ substantially from ours;
- a potential collaborator's evaluation of our financial stability and resources;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations in a timely manner, or at all, we may have to delay or curtail the commercialization of Auryxia or vadadustat, if and where approved, reduce or delay its development program or other of our other development programs, or increase our expenditures and undertake additional development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop or commercialize Auryxia or vadadustat, if approved.

Even if we enter into additional collaboration agreements and strategic partnerships or license our intellectual property, we may not be able to maintain them or they may be unsuccessful, which could delay our timelines or otherwise adversely affect our business.

Royalties from commercial sales of vadadustat under our MTPC Agreement will likely fluctuate and will impact our rights to receive future payments under our Royalty Agreement with HCR.

Pursuant to the Royalty Agreement with HCR, we sold to HCR our right to receive the Royalty Interest Payments payable to us under the MTPC Agreement, subject to the Annual Cap and the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, we will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or we pay the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to us, and HCR would have no further right to any Royalty Interest Payments. We received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and we are eligible to receive up to an additional $15.0 million under the Royalty Agreement if specified sales milestones are achieved for vadadustat in the territory covered by the MTPC Agreement, subject to the satisfaction of certain customary conditions.

The royalty revenues under the MTPC Agreement may fluctuate considerably because they depend upon, among other things, the rate of growth of sales of vadadustat in the territory covered by the MTPC Agreement. Negative fluctuations in these royalty revenues could delay, diminish or eliminate our right to receive up to the additional $15.0 million under the Royalty Agreement upon achievement of the specified sales milestones, our ability to receive 85% of the Royalty Interest Payments after the Annual Cap is achieved in a given calendar year, or our ability to receive 100% of the Royalty Interest Payments after the Aggregate Cap is achieved.

We rely upon third parties to conduct all aspects of our product manufacturing, and in many instances only have a single supplier, and the loss of these manufacturers, their failure to supply us on a timely basis, or at all, or their failure to successfully carry out their contractual duties or comply with regulatory requirements, cGMP requirements, or guidance could cause delays in or disruptions to our supply chain and substantially harm our business.

We do not have any manufacturing facilities and do not expect to independently manufacture any product or product candidates. We currently rely, and expect to continue to rely, on third party manufacturers to produce all of our commercial, clinical and preclinical supply. Our reliance on third party manufacturers, who have control over the manufacturing process, increases the risk that we will not have or be able to maintain sufficient quantities of Auryxia and vadadustat or the ability to obtain such quantities at an acceptable cost or quality, which could delay, prevent or impair our and our partners' development or commercialization efforts.

We currently rely on a single source supplier for each of Auryxia drug substance and drug product and vadadustat drug substance and drug product, and alternate sources of supply may not be readily available. If any of the following occurs, we may not have sufficient quantities of Auryxia and/or vadadustat to support our clinical trials, development, commercialization,

or obtaining and maintaining marketing approvals, which could materially and adversely impact our business and results of operations:

- we are unsuccessful in maintaining our current supply arrangements for commercial quantities of Auryxia and vadadustat;
- we are unsuccessful in validating new sites;
- our commercial supply arrangements for Auryxia or vadadustat are terminated;
- any of our third party manufacturers are unable to fulfill the terms of their agreements with us, including with respect to quality and quantity, or are unable or unwilling to continue to manufacture on the manufacturing lines included in our regulatory filings; or
- any of our third party manufacturers breach our supply agreements, do not comply with quality or regulatory requirements and guidance, including cGMP or are subject to regulatory review or ceases their operations for any reason.

If any of our third party manufacturers cannot or do not perform as agreed or expected, including as a result of catastrophic events, including pandemics, including the COVID-19 pandemic, terrorist attacks, wars or other armed conflicts, geopolitical tensions or natural disasters, if they misappropriate our proprietary information, if they terminate their engagements with us, if we terminate our engagements with them, or if there is a significant disagreement, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into agreements with other third party manufacturers, which we may not be able to do in a timely manner or on favorable or reasonable terms, if at all. For example, one of our manufacturers has notified us that it will be discontinuing operations at one site at a future date. In some cases, there may be a limited number of qualified replacement manufacturers, or the technical skills or equipment required to manufacture a product or product candidate may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party, or a feasible alternative may not exist. These factors would increase our reliance on our current manufacturers or require us to obtain necessary regulatory approvals and licenses in order to have another third party manufacture Auryxia or vadadustat. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays and costs associated with the qualification of a new manufacturer and validation of manufacturing processes would negatively affect our ability to supply clinical trials, obtain and maintain marketing approval, or commercialize or satisfy patient demand for Auryxia and vadadustat, where approved, in a timely manner, within budget, or at all.

In addition, the cost of obtaining Auryxia and vadadustat is subject to adjustment based on our third party manufacturers' costs of obtaining raw materials and producing the product. We have limited control over the production costs of Auryxia and vadadustat, including the costs of raw materials, and have seen increases in the production costs of Auryxia and vadadustat, and any significant increase in the cost of obtaining our products could materially adversely affect our revenue for Auryxia and vadadustat, if approved.

Moreover, issues that may arise in any scale-up and technology transfer and continued commercial scale manufacture of our products may lead to significant delays in our development, marketing approval and commercial timelines and negatively impact our financial performance. For example, a production-related issue resulted in an interruption in the supply of Auryxia in the third and fourth quarters of 2016. This supply interruption negatively impacted Keryx's revenues in 2016. This supply interruption was resolved, and we have taken and continue to take actions designed to prevent future interruptions in the supply of Auryxia. However, we recently experienced issues in manufacturing Auryxia, and if we continue to experience manufacturing issues or our actions to prevent future interruptions are not successful, we may experience additional supply issues. In addition, before we can manufacture product at a new site, we must validate the process at that site. If the process validation is unsuccessful, or takes longer than we anticipate, we may have to expend additional resources and could experience a supply interruption. Any future supply interruptions, whether quality or quantity based, for Auryxia or vadadustat, if and where approved, would negatively and materially impact our reputation and financial condition.

There are a limited number of manufacturers that are capable of manufacturing Auryxia and vadadustat for us and complying with cGMP regulations and guidance and other stringent regulatory requirements and guidance enforced by the FDA, EMA, PMDA and other regulatory authorities. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation, which occur in addition to our own quality assurance releases. The facilities and processes used by our third party manufacturers to manufacture Auryxia may be inspected by the FDA and other regulatory authorities at any time, and the facilities and processes used by our third party manufacturers to manufacture vadadustat will be inspected by the FDA, the EMA and other regulatory authorities prior to or after we submit our marketing applications. Although we have general visibility into the manufacturing processes of our third party manufacturers, we do not ultimately control such manufacturing processes of, and have little control over, our third party manufacturers, including, without limitation, their compliance with cGMP requirements and guidance for the manufacture of certain starting materials, drug substance and finished drug product. Similarly, although we review final production, we have little control over the ability of

our third party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Our third party manufacturers may experience problems with their manufacturing and distribution operations and processes, including, for example, quality issues, such as product specification and stability failures, procedural deviations, improper equipment installation or operation, utility failures, contamination, natural disasters and public health epidemics. We may also encounter difficulties relating to our own quality processes and procedures, including regulatory compliance, lot release, quality control and quality assurance, as well as shortages of qualified personnel. If our third party manufacturers cannot successfully manufacture material that conforms to our specifications and regulatory requirements and guidance, or if we or our third party manufacturers experience manufacturing, operations and/or quality issues, including an inability or unwillingness to continue manufacturing our products at all, in accordance with agreed-upon processes or on currently validated manufacturing lines, we may not be able to supply patient demand or maintain marketing approval for Auryxia, secure and maintain marketing approval for vadadustat, and we might be required to expend additional resources to obtain material from other manufacturers. If any of these events occur, our reputation and financial condition would be negatively and materially impacted. In addition, during the year ended December 31, 2022, we had higher write-downs to inventory reserves related to Auryxia drug substance that will not be forward processed into drug product. If we have additional write-downs to inventory reserves in the future, it could negatively impact our ability to supply Auryxia, and our financial condition could be harmed.

If the FDA, the EMA or other regulatory authorities do not approve the facilities being used to manufacture vadadustat, or if they withdraw any approval of the facilities being used to manufacture Auryxia or vadadustat, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or Vafseo in Japan, or develop, obtain marketing approval for or market vadadustat or our other product candidates, if approved.

Moreover, our failure or the failure of our third party manufacturers to comply with applicable regulations or guidance, or our failure to oversee or facilitate such compliance, could result in sanctions being imposed on us or our third party manufacturers, including, where applicable, clinical holds, fines, injunctions, civil penalties, delays in, suspension of or withdrawal of approvals, license revocation, seizures or recalls of Auryxia or Vafseo in Japan, operating restrictions, receipt of a Form 483 or warning letter, or criminal prosecutions, any of which could significantly and adversely affect the supply of Auryxia or vadadustat. For example, we previously conducted three limited, voluntary recalls of Auryxia. These and any other recalls or any supply, quality or manufacturing issues in the future and any related write-downs of inventory or other consequences could result in significant negative consequences, including reputational harm, loss of customer confidence, and a negative impact on our financials, any of which could have a material adverse effect on our business and results of operations, and may impact our ability to supply Auryxia, Vafseo in Japan or vadadustat for clinical and commercial use. Also, if our starting materials, drug substance or drug product are damaged or lost while in our or our third party manufacturers’ control, it may adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

In addition, Auryxia and vadadustat may compete with other products and product candidates for access to third party manufacturing facilities. A third party manufacturer may also encounter delays or operational issues brought on by sudden internal resource constraints, labor disputes, shifting priorities or shifting regulatory protocols including, in each case, relating to the COVID-19 pandemic. Certain of these third party manufacturing facilities may be contractually prohibited from manufacturing Auryxia or vadadustat due to exclusivity provisions in agreements with our competitors. Any of the foregoing could negatively impact our third party manufacturers' ability to meet our demand, which could adversely impact our ability to supply Auryxia or vadadustat, and we may incur significant financial harm.

Our current and anticipated future dependence on third parties for the manufacture of Auryxia and vadadustat may adversely affect our and our partners' ability to commercialize Auryxia and vadadustat, where approved, on a timely and competitive basis and may reduce any future profit margins.

We rely upon third parties to conduct our clinical trials and certain of our preclinical studies. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain or maintain marketing approval for Auryxia, vadadustat or any of our product candidates, and our business could be substantially harmed.

We do not have the ability to independently conduct certain preclinical studies and clinical trials. We are currently relying, and expect to continue to rely, upon third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our current and future preclinical studies and clinical trials. The third parties upon whom we rely may fail to perform effectively, or terminate their engagement with us, for a number of reasons, including the following:

- if they experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if they undergo changes in priorities or corporate structure including as a result of a merger or acquisition or other transaction, or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

If the third parties upon whom we rely to conduct our trials fail to adhere to clinical trial protocols or to regulatory requirements, the quantity, quality or accuracy of the data obtained by the third parties may be compromised. We are exposed to risk of fraud or other misconduct by such third parties.

Any of these events could cause our preclinical studies and clinical trials, including post-approval clinical trials, to be extended, delayed, suspended, required to be repeated or terminated, or we may receive untitled warning letters or be the subject of an enforcement action, which could result in our failing to obtain and maintain marketing approval of vadadustat or any other product candidates on a timely basis, or at all, or fail to maintain marketing approval of Auryxia, or any other products, any of which would adversely affect our business operations. In addition, if the third parties upon whom we rely fail to perform effectively or terminate their engagement with us, we may need to enter into alternative arrangements, which could delay, perhaps significantly, the development and commercialization of vadadustat, if approved, or any other product candidates.

Even though we do not directly control the third parties upon whom we rely to conduct our preclinical studies and clinical trials and therefore cannot guarantee the satisfactory and timely performance of their obligations to us, we are nevertheless responsible for ensuring that each of our clinical trials and preclinical studies is conducted in accordance with the applicable protocol, legal and regulatory requirements, including GXP requirements, and scientific standards, and our reliance on these third parties, including CROs, will not relieve us of our regulatory responsibilities. If we or any of our CROs, their subcontractors, or clinical or preclinical trial sites fail to comply with applicable GXP requirements, the clinical data generated in our trials may be deemed unreliable or insufficient, our clinical trials could be put on hold, and/or the FDA, the EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical and preclinical trials must be conducted with drug product that meets certain specifications and is manufactured under applicable cGMP regulations. These requirements include, among other things, quality control, quality assurance, and the satisfactory maintenance of records and documentation.

We also rely upon third parties to store and distribute drug product for our clinical trials. For example, we use third parties to store product at various sites in the United States to distribute to our clinical trial sites. Any performance failure on the part of our storage or distributor partners could delay clinical development, marketing approval or commercialization, resulting in additional costs and depriving us of potential product revenue.

If the licensor of certain intellectual property relating to Auryxia terminates, modifies or threatens to terminate existing contracts or relationships with us, our business may be materially harmed.

We do not own all of the rights to our product, Auryxia. We have licensed and sublicensed certain rights, patent and otherwise, to Auryxia from a third party, Panion & BF Biotech, Inc., or Panion, who in turn licenses certain rights to Auryxia from one of the inventors of Auryxia. The license agreement with Panion, or the Panion License Agreement, requires us to meet development milestones and imposes development and commercialization due diligence requirements on us. In addition, under the Panion License Agreement, we must pay royalties based on a mid-single digit percentage of net sales of product resulting from the licensed technologies, including Auryxia, and pay the patent filing, prosecution and maintenance costs related to the license. If we do not meet our obligations in a timely manner, or if we otherwise breach the terms of the Panion License Agreement, Panion could terminate the agreement, and we would lose the rights to Auryxia. For example, following announcement of the Merger, Panion notified Keryx in writing that Panion would terminate the Panion License Agreement on November 21, 2018 if Keryx did not cure the breach alleged by Panion, specifically, that Keryx failed to use commercially reasonable best efforts to commercialize Auryxia outside the United States. Keryx disagreed with Panion's claims, and the parties entered discussions to resolve this dispute. On October 24, 2018, prior to the consummation of the Merger, we, Keryx and Panion entered into a letter agreement, or the Panion Letter Agreement, pursuant to which Panion agreed to rescind any and all prior termination threats or notices relating to the Panion License Agreement and waived its rights to terminate the license agreement based on any breach by us of our obligation to use commercially reasonable efforts to commercialize Auryxia outside the United States until the parties executed an amendment to the Panion License Agreement in accordance with the terms of the Panion Letter Agreement, following consummation of the Merger. On April 17, 2019, we and Panion entered into an amendment and restatement of the Panion License Agreement, or the Panion Amended License Agreement, which reflects certain revisions consistent with the terms of the Panion Letter Agreement. See Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for additional information regarding the Panion Amended License Agreement. Even though we entered into the Panion Amended License Agreement, there are no assurances that Panion will not allege other breaches of the Panion Amended License Agreement or otherwise attempt to terminate the Panion Amended License Agreement in the future. In addition, if Panion breaches its agreement with the inventor from whom it licenses rights to Auryxia, Panion could lose its license, which could impair or delay our ability to develop and commercialize Auryxia.

From time to time, we may have disagreements with Panion, or Panion may have disagreements with the inventor from whom it licenses rights to Auryxia, regarding the terms of the agreements or ownership of proprietary rights, which could impact the

commercialization of Auryxia, could require or result in litigation or arbitration, which would be time-consuming and expensive, could lead to the termination of the Panion Amended License Agreement, or force us to negotiate a revised or new license agreement on terms less favorable than the original. In addition, in the event that the owners and/or licensors of the rights we license were to enter into bankruptcy or similar proceedings, we could potentially lose our rights to Auryxia or our rights could otherwise be adversely affected, which could prevent us from continuing to commercialize Auryxia.

Risks Related to our Intellectual Property

If we are unable to adequately protect our intellectual property, third parties may be able to use our intellectual property, which could adversely affect our ability to compete in the market.

Our commercial success will depend in part on our ability, and the ability of our licensors, to obtain and maintain patent protection on our drug product and technologies, and to successfully defend these patents against third party challenges. We seek to protect our proprietary products and technology by filing patent applications in the United States and certain foreign jurisdictions. The process for obtaining patent protection is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications in a cost effective or timely manner. In addition, we may fail to identify patentable subject matter early enough to obtain patent protection. Further, license agreements with third parties may not allow us to control the preparation, filing and prosecution of patent applications, or the maintenance or enforcement of patents. Such third parties may decide not to enforce such patents or enforce such patents without our involvement. Thus, these patent applications and patents may not, under these circumstances, be prosecuted or enforced in a manner consistent with the best interests of the company.

Our pending patent applications may not issue as patents and may not issue in all countries in which we develop, manufacture or potentially sell our product or in countries where others develop, manufacture and potentially sell products using our technologies. Moreover, our pending patent applications, if issued as patents, may not provide additional protection for our product.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in pharmaceutical and biotechnology patents has emerged to date. Changes in the patent laws or the interpretation of the patent laws in the United States and other jurisdictions may diminish the value of our patents or narrow the scope of our patent protection. Accordingly, the patents we own or license may not be sufficiently broad to prevent others from practicing our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative drug products or technologies or design around our patented drug product and technologies which may have an adverse effect on our business. If our competitors prepare and file patent applications in the United States that claim technology also claimed by us, we may have to participate in interference or derivation proceedings in front of the U.S. Patent and Trademark Office, or USPTO, to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that any related patent may expire prior to, or remain in existence for only a short period following, commercialization, which may significantly diminish our ability to exclude others from commercializing products that are similar or identical to ours. The patents we own or license may be challenged or invalidated or may fail to provide us with any competitive advantage. Since we have licensed or sublicensed many patents from third parties, we may not be able to enforce such licensed patents against third party infringers without the cooperation of the patent owner and the licensor, which may not be forthcoming. In addition, we may not be successful or timely in obtaining any patents for which we submit applications.

Generally, the first to file a patent application is entitled to the patent if all other requirements of patentability are met. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Since publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, the laws enacted by the Leahy-Smith America Invents Act of 2011, which reformed certain patent laws in the United States, introduce procedures that permit competitors to challenge our patents in the USPTO after grant, including inter partes review and post grant review. Similar laws exist outside of the United States. The laws of the European Patent Convention, for example, provide for post-grant opposition procedures that permit competitors to challenge, or oppose, our European patents administratively at the European Patent Office.

We may become involved in addressing patentability objections based on third party submission of references, or we may become involved in defending our patent rights in oppositions, derivation proceedings, reexamination, inter partes review, post grant review, interference proceedings or other patent office proceedings or litigation, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse result in any such proceeding or litigation could reduce

the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged on such a basis in the courts or patent offices in the United States and abroad. As a result of such challenges, we may lose exclusivity or freedom-to-operate or patent claims may be narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to prevent third parties from using or commercializing similar or identical products, or limit the duration of the patent protection for our products.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and governmental patent agencies in other jurisdictions also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse in many cases can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market sooner than we expect, which would have a material adverse effect on our business.

In addition, patents protecting our product candidate might expire before or shortly after such candidate is commercialized. Thus, our patent portfolio may not provide sufficient rights to exclude others from commercializing products similar or identical to ours.

We also rely on trade secrets and know-how to protect our intellectual property where we believe patent protection is not appropriate or obtainable. Trade secrets are difficult to protect. While we require our employees, licensees, collaborators and consultants to enter into confidentiality agreements, this may not be sufficient to adequately protect our trade secrets or other proprietary information. In addition, in some cases, we share certain ownership and publication rights to data relating to some of our products and product candidates with research collaborators, licensees and other third parties. If we cannot maintain the confidentiality of this information, our ability to receive patent protection or protect our trade secrets or other proprietary information will be at risk.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on our products and product candidates in all countries throughout the world would be prohibitively expensive. Consequently, the breadth of our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. As a result, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories where we have patent protection, but where enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or the marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in countries outside of the United States could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage for our products and product candidates from the intellectual property that we develop or license.

The intellectual property that we own or have licensed and related non-patent exclusivity relating to our current and future products is, and may be, limited, which could adversely affect our ability to compete in the market and adversely affect the value of Auryxia.

The patent rights and related non-patent exclusivity that we own or have licensed relating to Auryxia are limited in ways that may affect our ability to exclude third parties from competing against us. For example, a third party may design around our owned or licensed composition of matter patent claims or market a product for the methods of use not covered by our owned or licensed patents.

Obtaining proof of direct infringement by a competitor for a method of use patent requires us to demonstrate that the competitors make and market a product for the patented use(s). Alternatively, we can prove that our competitors induce or contribute to others in engaging in direct infringement. Proving that a competitor contributes to or induces infringement of a patented method by another has additional proof requirements. For example, proving inducement of infringement requires proof of intent by the competitor. If we are required to defend ourselves against claims or to protect our own proprietary rights against others, it could result in substantial costs to us and the distraction of our management. An adverse ruling in any litigation or administrative proceeding could prevent us from marketing and selling Auryxia, increase the risk that a generic or other similar version of Auryxia could enter the market to compete with Auryxia, limit our development and commercialization of Auryxia, or otherwise harm our competitive position and result in additional significant costs.

Moreover, physicians may prescribe a competitive identical product for indications other than the one for which the product has been approved, or "off-label" indications, that are covered by the applicable patents. Although such off-label prescriptions may directly infringe or contribute to or induce infringement of method of use patents, such infringement is difficult to prevent.

In addition, any limitations of our patent protection described above may adversely affect the value of our drug product and may inhibit our ability to obtain a collaboration partner at terms acceptable to us, if at all.

In addition to patent rights in the United States, we may seek non-patent exclusivity for vadadustat and other product candidates under other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, but there is no guarantee that vadadustat or any other product candidates will receive such exclusivity. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first sponsor to gain approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which consists of the molecule(s) or ion(s) responsible for the action of the drug substance (but not including those portions of the molecule that cause it to be a salt or ester or which are not bound to the molecule by covalent or similar bonds). During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company for another version of such drug where the sponsor does not own or have a legal right of reference to all the data required for approval.

An ANDA that references an NDA product with NCE exclusivity may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of exclusivity for an NDA, particularly a 505(b)(2) NDA or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the sponsor are deemed by the FDA to be essential to the approval of the application (for example, for new indications, dosages, or strengths of an existing drug). This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. The three-year exclusivity period, unlike five-year exclusivity, does not prevent the submission of a competing ANDA or 505(b)(2) NDA. Instead, it only prevents the FDA from granting final approval to such a product until expiration of the exclusivity period. Five-year and three-year exclusivity will not delay the submission (in the case of five-year exclusivity) or the approval (in the case of three-year exclusivity) of a full NDA submitted under section 505(b)(1) of the FDCA; however, a sponsor submitting a full NDA would be required to conduct all of its own studies needed to independently support a finding of safety and effectiveness for the proposed product, or have a full right of reference to all studies not conducted by the sponsor.

In cases where NCE exclusivity has been granted to a new drug product, the 30-month stay triggered by such litigation is extended by the amount of time such that seven years and six months will elapse from the date of approval of the NDA for that product. Without NCE exclusivity, the 30-month stay on FDA final approval of an ANDA runs from the date on which the sponsor of the reference listed drug receives notice of a Paragraph IV certification from the ANDA sponsor.

In addition to NCE, in the United States, the FDA has the authority to grant additional regulatory exclusivity protection for approved drugs where the sponsor conducts specified testing in pediatric or adolescent populations. If granted, this pediatric exclusivity may provide an additional six months which are added to the term of any non-patent exclusivity that has been awarded as well as to the regulatory protection related to the term of a relevant patent, to the extent these protections have not already expired.

We cannot assure you that Auryxia, vadadustat, if approved, or any of our potential future products will obtain such pediatric exclusivity, NCE exclusivity or any other market exclusivity in the United States, EU or any other territory, or that we will be the first to receive the respective regulatory approval for such drugs so as to be eligible for any non-patent exclusivity

protection. We also cannot assure you that Auryxia, vadadustat, if approved, or any of our potential future products will obtain patent term extension.

The market entry of one or more generic competitors or any third party's attempt to challenge our intellectual property rights will likely limit Auryxia sales and have an adverse impact on our business and results of operation.

Although the composition and use of Auryxia is currently claimed by 15 issued patents that are listed in the FDA's Orange Book, we cannot assure you that we will be successful in defending against third parties attempting to invalidate or design around our patents or asserting that our patents are invalid or otherwise unenforceable or not infringed, or in competing against third parties introducing generic equivalents of Auryxia or any of our potential future products. If our Orange Book-listed patents are successfully challenged by a third party and a generic version of Auryxia is approved and launched sooner than we anticipate, revenue from Auryxia could decline significantly, which would have a material adverse effect on our sales, results of operations and financial condition.

We previously received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg ferric iron per tablet). We filed complaints for patent infringement relating to such ANDAs, and subsequently entered into settlement and license agreements with all such ANDA filers that allow such ANDA filers to market a generic version of Auryxia in the United States beginning on March 20, 2025. It is possible that we may receive Paragraph IV certification notice letters from additional ANDA filers and may not ultimately be successful in an ANDA litigation. For example, in February 2023, we received another Paragraph IV certification notice letter regarding an ANDA submitted to the FDA. Generic competition for Auryxia or any of our potential future products could have a material adverse effect on our sales, results of operations and financial condition.

Litigation and administrative proceedings, including third party claims of intellectual property infringement and opposition/invalidation proceedings against third party patents, may be costly and time consuming and may delay or harm our drug discovery, development and commercialization efforts.

We may be forced to initiate litigation to enforce our contractual and intellectual property rights, or we may be sued by third parties asserting claims based on contract, tort or intellectual property infringement. Competitors may infringe our patents or misappropriate our trade secrets or confidential information. We may not be able to prevent infringement of our patents or misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. In addition, third parties may have or may obtain patents in the future and claim that our products or other technologies infringe their patents. If we are required to defend against suits brought by third parties, or if we sue third parties to protect our rights, we may be required to pay substantial litigation costs, and our management's attention may be diverted from operating our business. In addition, any legal action against our licensor, licensees or us that seeks damages or an injunction of commercial activities relating to Auryxia, vadadustat or any other product candidates or other technologies, including those that may be in-licensed or acquired, could subject us to monetary liability, a temporary or permanent injunction preventing the development, marketing and sale of such products or such technologies, and/or require our licensor, licensees or us to obtain a license to continue to develop, market or sell such products or other technologies. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. We cannot predict whether our licensor, licensees or we would prevail in any of these types of actions or that any required license would be made available on commercially acceptable terms, if at all.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. However, there may be patents of third parties of which we are currently unaware with claims to compounds, materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Also, because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We have in the past and may in the future become a party to, or be threatened with, future adversarial litigation or other proceedings regarding intellectual property rights with respect to our product and product candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

While our product candidates are in preclinical studies and clinical trials, we believe that the use of our product candidates in these preclinical studies and clinical trials in the United States falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e), which provides that it shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA. There is an increased possibility of a patent infringement claim against us with respect to commercial products. Our portfolio includes one commercial product, Auryxia. We received the CRL from the FDA regarding our NDA for vadadustat in March 2022, and, if in the future vadadustat is approved, vadadustat could be

commercialized. We attempt to ensure that our products and product candidates and the methods we employ to manufacture them, as well as the methods for their use which we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

FibroGen has filed patent applications in the United States and other countries directed to purportedly new methods of using previously known heterocyclic carboxamide compounds for purposes of treating or affecting specified conditions, and some of these applications have since issued as patents. To the extent any such patents issue or have been issued, we may initiate opposition or other legal proceedings with respect to such patents. We discuss the status of the opposition and/or invalidation proceedings against certain FibroGen patents in Part I, Item 3. Legal Proceedings of this Annual Report on Form 10-K.

Third parties, including FibroGen, may in the future claim that our product and product candidates and other technologies infringe upon their patents and may challenge our ability to commercialize Auryxia and vadadustat, if approved. Parties making claims against us or our licensees may seek and obtain injunctive or other equitable relief, which could effectively block our or their ability to continue to commercialize Auryxia or further develop and commercialize vadadustat or any other product candidates, including those that may be in-licensed or acquired. If any third party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product or product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or our intended methods of use, the holders of any such patent may be able to block or impair our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. We may also elect to enter into a license in order to settle litigation or in order to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our products or product candidates. Should a license to a third party patent become necessary, we cannot predict whether we would be able to obtain a license or, if a license were available, whether it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is unavailable on commercially reasonable terms, or at all, our ability to commercialize our product or product candidate may be impaired or delayed, which could in turn significantly harm our business.

Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products, which may be impossible or require substantial time and monetary expenditure.

In addition, there may be a challenge or dispute regarding inventorship or ownership of patents or applications currently identified as being owned by or licensed to us. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Interference proceedings provoked by third parties or brought by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications.

Various administrative proceedings are also available for challenging patents, including interference, reexamination, inter partes review, and post-grant review proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Competitors may initiate an administrative proceeding challenging our issued patents or pending patent applications, which can be expensive and time-consuming to defend. An adverse result in any current or future defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and held not infringed and could put our patent applications at risk of not issuing. In addition, an unfavorable outcome in any current or future proceeding in which we are challenging third party patents could require us to cease using the patented technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all. Even if we are successful, participation in interference or other administrative proceedings before the USPTO or a foreign patent office may result in substantial costs and distract our management and other employees.

We are currently involved in opposition and invalidation proceedings in the European Patent Office, Intellectual Property High Court of Japan, and the Patents Court of the UK. These proceedings may be ongoing for a number of years and may involve substantial expense and diversion of employee resources from our business. In addition, we may become involved in additional opposition proceedings or other legal or administrative proceedings in the future. For more information, see the other risk factors under "Risks Related to our Intellectual Property".

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation and some administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure during discovery. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from potential collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

Risks Related to our Business and Managing Growth

If we fail to attract, retain and motivate senior management and qualified personnel, we may be unable to successfully develop, obtain and/or maintain marketing approval of and commercialize vadadustat or commercialize Auryxia.

Recruiting and retaining qualified personnel is critical to our success. We are also highly dependent on our executives, certain members of our senior management and certain members of our commercial organization. The loss of the services of our executives, senior managers or other employees could impede the achievement of our research, development, regulatory and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Specifically, following receipt of the CRL, in April and May 2022, we implemented a reduction of our workforce by approximately 42% across all areas of our company (47% inclusive of the closing of the majority of open positions), including several members of management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. In addition, uncertainty related to the timing and outcome of regulatory decisions, could increase attrition. Losing members of management and other key personnel subjects us to a number of risks, including the failure to coordinate responsibilities and tasks, the necessity to create new management systems and processes, the impact on corporate culture, and the retention of historical knowledge.

Furthermore, replacing executives, senior managers and other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, obtain and/or maintain marketing approval of and commercialize Auryxia, vadadustat and other product candidates. Our future financial performance and our ability to develop, obtain and/or maintain marketing approval of and commercialize Auryxia and vadadustat and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to hire, train, integrate, and retain additional qualified personnel with sufficient experience. We may be unable to hire, train, retain or motivate these personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel, particularly in our geographic region.

We also experience competition for the hiring of personnel from universities and research institutions. In addition, we rely on contractors, consultants and advisors, including scientific and clinical advisors, to assist us in formulating and executing our research and development and commercialization strategy. Our contractors, consultants and advisors may become employed by companies other than ours and may have commitments with other entities that may limit their availability to us. If additional members of management or other personnel leave, or we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

Our cost savings plan and the associated workforce reductions implemented in April, May and November 2022 may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.

Following receipt of the CRL, in April and May 2022, we implemented a reduction in workforce by approximately 42% across all areas of our company (47% inclusive of the closing of the majority of open positions), including several members of

management. In November 2022, we also implemented a reduction of our workforce, by approximately 14% consisting of individuals within our commercial organization. The reductions in workforce reflect our strategic pillars to drive Auryxia revenue while also continuing to decrease operating costs. We may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our restructuring efforts due to unforeseen difficulties, delays or unexpected costs. We recorded a restructuring charge of approximately $15.9 million in the aggregate primarily related to contractual termination benefits including severance, non-cash stock-based compensation expense, healthcare and related benefits in the year ended December 31, 2022. If we are unable to realize the expected operational efficiencies and cost savings from the restructuring, our operating results and financial condition would be adversely affected. We also cannot guarantee that we will not have to undertake additional workforce reductions or restructuring activities in the future, including as a result of the FDA's decision related to our appeal of the CRL for vadadustat. Furthermore, our cost savings plan may be disruptive to our operations, including our commercialization of Auryxia, which could affect our ability to generate product revenue. In addition, our workforce reductions could yield unanticipated consequences, such as attrition beyond planned staff reductions, or disruptions in our day-to-day operations. Our workforce reductions could also harm our ability to attract and retain qualified management, scientific, clinical, manufacturing and sales and marketing personnel who are critical to our business. Any failure to attract or retain qualified personnel could prevent us from successfully commercializing Auryxia and from successfully developing and commercializing our product candidates in the future, including vadadustat, if approved. If we are ultimately successful in obtaining approval of vadadustat in the United States, we will need to hire additional employees to support the commercialization of vadadustat in the United States, and if we are unsuccessful or delayed in doing so, the potential launch of vadadustat could be delayed.

We may encounter difficulties in managing our growth, including with respect to our employee base, and managing our operations successfully.

In our day-to-day operations, we may encounter difficulties in managing the size of our operations as well as challenges associated with managing our business. We have strategic collaborations for the commercialization of Riona and the development and commercialization of vadadustat, which is now being marketed under the trade name Vafseo™ by our collaboration partner, MTPC, in Japan. Additionally, in the United States, we have a strategic relationship with CSL Vifor related to the commercialization of vadadustat, if approved. As our operations continue, we expect that we will need to manage our current relationships and enter into new relationships, especially in light of the termination of our collaboration agreements with Otsuka, with various strategic collaborators, consultants, vendors, suppliers and other third parties. These relationships are complex and create numerous risks as we deal with issues that arise.

Our future financial performance and our ability to commercialize Auryxia and vadadustat, if and where approved, and to compete effectively will depend, in part, on our ability to manage any future growth effectively. This future growth will impose significant added responsibilities on the business and members of management. To manage any future growth, we must continue to implement and improve our managerial, operational and financial systems, procedures and processes. We may not be able to implement these improvements in an efficient or timely manner and may discover deficiencies in existing systems, procedures and processes. Moreover, the systems, procedures and processes currently in place or to be implemented may not be adequate for any such growth. Any expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully managing and, as applicable, growing our company.

In addition, we may need to further adjust the size of our workforce as a result of changes to our expectations for our business, which can result in management being required to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth-related activities and related expenses. Further, we rely on independent third parties to provide certain services to us. We structure our relationships with these outside service providers in a manner that we believe results in an independent contractor relationship, not an employee relationship. If any of our service providers are later legally deemed to be employees, we could be subject to employment and tax withholding liabilities and other additional costs as well as other multiple damages and attorneys' fees.

If we fail to develop or maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, investors may lose confidence in us and the trading price of our common stock may decline.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and effectively prevent fraud and operate successfully as a public company. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If our internal control over financial reporting is not effective, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting could also restrict our future access to the capital markets.

A material weakness in internal control over financial reporting has in the past and could in the future lead to deficiencies in the preparation of financial statements. Deficiencies in the preparation of financial statements, could lead to litigation claims against us. The defense of any such claims may cause the diversion of management's attention and resources, and we may be required to pay damages if any such claims or proceedings are not resolved in our favor. Any litigation, even if resolved in our favor, could cause us to incur significant legal and other expenses. Such events could also affect our ability to raise capital to fund future business initiatives.

Security breaches and unauthorized use of our information technology systems and information, or the information technology systems or information in the possession of our collaborators and other third parties, could damage the integrity of our clinical trials, impact our regulatory filings, compromise our ability to protect our intellectual property, and subject us to regulatory actions that could result in significant fines or other penalties.

We, our collaborators, contractors and other third parties rely significantly upon information technology, and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively. In addition, we and our collaborators, contractors and other third parties rely on information technology networks and systems, including the Internet, to process, transmit and store clinical trial data, patient information, and other electronic information, and manage or support a variety of business processes, including operational and financial transactions and records, personal identifying information, payroll data and workforce scheduling information. We purchase most of our information technology from vendors, on whom our systems depend. We rely on commercially available systems, software, tools and monitoring to provide security for the processing, transmission and storage of company and customer information.

In the ordinary course of our business, we and our third party contractors maintain personal and other sensitive data on our and their respective networks, including our intellectual property and proprietary or confidential business information relating to our business and that of our clinical trial patients and business partners. In particular, we rely on CROs and other third parties to store and manage information from our clinical trials. We also rely on third parties to manage patient information for Auryxia. The secure maintenance of this sensitive information is critical to our business and reputation.

Companies and other entities and individuals have been increasingly subject to a wide variety of security incidents, cyber-attacks and other attempts to gain unauthorized access to systems and information. These threats can come from a variety of sources, ranging in sophistication from individual hackers to state-sponsored attacks. Cyber threats may be broadly targeted, or they may be custom-crafted against our information systems or those of our vendors or third party service providers. A security breach, cyberattack or unauthorized access of our clinical data or other data could damage the integrity of our clinical trials, impact our regulatory filings, cause significant risk to our business, compromise our ability to protect our intellectual property, and subject us to regulatory actions, including under the GDPR and CCPA discussed elsewhere in these risk factors and the privacy or security rules under federal, state, or other local laws outside of the United States protecting confidential or personal information, that could be expensive to defend and could result in significant fines or other penalties. Cyberattacks can include malware, computer viruses, hacking or other unauthorized access or other significant compromise of our computer, communications and related systems. Although we take steps to manage and avoid these risks and to be prepared to respond to attacks, our preventive and any remedial actions may not be successful and no such measures can eliminate the possibility of the systems' improper functioning or the improper access or disclosure of confidential or personally identifiable information such as in the event of cyberattacks. Security breaches, whether through physical or electronic break-ins, computer viruses, ransomware, impersonation of authorized users, attacks by hackers or other means, can create system disruptions or shutdowns or the unauthorized disclosure of confidential information.

Although we believe our collaborators, vendors and service providers, such as our CROs, take steps to manage and avoid information security risks and respond to attacks, we may be adversely affected by attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers to remedy any harm to our business caused by such event. Additionally, outside parties may attempt to fraudulently induce employees, collaborators, or other contractors to disclose sensitive information or take other actions, including making fraudulent payments or downloading malware, by using "spoofing" and "phishing" emails or other types of attacks. Our employees may be targeted by such fraudulent activities. Outside parties may also subject us to distributed denial of services attacks or introduce viruses or other malware through "trojan horse" programs to our users' computers in order to gain access to our systems and the data stored therein. Cyber-attacks have become more prevalent and much harder to detect and defend against and, because the techniques used to obtain unauthorized access, disable or degrade service, or sabotage systems change frequently and continuously become more sophisticated, often are not recognized until launched against a target and may be difficult to detect for a long time, we may be unable to anticipate these techniques or to implement adequate preventive or detective measures, and we might not immediately detect such incidents and the damage caused by such incidents.

Such attacks, whether successful or unsuccessful, or other compromises with respect to our information security and the measures we implement to prevent, detect and respond to them, could:

- result in our incurring significant costs related to, for example, rebuilding internal systems, defending against litigation, responding to regulatory inquiries or actions, paying damages or fines, or taking other remedial steps with respect to third parties;
- lead to public exposure of personal information of participants in our clinical trials, Auryxia patients and others;
- damage the integrity of our studies or delay their completion, disrupt our development programs, our business operations and commercialization efforts;
- compromise our ability to protect our trade secrets and proprietary information;
- damage our reputation and deter business partners from working with us; or
- divert the attention of our management and key information technology resources.

Any failure to maintain proper functionality and security of our internal computer and information systems could result in a loss of, or damage to, our data or marketing applications or inappropriate disclosure of confidential or proprietary information, interrupt our operations, damage our reputation, subject us to liability claims or regulatory penalties, under a variety of federal, state or other applicable privacy laws, such as HIPAA, the GDPR, or state data protection laws including the CCPA, harm our competitive position and delay the further development and commercialization of our products and product candidates, or impact our relationships with customers and patients.

Our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading. In addition, laws and regulations governing any international operations we have or may have in the future may require us to develop and implement costly compliance programs.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate applicable laws, including the following:

- FDA and other healthcare authorities' regulations, including those laws that require the reporting of true, complete and accurate information to regulatory authorities, and those prohibiting the promotion of unapproved drugs or approved drugs for an unapproved use;
- quality standards, including GXP;
- federal and state healthcare fraud and abuse laws and regulations and their non-U.S. equivalents;
- anti-bribery and anti-corruption laws, such as the FCPA and the UK Bribery Act or country-specific anti-bribery or anti-corruption laws, as well as various import and export laws and regulations;
- laws that require the reporting of true and accurate financial information and data; and
- U.S. state and federal securities laws and regulations and their non-U.S. equivalents, including those related to insider trading.

We are seeking regulatory approval for vadadustat with the EMA and countries in the ACCESS Consortium, and we conducted our global clinical trials for vadadustat, and may in the future conduct additional trials, in countries where corruption is prevalent, and violations of any of these laws by our personnel or by any of our vendors or agents, such as our CROs or CMOs, could have a material adverse impact on our clinical trials and our business and could result in criminal or civil fines and sanctions. We are subject to complex laws that govern our international business practices. These laws include the FCPA, which prohibits U.S. companies and their intermediaries, such as CROs or CMOs, from making improper payments to foreign government officials for the purpose of obtaining or keeping business or obtaining any kind of advantage for the company. The FCPA also requires companies to keep accurate books and records and maintain adequate accounting controls. A number of past and recent FCPA investigations by the Department of Justice and the SEC have focused on the life sciences sector.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. Some of the countries in which we have conducted clinical trials and in which we have CMOs have a history of corruption, which increases our risks of FCPA violations. In addition, the FCPA presents unique challenges in the pharmaceutical industry because in many countries' hospitals are operated by the government, and doctors and other hospital employees are considered foreign government officials. Certain payments made by pharmaceutical companies, or on their behalf by CROs, to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Additionally, the UK Bribery Act applies to our global activities and prohibits bribery of private individuals as well as public officials. The UK Bribery Act prohibits both the offering and accepting of a bribe and imposes strict liability on companies for failing to prevent bribery, unless the company can show that it had "adequate procedures" in place to prevent bribery. There are also local anti-bribery and anti-corruption laws in countries where we have conducted clinical trials, and many of these also carry the risk of significant financial or criminal penalties.

We are also subject to trade control regulations and trade sanction laws that restrict the movement of certain goods, currency, products, materials, services and technology to, and certain operations in, various countries or with certain persons. Our ability to transfer commercial and clinical product and other clinical trial supplies, and for our employees, independent contractors, principal investigators, CROs, CMOs, consultants and vendors ability to travel, between certain countries is subject to maintaining required licenses and complying with these laws and regulations.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state laws, and requirements of non-U.S. jurisdictions, including the GDPR. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us.

The internal controls, policies and procedures, and training and compliance programs we have implemented to deter prohibited practices may not be effective in preventing our employees, contractors, consultants, agents or other representatives from violating or circumventing such internal policies or violating applicable laws and regulations. The failure to comply with laws governing international business practices may impact any future clinical trials, result in substantial civil or criminal penalties for us and any such individuals, including imprisonment, suspension or debarment from government contracting, withdrawal of our products, if approved, from the market, or being delisted from The Nasdaq Capital Market. In addition, we may incur significant costs in implementing sufficient systems, controls and processes to ensure compliance with the aforementioned laws. The laws and regulations referenced above may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements that could adversely affect our business.

Additionally, it is not always possible to identify and deter misconduct by employees and third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling known or unknown risks or preventing losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, or if any such action is instituted against our employees, consultants, independent contractors, CROs, CMOs, vendors or principal investigators, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, curtailment of our operations, disclosure of our confidential information and imprisonment, any of which could adversely affect our ability to operate our business and our results of operations.

Our financial statements include goodwill and an intangible asset as a result of the Merger. The intangible asset has become impaired and could become further impaired in the future under certain conditions. In addition, goodwill could become impaired in the future under certain conditions. Any potential future impairment of goodwill or intangible assets may significantly impact our results of operations and financial condition.

As of December 31, 2022, we had approximately $127.1 million in the aggregate of goodwill and a definite lived intangible asset from the Merger. In accordance with generally accepted accounting principles, or GAAP, we are required annually, or more frequently upon certain indicators of impairment, to review our estimates and assumptions underlying the fair value of our goodwill and our definite lived intangible assets when indicators of impairment are present. Events giving rise to impairment of goodwill or intangible assets are an inherent risk in the pharmaceutical industry and often cannot be predicted.

Conditions that could indicate impairment and necessitate such a review include, but are not limited to, Auryxia's commercial performance, our inability to execute on our strategic initiatives, the deterioration of our market capitalization such that it is significantly below our net book value, a significant adverse change in legal factors, unexpected adverse business conditions, and an adverse action or assessment by a regulator. To the extent we conclude that goodwill and/or definite lived intangible assets have become impaired, we may be required to incur material write-offs relating to such impairment and any such write-offs could have a material impact on our future operating results and financial position. For example, in the second quarter of 2020, in connection with a routine business review, we reduced our short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the impact of the September 2018 CMS decision that Auryxia would no longer be covered by Medicare for the treatment of the IDA Indication. While this decision does not impact CMS coverage for the use of Auryxia for the control of serum phosphorus levels in adult patients with CKD on dialysis, or the Hyperphosphatemia Indication, it requires

all Auryxia prescriptions for Medicare patients to undergo a prior authorization to ensure their use of Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of $115.5 million during the three months ended June 30, 2020, which was entirely allocated to our only intangible asset, the developed product rights for Auryxia, and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia, which we again adjusted during the three months ended December 31, 2020. The estimates, judgments and assumptions used in our impairment testing, and the results of our testing, are discussed in Note 9 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K. If these estimates, judgments and assumptions change in the future, including if the Auryxia asset group does not meet its current forecasted projections, additional impairment charges related to goodwill or our intangible asset could be recorded in the future and additional corresponding adjustments may need to be made to the estimated useful life of the developed product rights for Auryxia, which could materially impact our financial position, certain of our material agreements, and our future operating results.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Auryxia or vadadustat, if approved.

We face an inherent risk of product liability as a result of the clinical and commercial use of Auryxia and vadadustat. For example, we may be sued if Auryxia or vadadustat allegedly causes injury or is found to be otherwise unsuitable during clinical trials, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product or product candidate, negligence, strict liability and breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of Auryxia or vadadustat, if approved. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, product liability claims may result in:

- decreased demand for Auryxia or vadadustat, if approved;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- delay or termination of clinical trials;
- our inability to continue to develop Auryxia or vadadustat;
- significant costs to defend the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to study subjects or patients;
- product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- decreased demand for Auryxia or vadadustat, if approved;
- loss of revenue;
- the inability to commercialize Auryxia or vadadustat, if approved; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance that we believe is appropriate for our company. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have insufficient or no coverage. If we have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, we may not have, or be able to obtain, sufficient capital to pay such amounts. In addition, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost. We also may not be able to obtain additional insurance coverage that will be adequate to cover additional product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to our business.

We will continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we operate in a demanding regulatory environment, and we have and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and certain corporate governance practices. In particular, our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting-related expenses and

expend significant management efforts. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner. If we are not able to comply with the requirements of the Sarbanes-Oxley Act, we could be subject to sanctions or investigations by the SEC, the Nasdaq Capital Market or other regulatory authorities, which would require additional financial and management resources and could adversely affect the market price of our securities. Furthermore, if we cannot provide reliable financial reports or prevent fraud, including as a result of remote working by our employees, our business and results of operations would likely be materially and adversely affected.

We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our Ninth Amended and Restated Certificate of Incorporation, as amended, or Charter, and our Amended and Restated By-Laws, or Bylaws, as amended to date, contain provisions that eliminate, to the maximum extent permitted by the General Corporation Law of the State of Delaware, or DGCL, the personal liability of our directors and executive officers for monetary damages for breach of their fiduciary duties as a director or officer. Our Charter and our Bylaws also provide that we will indemnify our directors and executive officers and may indemnify our employees and other agents to the fullest extent permitted by the DGCL.

In addition, as permitted by Section 145 of the DGCL our Bylaws and our indemnification agreements that we have entered into with our directors and executive officers provide that:

- We will indemnify our directors and officers, as defined in our Bylaws, for serving us in those capacities or for serving other related business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of Akebia and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.
- The rights conferred in our Bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.

Any claims for indemnification made by our directors or officers could impact our cash resources and our ability to fund the business.

Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.

Under Section 382 of the Internal Revenue Code, or Section 382, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. On December 12, 2018, we completed the Merger, which we believe has resulted in an ownership change under Section 382. In addition, the Tax Cuts and Jobs Act, including amendments made by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to fully offset taxable income in the future. Future changes in our stock ownership, many of which are outside of our control, could result in an additional ownership change under Section 382. As a result, if we generate taxable income, our ability to use our pre-change NOL carryforwards to offset federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. At the state level, state net operating losses generated in one state cannot be used to offset income generated in another state and there may be periods during which the use of NOL carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. taxable income. As described above under "—Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. taxable income necessary to utilize our NOLs.

Our Charter designates the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our Charter provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the DGCL our Charter or our Bylaws, or (iv) any other action asserting a claim against us, our directors, officers or other employees that is governed by the internal affairs doctrine. Under our Charter, this exclusive forum provision will not apply to claims that are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Exchange Act, or the rules and regulations thereunder. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our Charter described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our Charter inapplicable to, or unenforceable with respect to, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

We are currently subject to legal proceedings that could result in substantial costs and divert management's attention, and we could be subject to additional legal proceedings.

We are currently subject to legal proceedings, including those described in Part I, Item 3. Legal Proceedings in this Annual Report on Form 10-K, and additional claims may arise in the future. In addition, securities class action and derivative lawsuits and other legal proceedings are often brought against companies for any of the risks described in this Annual Report on Form 10-K following a decline in the market price of their securities. For example, we were party to a putative class action lawsuit in state court filed by purported Keryx stockholders challenging the disclosures made in connection with the Merger, including those that relate to vadadustat's safety, approvability and commercial viability. Oral argument was held on October 7, 2022, and the Court dismissed the complaint without prejudice on October 17, 2022, giving plaintiffs thirty days to amend their complaint. On November 16, 2022, plaintiffs filed an amended consolidated complaint, asserting the same claims and seeking the same relief as the consolidated complaint. On January 18, 2023, defendants moved to dismiss the amended consolidated complaint in its entirety. Briefing on defendants' motion to dismiss is scheduled to be completed by April 5, 2023. In connection with any litigation or other legal proceedings, we could incur substantial costs, and such costs and any related settlements or judgments may not be covered by insurance. Monetary damages or any other adverse judgment would have a material adverse effect on our business and financial position. In addition, if other resolution or actions taken as a result of legal proceedings were to restrain our ability to operate or market our products and services, our consolidated financial position, results of operations or cash flows could be materially adversely affected. We could also suffer an adverse impact on our reputation, negative publicity and a diversion of management's attention and resources, which could have a material adverse effect on our business.

Risks Related to our Common Stock

Our stock price has been and may continue to be volatile, which could result in substantial losses for holders or future purchasers of our common stock and lawsuits against us and our officers and directors.

Our stock price has been and will likely continue to be volatile. The stock market in general and the market for similarly situated biopharmaceutical companies specifically have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. Since our initial public offering in March 2014, the price of our common stock as reported on The Nasdaq Stock Market has ranged from a low of $0.24 on October 24, 2022 to a high of $31.00 on June 20, 2014. The daily closing market price for our common stock varied between a high price of $2.93 on March 9, 2022 and a low price of $0.25 on November 17, 2022 in the twelve-month period ending on December 31, 2022. During that time, the price of our common stock ranged from an intra-day low of $0.24 per share to an intra-day high of $2.93 per share. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section,

including, among others, developments related to and results of our research or clinical trials, developments related to our regulatory submissions and meetings with regulatory authorities, in particular as it relates to vadadustat, commercialization of Auryxia, vadadustat, if and as approved in the U.S. and foreign markets including Europe, and any other product candidates, announcements by us or our competitors of significant transactions or strategic collaborations, negative publicity around Auryxia or vadadustat, regulatory or legal developments in the United States and other countries, developments or disputes concerning our intellectual property, the recruitment or departure of key personnel including as a result of our recent reduction in workforce, actual or anticipated changes in estimates as to financial results, changes in the structure of healthcare payment systems, market conditions in the biopharmaceutical sector and other factors beyond our control. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price at which they purchased it.

In addition, companies that have experienced volatility in the market price of their stock have frequently been the subject of securities class action and shareholder derivative litigation. See Part I, Item 3. Legal Proceedings of this Annual Report on Form 10-K for information concerning securities class action initiated against Keryx and certain current and former directors and officers of ours and Keryx's. In addition, we could be the target of other such litigation in the future. Class action and shareholder derivative lawsuits, whether successful or not, could result in substantial costs, damage or settlement awards and a diversion of our management's resources and attention from running our business, which could materially harm our reputation, financial condition and results of operations.

The issuance of additional shares of our common stock or the sale of shares of our common stock by any of our directors, officers or significant stockholders will dilute our stockholders' ownership interest in Akebia and may cause the market price of our common stock to decline.

Most of our outstanding common stock can be traded without restriction at any time. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell such shares, could reduce the market price of our common stock.

As of December 31, 2022 and based on the amounts reported in the most recent filings made under Section 13(d) and 13(g) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, Satter Management Co., L.P., or Satter, beneficially owned approximately 8.2% of our outstanding shares of common stock, the Vanguard Group, or Vanguard, beneficially owned approximately 6.1% of our outstanding shares of common stock, and CSL Vifor beneficially owned approximately 4.1% of our outstanding shares of common stock. By selling a large number of shares of common stock, Satter or Vanguard could cause the price of our common stock to decline. The shares beneficially owned by CSL Vifor have not been registered pursuant to the Securities Act and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder, but if they are registered in the future, those shares would become freely tradable and, if a large portion of such shares are sold, could cause the price of our common stock to decline.

We have a significant number of shares that are subject to outstanding options and restricted stock units, and in the future we may issue additional options, restricted stock units, or other derivative securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, or other derivative securities, and the subsequent sale of the underlying common stock, could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. Such sales of our common stock could result in higher than average trading volume and may cause the market price for our common stock to decline.

In addition, we currently have on file with the SEC a shelf registration statement, which allows us to offer and sell up to $300 million in registered securities, such as common stock, preferred stock, debt securities, warrants and units, from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale, including a sales agreement prospectus that covers the offering, issuance and sale by us of up to a maximum aggregate offering price of up to $26 million of our common stock that may be issued and sold from time to time under a sales agreement with Jefferies LLC.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other stockholders or by us under our shelf registration statement, pursuant to at-the-market offerings or otherwise, could dilute our stockholders, lower the market price of our common stock and impair our ability to raise capital through the sale of equity securities.

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of December 31, 2022, our executive officers, directors and principal stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons could significantly influence the election of directors and approval of any merger,

consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Provisions in our organizational documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our Charter and our Bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our Board of Directors is responsible for appointing certain members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our Board of Directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our Board of Directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified Board of Directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our Board of Directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our Board of Directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our Board of Directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of 75% of the holders of our capital stock entitled to vote or the majority vote of our Board of Directors to amend our Bylaws; and
- require a supermajority vote of 85% of the holders of our capital stock entitled to vote to amend the classification of our Board of Directors and to amend certain other provisions of our Charter.

These provisions, alone or together, could delay or prevent hostile takeovers, changes in control or changes in our management.
In addition, Section 203 of the DGCL prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person which together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock and we currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. Any payment of cash dividends in the future would be at the discretion of our Board of Directors and would depend on, among other things, our earnings, financial condition, capital requirements, level of indebtedness, statutory and contractual restrictions applying to the payment of dividends and other considerations that the Board of Directors deems relevant. In addition, the terms of the Loan Agreement preclude us from paying cash dividends and future debt agreements may preclude us from paying cash dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate headquarters are located in Cambridge, Massachusetts. We currently lease approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts, and 27,300 square feet of office space in Boston, Massachusetts. Excluding renewal options, the lease for our Cambridge, Massachusetts office space expires on September 11, 2026 and the lease for the Cambridge, Massachusetts lab space expires on January 31, 2025. In February 2022 we extended the term of the lease for our Boston, Massachusetts office space, such that the lease expires on July 31, 2031. In September 2019, we entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., which expired on February 28, 2023. We believe that our existing facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings

Legal Proceedings Relating to Vadadustat

Opposition Proceedings Against Akebia

In September 2018, Dr. Reddy's Laboratories Limited filed an opposition to our issued Indian Patent No. 287720 in the Indian Patent Office.

On July 26, 2022, Sandoz AG filed an opposition against our issued European Patent No. 3277270 in the European Patent Office.

On February 13, 2023, FibroGen, Inc., or FibroGen, filed an opposition against our issued European Patent No. 3357911 in the European Patent Office.

Proceedings Filed by Akebia Against FibroGen, Inc.

Europe

We filed an opposition in the European Patent Office, or the EPO, against FibroGen's European Patent No. 1463823, or the '823 EP Patent on December 5, 2013, and an oral proceeding took place March 8 and 9, 2016. Following the oral proceeding, the Opposition Division of EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. FibroGen appealed that decision. On February 27, 2023, FibroGen withdrew its appeal, and the patent remains revoked.

On May 13, 2015, May 20, 2015 and July 6, 2015, we filed oppositions to FibroGen's European Patent Nos. 2322155, or the '155 EP Patent, 1633333, or the '333 EP Patent, and 2322153, or the '153 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. These method of use patents do not prevent persons from using the compound for other uses, including any previously known use of the compound. In particular, these patents do not claim methods of using any of our product candidates for purposes of inhibiting HIF-PH for the treatment of anemia due to chronic kidney disease, or CKD. While we do not believe these patents will prevent us from commercializing vadadustat for the treatment of anemia due to CKD, we filed these oppositions to provide us with maximum flexibility for developing vadadustat and our pipeline of investigational oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor compounds.

With regard to the opposition that we filed in Europe against the '333 EP Patent, an oral proceeding took place on December 8 and 9, 2016. Following the oral proceeding, the Opposition Division of the EPO ruled that the patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore, revoked the patent in its entirety. On December 9, 2016, FibroGen filed a notice to appeal the decision to revoke the '333 EP Patent. The Board of Appeal held an oral proceeding on this appeal on February 24 and 25, 2022, during which proceeding the '333 EP Patent was maintained in restricted form. The '333 EP patent was originally granted with four independent claims, one of which was found obvious on appeal. The remaining claims are directed to: treatment of anemia of chronic disease in subjects having a percent transferrin saturation of less than 20% (claim 1), treatment of anemia that is refractory to treatment with exogenously administered erythropoietin (claim 6), and treatment of iron deficiency (claim 15).

In oral proceedings held on May 29, 2017, regarding the '155 EP Patent, the European Opposition Division ruled that the '155 EP Patent as granted did not meet the requirements for patentability under the European Patent Convention and, therefore,

revoked the patent in its entirety. FibroGen filed a notice to appeal the decision to revoke the ’155 EP Patent on May 29, 2017. An oral proceeding for the appeal was held on February 22, 2022, during which proceeding the Board of Appeal maintained the revocation of the ‘155 EP Patent in its entirety.

In related oral proceedings held on May 31, 2017 and June 1, 2017 for the ’153 EP Patent, the Opposition Division of the EPO maintained the patent after FibroGen significantly narrowed the claims to an indication for which vadadustat is not intended to be developed. We and Glaxo separately filed notices to appeal the decision to maintain the ’153 EP Patent on November 9, 2017. Bayer filed a notice to appeal the decision on November 14, 2017. Glaxo withdrew its appeal on March 2, 2020 and Bayer withdrew its appeal on June 30, 2021. An oral proceeding for the appeal was held on February 21, 2022, during which proceeding the Board of Appeal revoked the ‘153 patent in its entirety.

On April 3, 2019, we filed oppositions to FibroGen’s European Patent Nos. 2289531, or the ’531 EP Patent, and 2298301, or the ’301 EP Patent in the EPO, respectively, requesting the patents be revoked in their entirety. Oral proceedings for oppositions to the two patents were held on September 7-8 and 10, 2021. Following oral proceedings, the Opposition Division of the EPO maintained certain claims in amended form in the two patents. On January 26, 2022, we filed notice to appeal the Opposition Division’s decision for ’531 EP Patent. On July 8, 2022, FibroGen filed notice to appeal the Opposition Division’s decision for the ’301 EP Patent, which it withdrew on August 17, 2022. These two patents expired in December 2022, and we do not expect the Opposition Division’s decision on the two patents to have any effect on our commercialization of vadadustat in Europe.

Japan

In 2018, we and our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, jointly filed a Request for Trial before the JPO to challenge the validity of certain of FibroGen’s HIF-related patents in Japan: JP4845728, JP5474872 and JP5474741. On September 26, 2019, the JPO conducted an invalidation trial for JP5474872 and JP4845728. On November 11, 2019, the JPO conducted an invalidation trial for JP5474741. On April 1, 2022, the JPO issued a final decision for JP4845728, which invalidated all claims except claims directed to the medical use to treat anemia that does not respond to erythropoiesis. On May 18, 2022, the JPO issued a final decision for JP5474741 and JP5474872, which maintained the claims in amended form. In May 2022, MTPC filed revocation lawsuits for the three patents in the Intellectual Property High Court requesting cancellation of the JPO’s decisions. In July 2022, we filed a revocation lawsuit for JP4845728 in the Intellectual Property High Court requesting cancellation of the JPO’s decision. In August 2022, we filed revocation lawsuits for JP5474741 and JP5474872 in the Intellectual Property High Court requesting cancellation of the JPO’s decisions. In September 2022, FibroGen filed a revocation lawsuit for JP4845728 in the Intellectual Property High Court requesting cancellation of the JPO’s decision on the claims that were invalidated. We do not believe the JPO’s decisions will prevent our collaboration partner MTPC from continuing to commercialize vadadustat for the treatment of anemia due to CKD in Japan.

United Kingdom

On December 13, 2018, we filed Particulars of Claim in the Patents Court of the United Kingdom to challenge the validity of FibroGen’s six HIF-related patents in the UK: the ’823 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), the ’155 EP Patent (UK), European Patent (UK) No. 2,289,531, or the ’531 EP Patent (UK), and European Patent (UK) No. 2,298,301, or the ’301 EP Patent (UK). In May 2019, Astellas Pharma Inc., or Astellas, the exclusive licensee of FibroGen’s HIF-related patents, sued Akebia for patent infringement in the Patents Court of the UK. In September 2019, we filed an Amended Particulars of Claim to include FibroGen’s European Patent No. 1487472, or the ’472 EP Patent (UK). On February 28, 2020, the parties agreed to dismiss the ’472 EP Patent (UK) from the trial.

A trial was conducted in March 2020. On April 20, 2020, the Patents Court of the UK issued a judgment in favor of Akebia, which invalidated all the claims at issue in each of the ’823 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), the ’155 EP Patent (UK) and the ’301 EP Patent (UK). The ’531 EP Patent (UK) was amended to a single claim to recite one specific compound; this claim was held to be valid but not infringed by vadadustat. On June 11, 2020, FibroGen and Astellas appealed the Patents Court’s judgment on the invalidity of the ’823 EP Patent (UK), the ’301 EP Patent (UK), the ’333 EP Patent (UK), the ’153 EP Patent (UK), and the ’155 EP Patent (UK) in the Court of Appeal (Civil Division). On June 8, 2021 - June 10, 2021, the United Kingdom Court of Appeal held a three-day hearing for the appeal. On August 24, 2021, the Court of Appeal issued a judgment, which reversed the Patents Court’s judgment on the invalidity of the ’823 EP Patent (UK) and maintained certain claims of the ’823 EP Patent (UK) and the ’301 EP Patent (UK) in amended form, and which affirmed the Patents Court’s judgment on the invalidity of the ’333 EP Patent (UK), the ’155 EP Patent (UK), and the ’153 EP Patent (UK). Akebia sought permission to appeal to the UK Supreme Court, which was granted on October 3, 2022. Hearing for the appeal is scheduled for March 5-7, 2024. We do not expect the UK Court of Appeal’s judgment to have any effect on our commercialization of vadadustat in the UK because the patents expired in December 2022.

Stockholder Litigation Relating to the Merger

On June 28, 2018, we entered into an Agreement and Plan of Merger with Keryx and Alpha Therapeutics Merger Sub, Inc., or the Merger Sub, pursuant to which the Merger Sub would merge with and into Keryx, with Keryx becoming a wholly owned subsidiary of ours, or the Merger. On December 12, 2018, we completed the Merger.

On July 15, 2021, a purported former Keryx stockholder filed a putative class action in the Supreme Court of the State of New York against Akebia, a current officer of Akebia (John P. Butler), a former officer of Akebia (Jason A. Amello), former directors of Akebia (Muneer A. Satter, Scott A. Canute, Michael D. Clayman, Maxine Gowen, Duane Nash, Ronald C. Renaud, Jr., and Michael S. Wyzga), a current director of Akebia (Cynthia Smith), a former director and officer of Keryx (Jodie P. Morrison), a former officer of Keryx (Scott A. Holmes) and former directors of Keryx (Michael Rogers, Kevin J. Cameron, Steven C. Gilman, Daniel P. Regan, Mark J. Enyedy, and Michael T. Heffernan, some of whom are current members of our Board of Directors). The action is captioned Loper v. Akebia Therapeutics, Inc., et al., or the *Loper* Action. The complaint in the *Loper* Action alleges that the registration statement filed in connection with the Merger contained allegedly false and misleading statements or failed to disclose certain allegedly material information in violation of Section 11, 12(a)(2), and 15 of the Securities Act of 1933, as amended. It alleges, among other things, that Akebia failed to disclose heightened safety risks that allegedly threatened the prospects of the Phase 3 PRO2TECT clinical trial and the commercial viability of vadadustat. The complaint in the *Loper* Action seeks damages including interest thereon, an award of plaintiffs' and the class's costs and expenses, including counsel fees and expert fees, and rescission, disgorgement, or such other equitable or injunctive relief that the Court deems appropriate.

On August 16, 2021, another purported former Keryx stockholder filed a putative class action making substantially similar allegations and asserting the same claims as the *Loper* Action, also in the Supreme Court of the State of New York against Akebia and many of the same individual defendants named in the *Loper* Action. The action is captioned Panicho v. Akebia Therapeutics, Inc., et al., or the *Panicho* Action.

On September 13, 2021, the parties in the *Loper* Action and *Panicho* Action entered into a joint stipulation and proposed order, which provided for the consolidation of the two actions under the caption In re Akebia Therapeutics, Inc. Securities Litigation, or the Consolidated State Action. On October 27, 2021, plaintiffs filed a consolidated complaint in the Consolidated State Action. On January 10, 2022, defendants moved to dismiss the consolidated complaint in its entirety. Briefing on defendants' motion to dismiss was completed on April 22, 2022. Oral argument was held on October 7, 2022, and the Court dismissed the complaint without prejudice on October 17, 2022, giving plaintiffs thirty days to amend their complaint. On November 16, 2022, plaintiffs filed an amended consolidated complaint, asserting the same claims and seeking the same relief as the consolidated complaint. On January 18, 2023, defendants moved to dismiss the amended consolidated complaint in its entirety, and the plaintiffs filed their opposition on March 6, 2023. Briefing on defendants' motion to dismiss is scheduled to be completed by April 5, 2023.

We deny any allegations of wrongdoing and intend to continue vigorously defending against the one active stockholder lawsuit described in this Legal Proceedings section, the Consolidated State Action. There is no assurance, however, that we will be successful in the defense of this action, or any associated appeals, or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of this action. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible losses at this time. A resolution of the Consolidated State Action in a manner adverse to us, however, could have a material effect on our financial position and results of operations in the period in which the action is resolved.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is traded on The Nasdaq Capital Market under the symbol "AKBA".

Holders

At February 17, 2023, there were approximately 28 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. In addition, the terms of our loan agreement with funds managed by Pharmakon Advisors, LP preclude us from paying cash dividends and future debt agreements may preclude us from paying cash dividends. Payment of future dividends, if any, on our common stock will be at the discretion of our Board of Directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

Issuer Purchases of Equity Securities

None.

Recent Sales of Unregistered Securities

None.

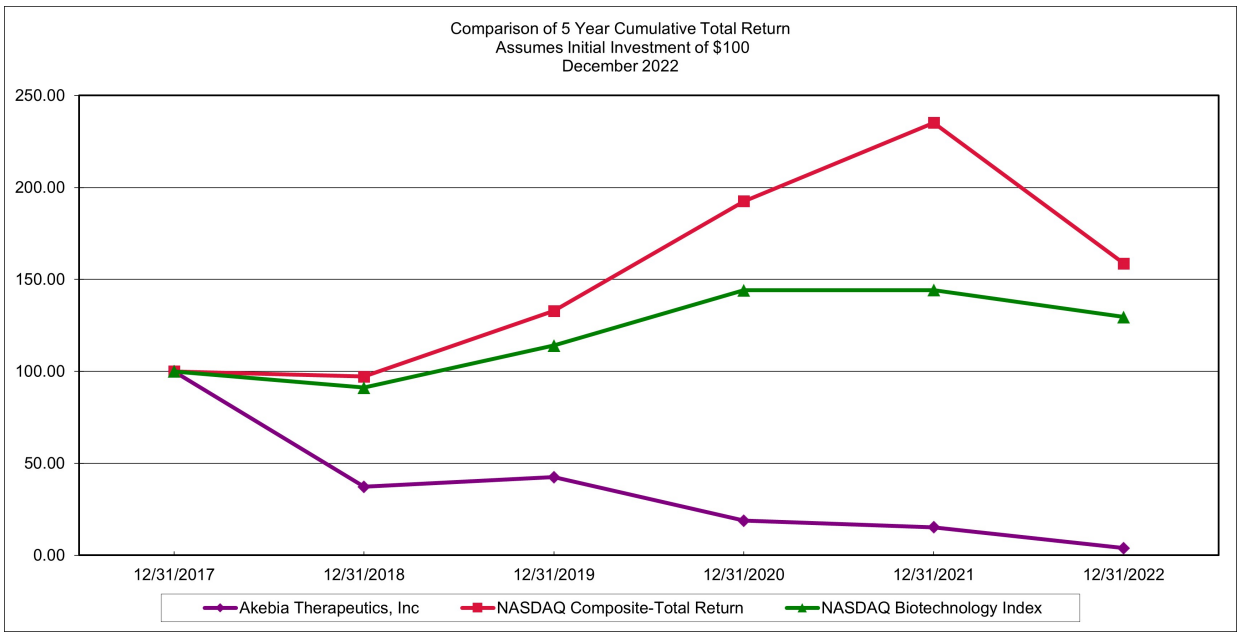
Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or "filed" with the SEC or subject to Regulation 14A or 14C, or to the liabilities of Section 18 of the Exchange Act, except to the extent that we specifically request that this information be treated as soliciting material or we specifically incorporate it by reference into a filing under the Securities Act of 1933, as amended, or the Exchange Act.

Set forth below is a graph* comparing the total cumulative returns of Akebia Therapeutics, Inc., the Nasdaq** Composite Index and the Nasdaq Biotechnology Index. The graph assumes $100 was invested on December 31, 2017 in our common stock and each of the indices and that all dividends, if any, are reinvested. The performance shown represents past performance and should not be considered an indication of future performance.



*Prepared by Zack's Investment Research, Inc. Used with permission. All rights reserved. Copyright 1980-2023

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Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12, Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters, of this Annual Report on Form 10-K.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve significant risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also refer to the section under the heading "Note Regarding Forward-Looking Statements."

Business Overview

We are a fully integrated biopharmaceutical company committed to addressing patients' unmet needs. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative therapeutics that we believe serves as a foundation for future growth. Our purpose is to better the life of each person impacted by kidney disease, and we have established ourselves as a leader in the kidney community. We believe our demonstrated ability to deliver value broadly to the kidney community has enabled us to build a sustainable company. While our current focus centers on people living with kidney disease, we believe our continued commitment to our products and pipeline assets, focusing on all patients who can realize a meaningful benefit from our medicines, will result in delivering value for shareholders.

Our current portfolio includes:

- ***Auryxia® (ferric citrate)***, a medicine approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with dialysis dependent chronic kidney disease, or DD-CKD, or the

Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with non-dialysis-dependent chronic kidney disease, or NDD-CKD. The product is also available in Japan and Taiwan.

- ***Vafseo™ (vadadustat)***, an oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor, is approved in Japan for the treatment of anemia due to chronic kidney disease, or CKD, in adult patients. Vadadustat is under regulatory review for the treatment of anemia due to CKD in Europe, where it has received a positive opinion from the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA, in adult patients on dialysis. Vadadustat is also under regulatory review for the treatment of anemia due to CKD in Australia, Korea, Taiwan and other countries. We continue to pursue a path to potentially gain approval for vadadustat in the U.S. Further, we have several lifecycle management and indication expansion opportunities currently under evaluation or in development for vadadustat.
- ***HIF-PH inhibitors*** in preclinical development. The discovery of hypoxia-inducible factor, or HIF, laid the foundation to explore the central role of oxygen sensing in many diseases. As we have seen through the development of vadadustat as a treatment for anemia due to CKD, when stabilized, HIF triggers wide-ranging adaptive, protective responses during hypoxic or ischemic conditions. Our clinical team and research scientists are eager to further develop HIF-PH inhibitors for various indications including acute kidney injury, or AKI, and retinopathy of prematurity, or ROP.

We continue to explore additional commercial and development opportunities to expand our pipeline and portfolio of novel therapeutics through both internal research and external innovation to leverage our fully integrated team.

Auryxia

Today we market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Auryxia is a non-calcium, non-chewable, orally administered tablet that was approved for marketing by the U.S. Food and Drug Administration, or FDA, in September 2014 as a phosphate binder for the Hyperphosphatemia Indication and was commercially launched in the United States shortly thereafter. In November 2017, Auryxia received marketing approval from the FDA for a second indication, the treatment of iron deficiency anemia, and was commercially launched for this indication in the United States shortly thereafter. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize ferric citrate hydrate as Riona® in Japan. Averoa SAS, or Averoa, has an exclusive license to develop and commercialize ferric citrate in the European Economic Area, or EEA, Turkey, Switzerland and the United Kingdom.

In 2022, Auryxia product revenue increased approximately 24.5% over 2021 due to the company's focus on implementing a new contracting strategy in late 2021. Since 2018, Auryxia product revenue has grown at a compounded annual growth rate of approximately 17% due to market share gains and improved net price per pill, despite a 13% decline in total prescriptions for phosphate binders in the United States since 2018.

Vadadustat

We are seeking regulatory approval in the European Union and the United States for vadadustat as an oral treatment of anemia in adult DD-CKD patients. We and Mitsubishi Tanabe Pharma Corporation, or MTPC, are also seeking regulatory approval for vadadustat as a treatment for anemia in adult DD-CKD and NDD-CKD patients in the United Kingdom, Switzerland and Australia, and Korea and Taiwan, respectively.

Vadadustat is currently pending an European Commission, or EC, approval decision. On February 23, 2023, the CHMP of the EMA adopted a positive opinion recommending the EC approve Vafseo™ for the treatment of symptomatic anemia associated with CKD in adults on chronic maintenance dialysis. We anticipate that the EC will issue a decision on the marketing authorization for Vafseo in May 2023, which would be applicable to all 27 European Union member states and Iceland, Norway and Liechtenstein. Following the termination of our U.S. and international collaboration agreements with Otsuka in June 2022, we regained full rights to vadadustat in Europe, Australia, China, Canada, Latin America, the Middle East and Russia. As we do not have a commercial presence in Europe, we are seeking a partner in Europe and will support the partner's launch of vadadustat, if approved. We are seeking to identify and secure a partner that can effectively facilitate treatment of as many people as would benefit from vadadustat, if approved, thus maximizing the value of the asset.

We submitted a New Drug Application, or NDA, to the FDA for vadadustat in March of 2021. On March 29, 2022, the FDA issued a complete response letter, or CRL, to our NDA for vadadustat. The FDA concluded that the data in the NDA do not

support a favorable benefit-risk assessment of vadadustat for dialysis and non-dialysis patients. The FDA expressed safety concerns noting failure to meet non-inferiority in MACE in the non-dialysis patient population, the increased risk of thromboembolic events, driven by vascular access thrombosis in dialysis patients, and the risk of drug-induced liver injury. We believe there are compelling data supporting a positive benefit-risk profile for the use of vadadustat broadly in patients with CKD, including non-dialysis patients though we have always remained cautious about receiving a broad label for vadadustat that would extend to non-dialysis patients with anemia due to CKD. As such, we began the process to dispute the FDA ruling, and in October 2022, we submitted a Formal Dispute Resolution Request, or FDRR, with the FDA regarding the CRL, specifically related to DD-CKD adult patients. The appeal focused on the favorable balance of the benefits and risks of vadadustat for the treatment of adult DD-CKD patients in light of safety concerns expressed by the FDA in the CRL related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR, which is still under consideration by the FDA at the time of this filing.

Following the termination of our collaboration agreement with Otsuka Pharmaceutical Co. Ltd., or Otsuka, we own full rights to vadadustat in the U.S., subject to our licensing agreement with Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor. If we obtain FDA approval of vadadustat for DD-CKD adult patients, we plan to commercialize vadadustat in the United States with CSL Vifor.

Leveraging our learnings from the research and development of vadadustat, and a breadth of scientific expertise on the HIF pathway, we believe there is potential to leverage HIFs to treat other hypoxic conditions and to explore the use of HIFs in acute settings. We believe this potential applies to vadadustat as well as other preclinical assets we are internally developing.

Regarding broader uses of vadadustat, in July 2020 we partially funded an investigator-sponsored clinical study conducted by The University of Texas Health Science Center at Houston, or UTHealth, in Houston, Texas, evaluating the use of vadadustat as a potential therapy to prevent and treat acute respiratory distress syndrome, or ARDS, in adult patients who have been hospitalized due to COVID-19 and hypoxemia (O2 saturation ≤94%). The study was a phase 2, randomized, double-blind, placebo-controlled trial that measured the proportion of patients who had scores of 6, 7, or 8 on the National Institute of Allergy and Infectious Disease Ordinal Scale, or NIAID-OS, at Day 7 and Day 14, with Day 14 being the primary endpoint. While the study missed the primary endpoint, the data, detailed in the Clinical Development Program section, were encouraging. For reference, subjects receiving vadadustat demonstrated 94% probability for conferring benefit on the NIAID-OS at Day 14, slightly below the primary superiority threshold of >95% probability. We believe vadadustat has the potential to prevent the worsening of ARDS more broadly since the mechanism underlying the benefits are not specific to COVID-19, and we will further explore vadadustat in an acute care setting.

Operating Overview

We have incurred net losses in each year since inception. Our net losses were $92.6 million, $282.8 million and $383.5 million for the years ended December 31, 2022, 2021 and 2020, respectively. Substantially all of our net losses resulted from costs incurred in connection with the continued commercialization of Auryxia and development efforts relating to vadadustat, including conducting clinical trials of, and seeking regulatory approval for, vadadustat, providing general and administrative support for these operations and protecting our intellectual property.

Our ability to achieve profitability depends in part on our ability to manage our expenses. Following receipt of the CRL, in April 2022 and May 2022, we implemented a reduction of our workforce by approximately 42% across all areas of our company including several members of management (47% inclusive of the closing of the majority of open positions). These actions reflect our determination to refocus our strategic priorities around our commercial product, Auryxia®, and our development portfolio, and are steps in a cost savings plan to significantly reduce our expense profile. The workforce reduction included net charges totaling approximately $14.5 million, including costs for one-time termination benefits and contractual termination benefits for severance, healthcare, and related benefits of $11.3 million and non-cash stock-based compensation expense of $3.2 million. On November 7, 2022, we implemented a further reduction in workforce by approximately 14% consisting solely of individuals within the commercial organization as a result of our decision to shift to a strategic account management focused model for our commercial efforts. The workforce reduction included net charges totaling approximately $1.4 million, primarily related to one-time and contractual termination benefits including severance, non-cash stock-based compensation expense, healthcare and related benefits in the fourth quarter of 2022. During the year ended December 31, 2022, we recognized an aggregate of $15.9 million of restructuring charges in the consolidated statement of operations and comprehensive loss. See Note 5 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for further details of the reductions in workforce.

We expect to continue to incur additional operating expenses, including additional research and development expenses to our pipeline, additional costs related to vadadustat, and research and development and selling, general and administrative expenses

for ongoing development and commercialization of Auryxia, which could lead to operating losses for the foreseeable future. In addition to any additional costs not currently contemplated due to the events associated with or resulting from the workforce reductions noted above, our ability to achieve profitability and our financial position will depend, in part, on the rate of our future expenditures, on our product revenue from Auryxia, our collaboration revenue, our ability to successfully implement cost avoidance measures and reduce overhead costs and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- continue our commercialization activities for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product or product candidate, including those that may be in-licensed or acquired;
- address the issues identified in the CRL for vadadustat that we received from the FDA and pursue our appeal of the CRL for vadadustat with the FDA;
- conduct and enroll patients in any clinical trials, including post-marketing studies or any other clinical trials for Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired;
- maintain marketing approvals for Auryxia and vadadustat, if we are able to obtain marketing approval for vadadustat following receipt of the CRL from the FDA in March 2022, and any other product, including those that may be in-licensed or acquired;
- manufacture Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, for commercial sale and clinical trials;
- conduct discovery and development activities for additional product candidates or platforms that may lead to the discovery of additional product candidates;
- engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would market and develop commercial products, or develop and commercialize other product candidates and technologies;
- continue to repay, and pay any associated pre-payment penalties, if applicable, the senior secured term loans in an aggregate principal amount of $67.0 million as of December 31, 2022, or the Term Loans, that were made available to us pursuant to the Loan Agreement;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- make decisions with respect to our personnel, including the retention of key employees;
- make decisions with respect to our infrastructure, including to support our operations as a fully integrated publicly traded biopharmaceutical company; and
- experience any additional delays or encounter issues with any of the above.

We have not generated, and may not generate, enough product revenue to realize net profits from product sales. We have no manufacturing facilities, and all of our manufacturing activities are contracted out to third parties. Additionally, we currently utilize contract research organizations, or CROs, to carry out our clinical development activities. If we obtain marketing approval for vadadustat, and as we continue to commercialize Auryxia, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, royalty transactions, strategic transactions, or a combination of these approaches. If we are unable to raise additional capital in sufficient amounts when needed or on attractive terms, we may not be able to pursue development and commercial activities related to Auryxia and vadadustat, if approved, or any additional products and product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

From inception through December 31, 2022, we raised approximately $793.5 million of net proceeds from the sale of equity, including $519.8 million from various underwritten public offerings, $223.7 million from at-the-market offerings, or ATM offerings, pursuant to prior sales agreements with Cantor Fitzgerald & Co., and $70.0 million from the sale of 7,571,429 shares of common stock to CSL Vifor. As of December 31, 2022, through our collaboration agreement with MTPC and our prior collaboration agreements with Otsuka, we received approximately $837.1 million in cost-share funding, and are not entitled to

receive any additional cost-share funding. On June 30, 2022, we entered into a Termination and Settlement Agreement, or the Termination Agreement, with Otsuka, pursuant to which we received a nonrefundable and non-creditable payment of $55.0 million in consideration for the covenants and agreements set forth in the Termination Agreement.

On November 11, 2019, we entered into a loan agreement, or the Loan Agreement, with funds managed by Pharmakon Advisors LP, or Pharmakon, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in two tranches, subject to certain terms and conditions, or the Term Loans. On July 15, 2022, or the Effective Date, we entered into the Second Amendment and Waiver with BioPharma Credit PLC, or the Collateral Agent, BPCR Limited Partnership, as a Lender, and BioPharma Credit Investments V (Master) LP, as a Lender, or the Second Amendment and Waiver, which amends and waives certain provisions of the Loan Agreement as amended by the First Amendment and Waiver between the Collateral Agent, the Lenders and us, dated February 18, 2022. The Collateral Agent and the Lenders are collectively referred to as Pharmakon. Pursuant to the Second Amendment and Waiver, we made prepayments totaling $25.0 million together with a prepayment premium of $0.5 million plus all accrued and unpaid interest on such prepayments of principal to the Effective Date, and Pharmakon agreed to waive or modify certain covenants in the Loan Agreement. In addition, on February 25, 2021, we received an upfront payment of $44.8 million (net of certain transaction expenses) in connection with our sale to HealthCare Royalty Partners IV, L.P., or HCR, of the right to receive all royalties and sales milestones payable to us under our collaboration agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions described in Note 6 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K. Finally, on February 18, 2022, we entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement, with CSL Vifor. Pursuant to the Vifor Second Amended Agreement, CSL Vifor made an upfront payment to us of $25.0 million in lieu of the previously disclosed milestone payment of $25.0 million that CSL Vifor was to pay to us following approval of vadadustat by the FDA. Also pursuant to the Vifor Second Amended Agreement, Vifor contributed $40 million to a working capital fund established to partially fund our costs of purchasing vadadustat from our contract manufacturers, or the Working Capital Fund, which amount of funding will fluctuate, and which funding we are required to repay to CSL Vifor over time.

Impacts of COVID-19 Pandemic

The COVID-19 pandemic has presented a substantial public health and economic challenge around the world and continues to affect our patients, healthcare providers with whom we interact, customers, collaboration partners, CROs, contract manufacturing organizations, or CMOs, vendors, communities and business operations.

We believe our revenue growth was negatively impacted by the COVID-19 pandemic in 2021 and 2022 primarily as the CKD patient populations that we serve experienced both high hospitalization and mortality rates due to COVID-19, and the pandemic had an adverse impact on the phosphate binder market in which Auryxia competes. Labor shortages and costs have adversely impacted dialysis providers. These impacts have refocused clinical efforts in addressing bone and mineral disorders like hyperphosphatemia to more acute operational issues to ensure patients receive dialysis treatments and still some patients have been rescheduled or missed treatments due to labor shortages. We believe, this and potentially other factors, has led to the reduction in the phosphate binder market, which has not experienced growth since early 2020. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, the COVID-19 pandemic and the ongoing impacts from the COVID-19 pandemic continue to adversely and disproportionately impact CKD patients and the phosphate binder market; therefore, we expect the COVID-19 pandemic and the ongoing impacts from the pandemic to continue to have a negative impact on our revenue growth for the foreseeable future.

In addition, several healthcare facilities have previously restricted access for non-patients, including the members of our sales force. For example, DaVita, Inc., or DaVita, and Fresenius Medical Care, or Fresenius, which account for a vast majority of the dialysis population in the United States, have previously restricted access to their clinics. As a result, we continue to engage with some healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers have, and could continue to, negatively impact our access to healthcare providers and, ultimately, our sales, including with respect to vadadustat, if approved. Recently, such precautionary measures have been relaxed at certain healthcare facilities and, as a result, members of our sales force have resumed in person interactions with certain customers. Nevertheless, some restrictions remain, and more restrictions may be put in place again due to a resurgence in COVID-19 cases, including those involving new variants of COVID-19 which may be more contagious and more severe than prior strains of the virus. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand in the United States for Auryxia and will be for vadadustat, if approved, including the potential for further declines or changes in prescription trends and customer orders, which could have a material adverse effect on our business, results of operations and financial condition.

In addition, the direct and indirect impacts of the pandemic or the response efforts to the pandemic, including, among others, competition for labor and resources and increases in labor, sourcing, manufacturing and shipping costs, may cause disruptions to, closures of, or other impacts on our CMOs and other vendors in our supply chain on which we rely for the supply of our

products and product candidates. For example, areas of China have recently continued to implement lockdowns for COVID-19, which could impact the global supply chain. At this time, our third party contract manufacturers continue to operate at or near normal levels. However, it is possible that the COVID-19 pandemic and response efforts may have an impact in the future on our contract manufacturers' ability to manufacture and deliver Auryxia and vadadustat (if approved in the United States and EMA and which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in increased costs and delays, or disruptions to the manufacturing and supply of our products and product candidates.

COVID-19 pandemic precautions have caused moderate delays in enrolling new clinical trials and may cause delays in enrolling other new clinical trials. We are using remote monitoring and central monitoring, where possible.

This uncertain pandemic environment has presented new risks to our business. While we are working aggressively to mitigate the impacts on our business, we are mindful that many of these risks and the impact to the larger healthcare market are outside of our control.

For additional information on the various risks posed by the COVID-19 pandemic, please refer to Part I, Item 1A. Risk Factors.

Financial Overview

Revenue

To date, our revenues have been derived from product revenue from commercial sales of Auryxia, collaboration revenues, which include license and milestone payments, royalty and cost-sharing revenue generated through collaboration and license agreements with partners for the development and commercialization of vadadustat, a nonrefundable, non-creditable termination fee pursuant to the terms of the Termination Agreement with Otsuka, and royalty revenue from sales of Riona in Japan. Cost-sharing revenue represents amounts reimbursed by our collaboration partners for expenses incurred by us for research and development activities and, potentially, co-promotion activities, under our collaboration agreements.

We expect our revenue to continue to be generated primarily from our commercial sales of Auryxia, our collaborations with MTPC and Japan Tobacco, Inc., and its subsidiary, Torii Pharmaceutical Co., Ltd., collectively JT and Torii, and any other collaborations into which we may enter. We will not recognize any future revenue pursuant to our former collaboration with Otsuka.

Cost of Goods Sold

Cost of goods sold includes direct costs to manufacture commercial drug substance and drug product for Auryxia, as well as indirect costs, including costs for packaging, shipping, insurance and quality assurance, idle capacity charges, write-offs for inventory that fails to meet specifications or is otherwise no longer suitable for commercial sale, changes in our excess purchase commitment liability, and royalties due to the licensor of Auryxia related to U.S. and Japan product sales recognized during the period. Cost of goods sold also includes costs to manufacture drug product provided to MTPC for commercial sale of Vafseo in Japan.

As a result of the Merger and the application of purchase accounting, costs of goods sold also includes both amortization expense and, if applicable, impairment charges associated with the fair value of the developed product rights for Auryxia as well as expense associated with the fair value inventory step-up. The fair value of the developed product rights for Auryxia is being amortized over its estimated useful life, which as of December 31, 2022 is estimated to be six years. The fair value inventory step-up as a result of the Merger was fully amortized as of the first quarter of 2021.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of vadadustat, which include:

- personnel-related expenses, including salaries, benefits, recruiting fees, travel and stock-based compensation expense of our research and development personnel;
- expenses incurred under agreements with CROs and investigative sites that conduct our clinical trials;
- the cost of acquiring, developing and manufacturing clinical study materials through CMOs;
- facilities, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other supplies;
- costs associated with preclinical, clinical and regulatory activities; and

- costs associated with pre-launch inventory build for vadadustat in the United States and Europe, for which we received the CRL from the FDA in the United States in March 2022.

Research and development costs are expensed as incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and our clinical sites.

We cannot determine with certainty the duration and completion costs of current or future clinical trials of Auryxia and vadadustat or if, when, or to what extent we will receive marketing approval for vadadustat or generate revenue from the commercialization and sale of vadadustat, if approved. We may never succeed in achieving marketing approval for vadadustat.

The duration, costs and timing of clinical trials and development of Auryxia and vadadustat will depend on a variety of factors including, but not limited to, those described in Part I, Item 1A. Risk Factors. A change in the outcome of any of these variables with respect to the development of Auryxia and vadadustat could mean a significant change in the costs and timing associated with that development. For example, if the FDA, the EMA, or other regulatory authorities were to require us to conduct clinical trials in addition to or different from those that we currently anticipate, or if we experience delays in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

From inception through December 31, 2022, we have incurred $1.6 billion in research and development expenses. We expect to have significant research and development expenditures for the foreseeable future as we continue the development of Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired.

Our direct research and development expenses consist principally of external costs, such as fees paid to clinical trial sites, consultants, central laboratories and CROs in connection with our clinical trials, and drug substance and drug product manufacturing for clinical trials.

In 2020, we completed our global Phase 3 clinical program for vadadustat to which the majority of our research and development costs are attributable. A significant portion of our research and development costs have been external costs, which we track on a program-by-program basis. These external costs include fees paid to investigators, consultants, central laboratories and CROs in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials. Our internal research and development costs are primarily personnel-related costs, depreciation and other indirect costs. We do not track our internal research and development expenses on a program-by-program basis as they are deployed across multiple projects under development.

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for the years ended December 31, 2022 and 2021:

	Year ended December 31,	
	2022	2021
	(in thousands)	
Vadadustat external costs	$ 58,107	$ 48,506
External costs for other programs	21,228	25,907
Total external research and development expenses	79,335	74,413
Headcount, consulting, facilities and other	49,779	73,439
Total research and development expenses	$ 129,114	$ 147,852

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and related costs for personnel, including stock-based compensation and travel expenses for our commercial personnel, including our field sales force and other commercial support personnel, as well as personnel in executive and other administrative or non-research and development functions. Other selling, general and administrative expenses include facility-related costs, fees for directors, accounting and legal services fees, recruiting fees and expenses associated with obtaining and maintaining patents.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

	Year ended December 31,		
	2022	2021	Increase (Decrease)
	(In Thousands)		
Revenues:			
Product revenue, net	$ 177,067	$ 142,216	$ 34,851
License, collaboration and other revenue	115,535	71,362	44,173
Total revenues	292,602	213,578	79,024
Cost of goods sold:			
Product	48,754	117,352	(68,598)
Amortization of intangibles	36,042	36,042	—
Total cost of goods sold	84,796	153,394	(68,598)
Operating expenses:			
Research and development	129,114	147,852	(18,738)
Selling, general and administrative	138,699	174,161	(35,462)
License expense	3,175	3,489	(314)
Restructuring	15,933	—	15,933
Total operating expenses	286,921	325,502	(38,581)
Operating loss	(79,115)	(265,318)	186,203
Other expense, net	(12,541)	(17,522)	4,981
Loss on extinguishment of debt	(906)	—	(906)
Net loss before income taxes	(92,562)	(282,840)	190,278
Benefit from income taxes	—	—	—
Net loss	$ (92,562)	$ (282,840)	$ 190,278

Product Revenue, Net. Net product revenue is derived from sales of our only commercial product in the United States, Auryxia. We distribute our product principally through a limited number of wholesale distributors as well as certain specialty pharmacy providers. Net product revenue was $177.1 million for the year ended December 31, 2022, compared to net product revenue of $142.2 million for the year ended December 31, 2021. The increase was primarily due to pricing, improved payor mix, and a 2022 year-end inventory build by a customer that exceeded 2021, partially offset by a decline in volume during 2022.

License, Collaboration and Other Revenue. License, collaboration and other revenue was $115.5 million for the year ended December 31, 2022, compared to $71.4 million for the year ended December 31, 2021. On June 30, 2022, we and Otsuka entered into the Termination Agreement, which, among other things, terminated the cost sharing arrangement under the Otsuka collaboration agreement for the United States, or the Otsuka U.S. Agreement and the Otsuka collaboration agreement for certain territories outside of the United States, or the Otsuka International Agreement. During the year ended December 31, 2022, we recognized $55.0 million in collaboration revenue related to a payment received pursuant to the terms of the Termination Agreement with Otsuka, $15.5 million related to previously deferred revenue as of the date of termination and $9.6 million of non-cash consideration related to Otsuka's obligations to complete certain agreed upon clinical activities related to the Phase 3b clinical trial of vadadustat Otsuka is conducting, in accordance with the current study protocol, at its own cost and expense. We also recognized $19.1 million in collaboration revenue for the year ended December 31, 2022 from the Otsuka U.S. Agreement and the Otsuka International Agreement prior to the termination. We also recognized royalty revenue under the MTPC Agreement, and revenue under our supply agreement with MTPC, or the MTPC Supply Agreement, totaling $18.0 million. On December 16, 2022, we, MTPC, and Esteve Química, S.A., or Esteve, executed an Assignment of Supply Agreement, or the Assignment Agreement, pursuant to which the supply agreement between us and Esteve, or the Esteve Agreement, was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Esteve Agreement to MTPC, including the obligations under certain purchase orders issued by us and accepted by Esteve. Therefore, we expect significantly less revenue in the future under the MTPC Supply Agreement. We recognized $65.5 million in collaboration revenue for the year ended December 31, 2021 from the Otsuka U.S. Agreement and the Otsuka International Agreement, royalty revenue earned under the MTPC Agreement, and revenue under our Supply Agreement with MTPC.

Cost of Goods Sold - Product. Cost of goods sold of $48.8 million for the year ended December 31, 2022 primarily consisted of costs associated with the manufacturing of Auryxia and supply of Vafseo to MTPC for commercial sale in Japan, $28.7 million

in termination fees in connection with the BioVectra Termination Agreement in the fourth quarter of 2022, and $30.2 million primarily related to inventory reserves associated with drug substance that will not be forward processed into drug product. These costs were offset by a non-cash reduction of our excess purchase commitment liability of $67.6 million driven by the reduction in purchase commitments due to execution of the Termination Agreement with BioVectra. See Note 15 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K for further details of the BioVectra termination fees and decrease to the liability for excess purchase commitments.

Cost of goods sold of $117.4 million for the year ended December 31, 2021 primarily consisted of costs associated with the manufacturing of Auryxia and supply of Vafseo to MTPC for commercial sale in Japan, $33.4 million in non-cash charges related to our excess purchase commitment liability, $21.6 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, and $15.6 million primarily related to excess and obsolescence reserves associated with Auryxia as well as inventory reserves associated with a previously disclosed manufacturing quality issue related to Auryxia.

Cost of Goods Sold - Amortization of Intangibles. Amortization of intangibles relates to the acquired developed product rights for Auryxia, which is being amortized using a straight-line method over its estimated useful life of approximately six years. Amortization of intangibles during each of the years ended December 31, 2022 and 2021 was $36.0 million.

Research and Development Expenses. Research and development expenses were $129.1 million for the year ended December 31, 2022, compared to $147.9 million for the year ended December 31, 2021. The net decrease of $18.7 million was due to the following changes as compared to the year ended December 31, 2021:

	(in millions)
Vadadustat external development expenses	$ 9.6
Headcount, consulting, facilities and other	(28.3)
Total net decrease	$ (18.7)

The decrease in research and development expense was primarily due to decreased headcount related costs as a result of the April 2022 reduction in force, decreased consulting costs, and decreased outsourced contract services. Also during the year ended December 31, 2021, we made an upfront payment of $3.0 million to Cyclerion for an exclusive global license to develop and commercialize praliciguat, an investigational oral sGC stimulator, which was recorded to research and development expense which did not reoccur during the year ended December 31, 2022. Although we expect our research and development expenses to continue to decrease in the near term, we will continue to incur significant research and development expenses in future periods in support of ongoing or planned studies with respect to Auryxia and vadadustat and development of other product candidates.

Selling, General and Administrative Expenses. Selling, general and administrative expenses were $138.7 million for the year ended December 31, 2022, compared to $174.2 million for the year ended December 31, 2021. The decrease of $35.5 million was primarily due to decreased headcount related costs as a result of both the April 2022 and November 2022 reductions in force, decreased one-time legal costs, and lower marketing expenses following receipt of the CRL for vadadustat. We expect our selling, general and administrative expenses to continue to decrease as we reduce our expense profile.

License Expenses. License expense related to royalties due to Panion relating to sales of Riona in Japan were $3.2 million and $3.5 million for the years ended December 31, 2022 and 2021, respectively.

Restructuring. Restructuring expenses were $15.9 million for the year ended December 31, 2022 due to one-time termination benefits and contractual termination benefits for severance, healthcare, and non-cash stock-based compensation related to the April 2022 and November 2022 reductions in force. There were no restructuring expenses for the year ended December 31, 2021.

Other Expense, Net. Other expense, net, was $12.5 million for the year ended December 31, 2022, compared to $17.5 million for the year ended December 31, 2021. The decrease was primarily due to a decrease in interest expense as a result of principal prepayments totaling $25.0 million made on the Term Loans pursuant to the Second Amendment and Waiver in the year ended December 31, 2022, as well as an additional $8.0 million of quarterly principal payments made on the Term Loans pursuant to the Loan Agreement with Pharmakon, reducing our outstanding balance on the Term Loans. The decrease was also related to a decrease in the fair value of our derivative liability related to the Loan Agreement with Pharmakon during the year ended December 31, 2022.

Loss on Extinguishment of Debt. During the year ended December 31, 2022, we recorded a debt extinguishment loss of $0.9 million related to the principal prepayments made on the Term Loans pursuant to the Second Amendment and Waiver.

Comparison of the Years Ended December 31, 2021 and 2020

For discussion of our 2021 results and a comparison with 2020 results please refer to Part II, Item 7, "Management's Discussion and Analysis of Financial Conditions and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 that was filed with the SEC on March 1, 2022, or the 2021 Form 10-K.

Liquidity and Capital Resources

We have funded our operations principally through sales of our common stock, payments received from our collaboration partners, product sales, debt, a royalty transaction, and a refund liability to a customer. As of December 31, 2022, we had cash and cash equivalents of approximately $90.5 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. On April 7, 2022, we entered into an Open Market Sale Agreement℠, or the Sales Agreement, with Jefferies LLC, or Jefferies, as agent, for the offer and sale of common stock at current market prices in amounts to be determined from time to time. Also, on April 7, 2022, we filed a prospectus supplement relating to the Sales Agreement, pursuant to which we are able to offer and sell under the Sales Agreement up to $26.0 million of our common stock at current market prices from time to time. From the date of filing of the prospectus supplement through the date of the filing of this Annual Report on Form 10-K, we have not sold any shares of our common stock under this program. As of December 31, 2022, through our collaboration agreements with Otsuka and MTPC we received approximately $837.1 million in cost-share funding, and are not entitled to receive any additional cost-share funding.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods set forth below:

	Year ended December 31,		
	2022	2021	2020
	(In Thousands)		
Net cash provided by (used in):			
Operating activities	$ (73,154)	$ (252,965)	$ (110,388)
Investing activities	(114)	39,941	(40,004)
Financing activities	14,598	133,731	231,720
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (58,670)	$ (79,293)	$ 81,328

Operating Activities. Net cash used in operating activities during the year ended December 31, 2022 was $73.2 million as compared to $253.0 million for the year ended December 31, 2021. The decrease in cash used was primarily due to a lower net loss driven by increased revenue as well as decreased operating expenses. The decrease in cash used was also due to lower accounts receivable and decreased inventory purchases. This was partially offset by payments made related to the reductions in force as well as decreases in accounts payable and accrued expenses.

Net cash used in operating activities during the year ended December 31, 2021 of $253.0 million was largely driven by net payroll-related expenses, rebate payments and payments for inventory.

Investing Activities. Net cash used in investing activities during the year ended December 31, 2022 of $0.1 million was comprised of purchases of equipment.

Net cash provided by investing activities during the year ended December 31, 2021 of $39.9 million was comprised of proceeds from the maturities of available for sale securities of $40.0 million, partially offset by immaterial purchases of equipment.

Financing Activities. Net cash provided by financing activities for the year ended December 31, 2022 was $14.6 million and consisted of net proceeds from a refund liability to a customer of $40.0 million, net proceeds from the issuance of common stock of $7.1 million, and proceeds from the sale of stock under our employee stock purchase plan, partially offset by principal payments of debt of $33.0 million.

Net cash provided by financing activities for the year ended December 31, 2021 was $133.7 million and consisted of net proceeds from the sale of future royalties of $44.8 million, net proceeds from the public issuance of common stock in connection with our prior ATM sales agreement of $88.2 million, and proceeds from the exercise of stock options and from the sale of stock under our employee stock purchase plan.

A discussion of changes in our cash flow from the year ended December 31, 2020 to the year ended December 31, 2021 can be found in Part II, Item 7, "Management's Discussion and Analysis of Financial Conditions and Results of Operations" of the 2021 Form 10-K.

Operating Capital Requirements

We have one product, Auryxia, approved for commercial sale in the United States. While we expect to be able to generate positive cash flows from our existing operations, we have not generated, and may not generate, enough product revenue from the sale of Auryxia to realize net profits from product sales. We currently have exclusive rights under a series of patents and patent applications to commercialize Auryxia in the U.S. that currently protect us from generic drug competition until March 2025. Following loss of exclusivity in the U.S., we may not be able realize enough product revenue from sales of Auryxia to realize net profits from product sales after March 2025. We have incurred losses and cumulative negative cash flows from operations in each year since our inception in February 2007, and as of December 31, 2022, we had an accumulated deficit of $1.6 billion. Our current operating plan anticipates continued increasing levels of cash flows from operations. We expect to continue to incur additional research and development expenses related to our pipeline, additional costs related to vadadustat, and research and development and selling, general and administrative expenses for our ongoing development and commercialization of Auryxia.

We expect our cash resources to fund our current operating plan for at least twelve months from the date of this filing. Our operating plan includes the effects of certain cost avoidance measures and the reduction of overhead costs that resulted from the amendment or termination of contractual arrangements with certain supply and collaboration partners and the reduction of operating expenses. During 2022, we implemented certain cost avoidance measures. For example, during the fourth quarter of 2022, we and BioVectra entered into a Termination Agreement, pursuant to which the parties agreed, among other things, to terminate, effective immediately, any and all existing agreements entered into between the parties in connection with the manufacture and supply, by BioVectra to us, of Auryxia drug substance, which eliminated future contractual commitments with this supply partner. We, MTPC, and Esteve also executed an Assignment Agreement, pursuant to which the Supply Agreement between us and Esteve was assigned to MTPC. The Assignment Agreement transferred our rights and obligations under the Supply Agreement to MTPC, specifically including the obligations under certain purchase orders issued by us and accepted by Esteve. In addition, in April, May and November of 2022, the Board of Directors approved reductions of our workforce by a combined total of approximately 56% consisting of individuals across our company. These actions reflect our determination to refocus our strategic priorities and drive revenue around our commercial product, Auryxia®, and our development portfolio, and are steps in a cost savings plan to significantly reduce our expense profile in line with being a single commercial product company (see Note 5 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K). We expect to finance future cash needs through product revenue, potential strategic transactions, public or private equity or debt transactions, expense management, or a combination of these approaches. We plan to reduce our need for future financing through product sales, expense management, and cost avoidance measures in line with being a single commercial product company.

We believe that the execution of further cost avoidance measures, future decisions by the FDA or foreign regulatory agencies related to the potential regulatory approval of vadadustat, and our ability to generate additional value from vadadustat, if approved, through partnerships or other strategic transactions could potentially further extend our cash runway for a period greater than twelve months. However, these future decisions and transactions are not contemplated in our operating plan and are outside of our control. Additionally, with Loss of Exclusivity, or LOE, in March of 2025, we believe the CMS decision to include phosphate binders in the dialysis bundle could potentially lead to higher sales of Auryxia after the LOE date than in other LOE scenarios, and plan to work with payors and providers to continue the use of Auryxia beyond LOE. Assuming we are successful in those endeavors, we will require additional funding to fund our strategic growth beyond Auryxia or to pursue later stage development and commercial activities for our product candidates and any additional product or product candidates, including those that may be in-licensed or acquired.

There can be no assurance that the current operating plan will be achieved in the time frame anticipated by us, or that our cash resources will fund our operating plan for the period of time anticipated by us, or that additional funding will be available on terms acceptable to us, or at all. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves numerous risks and uncertainties, and actual results could vary as a result of a number of factors, many of which are outside our control. We have based this estimate on assumptions that may be substantially different than actual results, and we could utilize our available capital resources sooner than we currently expect. If our operating performance deteriorates significantly from the levels achieved in 2022, it could have an effect on our liquidity and our ability to continue as a going concern in the future. Our future funding requirements, both near- and long-term,

will depend on many factors including, but not limited to, those described under Part I, Item 1A. Risk Factors under the heading "Risks Related to our Financial Position, Need for Additional Capital and Growth Strategy."

Contractual Obligations and Commitments

Leases

We lease approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in November 2020, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to us and did not impact rent payments. In April 2018, we entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12th floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by us was delivered in September 2018 and additional monthly lease payments of approximately $135,000 commenced in February 2019 and are subject to annual rent escalations, which commenced in September 2019. In November 2020, we entered into a Sixth Amendment to the Cambridge Lease, or the Sixth Amendment, to extend the term of the Cambridge Lease with respect to the lab space from November 30, 2021 to January 31, 2025. The Sixth Amendment includes two months of free rent starting in December 2020 and additional monthly lease payments of approximately $48,000 which commenced in December 2021, and is subject to annual rent escalations, which commenced in December 2022.

Additionally, as a result of the Merger, we have a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease. The total monthly lease payments under the Boston Lease are approximately $136,000 and are subject to annual rent escalations. On February 24, 2022, we entered into a First Amendment to Lease, or the First Lease Amendment, with CLPF One Marina Park Drive LLC (successor-in-interest to Fallon Cornerstone One MPD LLC), or the Landlord, amending the Boston Lease. Pursuant to the First Lease Amendment, we agreed to extend the term of the Boston Lease until July 31, 2031. The monthly lease payment pursuant to the First Amendment will be $200,122 commencing on August 1, 2023 and subject to annual rent escalation of approximately 2% commencing on August 1, 2024. The First Lease Amendment also includes a Landlord’s allowance for certain leasehold improvements to the Premises in an amount of up to $1,954,680, provided that such allowance must be used prior to August 1, 2024.

In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., or Foundation. The sublease is subject and subordinate to the Boston Lease between Keryx and the landlord. The term of the sublease commenced on October 16, 2019, upon receipt of the required consent from the landlord for the sublease agreement, and expired on February 27, 2023. Keryx continues to be obligated for all payment terms pursuant to the Boston Lease, and we will guaranty Keryx’s obligations under the sublease.

Term Loans

On November 11, 2019, Akebia, with Keryx as guarantor, entered into a loan agreement, or the Loan Agreement, with BioPharma Credit PLC as collateral agent and a lender, or the Collateral Agent, and BioPharma Credit Investments V (Master) LP as a lender, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to us in two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term Loans, solely in its capacity as a lender, to its affiliate, BPCR Limited Partnership. The Collateral Agent and the lenders are collectively referred to as Pharmakon. The first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. During the twelve months ended December 31, 2022, we made our first quarterly principal payment under the Term Loans of $8.0 million. In addition, on July 15, 2022, pursuant to the Loan Agreement, as amended, we made prepayments totaling $25.0 million together with a prepayment premium of $0.5 million plus all accrued and unpaid interest on such prepayments of principal to the Effective Date, and Pharmakon agreed to waive or modify certain covenants in the Loan Agreement. A more detailed description of the Term Loans can be found in Note 11 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Liability Related to Sale of Future Royalties

On February 25, 2021, we entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HCR, pursuant to which we sold to HCR our right to receive royalties and sales milestones for vadadustat in the MTPC Territory, such payments collectively the Royalty Interest Payments, in each case, payable to us under the MTPC Agreement, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, we will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or we pay the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to us, and HCR would have no further right to any Royalty Interest Payments. We received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and we are eligible to receive an additional $5.0 million in 2023 under the Royalty Agreement if specified annual sales milestones are achieved for vadadustat in the MTPC Territory, subject to the satisfaction of certain customary conditions. We retain the right to receive all potential future regulatory milestones for vadadustat under the MTPC Agreement. A more detailed description of the Royalty Agreement can be found in Note 6 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Refund Liability to Customer

On February 18, 2022, pursuant to the Vifor Second Amended Agreement, CSL Vifor contributed $40.0 million to the Working Capital Fund, established to partially fund our costs of purchasing vadadustat from our contract manufacturers, which amount of funding will fluctuate, and which funding we are required to repay to CSL Vifor over time. The $40.0 million initial contribution to the Working Capital Fund represented 50% of the amount of purchase orders that we had placed with our contract manufacturers for the supply of vadadustat for the United States, or the Territory, already delivered as of the effective date of the Vifor Second Amended Agreement, and to be delivered through the end of 2023.

We have recorded the Working Capital Fund as a refund liability under ASC 606, *Revenue from Contracts with Customers*. We accounted for the refund liability as a debt arrangement with zero coupon interest. We imputed interest on the refund liability to the customer at a rate of 15.0% per annum and recorded an initial discount on the refund liability to the customer and a related deferred gain as of the date the funds were received from CSL Vifor, which was March 18, 2022. The discount on the note payable is being amortized to interest expense using the effective interest method over the expected term of the refund liability. The deferred gain is being amortized to interest income on a straight-line basis over the expected term of the refund liability. A more detailed description of the Working Capital Fund can be found in Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Manufacturing Agreements

As a result of the Merger, our contractual obligations include Keryx's commercial supply agreement with Siegfried Evionnaz SA, or Siegfried, and previously included a commercial supply agreement with BioVectra Inc., or BioVectra, to supply commercial drug substance for Auryxia.

On December 22, 2022, we entered into a Termination Agreement with BioVectra, pursuant to which we and BioVectra agreed, among other things, to terminate, effective immediately, any and all existing agreements entered into between us in connection with the manufacture and supply, by BioVectra to us, of Auryxia drug substance. Under the terms of the BioVectra Termination Agreement, we agreed to pay BioVectra a total of $32.5 million consisting of (i) an upfront payment of $17.5 million and (ii) six quarterly payments of $2.5 million commencing in April 2024. We made the initial payment of $17.5 million in December 2022. In addition, we and BioVectra have released one another from all existing and future claims and liabilities and agreed to return certain materials and documents. Furthermore, as it relates to all open purchase orders, BioVectra is relieved from any obligations to manufacture any product or perform services under any such open purchase orders, and we are relieved from any obligations to purchase any product under such open purchase orders. We are also relieved from any obligations to pay any outstanding purchase orders or invoices related to performance by BioVectra of services and all other obligations under our agreements with BioVectra.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, as amended through December 31, 2022, or the Siegfried Agreement, we have agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The term of the Siegfried Agreement was to expire on December 31, 2022, but was automatically extended into 2023 as a result of Siegfried's updated production schedule for delivery of product originally scheduled for delivery in 2022. The Siegfried Agreement provides us and Siegfried with certain termination rights. As of December 31, 2022, we are required to purchase a minimum quantity of drug substance under the Siegfried Agreement for Auryxia annually at a total cost of approximately $8.4 million through the third quarter of 2023. As of the date of the filing of this Annual Report on Form 10-K, we have amended the Siegfried Agreement pursuant to which, we agreed to extend the term and purchase a minimum quantity of drug substance of Auryxia at a predetermined price as further described in Note 17 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

On April 9, 2019, we entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement included the terms and conditions under which Esteve would manufacture vadadustat drug substance for commercial use. On December 16, 2022, we, MTPC, and Esteve executed an assignment agreement, or the Assignment Agreement, pursuant to which the Esteve Agreement was assigned to MTPC. The Assignment Agreement transferred our rights and obligations under the Esteve Agreement to MTPC, including the obligations under certain purchase orders issued by us and accepted by Esteve. We will have no further obligation to take delivery of, or pay for, product delivered by Esteve under the Esteve Agreement or the transferred purchase orders.

On March 11, 2020, we entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement. The Patheon Agreement includes the terms and conditions under which Patheon will manufacture vadadustat drug product for commercial use. Pursuant to the Patheon Agreement, we provide Patheon a long-term forecast on an annual basis, as well as short-term forecasts on a quarterly basis, or the Patheon Forecast. The Patheon Forecast reflects our needs for commercial supply of vadadustat drug product produced by Patheon, represented as a quantity of drug product per calendar quarter. The parties have agreed to a volume-based pricing structure under the Patheon Agreement. The Patheon Agreement had an initial term beginning March 11, 2020 and ending June 30, 2023 and automatically renews for successive one-year terms unless either party gives the other party eighteen months' prior written notice. The current term of the Patheon Agreement ends June 30, 2025. Pursuant to the Patheon Agreement, we have agreed to purchase a certain percentage of the global demand for vadadustat drug product from Patheon. As of December 31, 2022, we had a minimum commitment with Patheon for $3.1 million through the third quarter of 2023.

On April 2, 2020, we entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, as amended on April 15, 2021, or the WuXi STA DS Agreement. The WuXi STA DS Agreement includes the terms and conditions under which WuXi STA will manufacture vadadustat drug substance for commercial use. Pursuant to the WuXi STA DS Agreement, we provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DS Forecast. The WuXi STA DS Forecast reflects our needs for vadadustat drug substance produced by WuXi STA over a certain number of quarters. The parties have agreed to a volume-based pricing structure under the WuXi STA DS Agreement. The WuXi STA DS Agreement has an initial term of four years, beginning April 2, 2020 and ending April 2, 2024. Pursuant to the WuXi STA DS Agreement, we have agreed to purchase a certain percentage of the global demand for vadadustat drug substance from WuXi STA. As of December 31, 2022, we have committed to purchase $15.3 million of vadadustat drug substance from WuXi STA through the end of 2023.

On February 10, 2021, we entered into a Supply Agreement with WuXi STA, or the WuXi STA DP Agreement. The WuXi STA DP Agreement includes the terms and conditions under which WuXi STA will manufacture and supply vadadustat drug product for commercial purposes. Pursuant to the WuXi STA DP Agreement, we will provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DP Forecast. Each WuXi STA DP Forecast will reflect the quantities of vadadustat drug product that we expect to order from WuXi STA over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. Pursuant to the WuXi STA DP Agreement, we have agreed to purchase a certain percentage of global demand for vadadustat drug product from WuXi STA. The parties have agreed to a volume-based pricing structure under the WuXi STA DP Agreement. The vadadustat drug product price will remain fixed for the first 12 months and thereafter shall be annually reviewed by us and WuXi STA. We will also reimburse WuXi STA for certain reasonable expenses. The WuXi STA DP Agreement has an initial term of four years, beginning February 10, 2021 and ending February 10, 2025. The WuXi STA DP Agreement may be renewed or extended by mutual agreement of us and WuXi STA with at least 18 months' prior written notice. The WuXi STA DP Agreement allows us to terminate the relationship on 180 calendar days' prior written notice to WuXi STA for any reason. In addition, each party has the ability to terminate the WuXi STA DP Agreement upon the occurrence of certain conditions.

Other Third Party Contracts

We contract with various organizations to conduct research and development activities with remaining contract costs to us of approximately $90.2 million as of December 31, 2022. The scope of the services under these research and development contracts can be modified and the contracts cancelled by us upon written notice, and therefore not included in the table of contractual obligations and commitments. In some instances, the contracts may be cancelled by the third party upon written notice.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported

amounts of assets, liabilities, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue, inventory, our excess purchase commitment liability, liabilities related to sale of future royalties, refund liabilities to customers, impairment of intangible assets, and income taxes. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. In making estimates and judgments, management employs critical accounting policies.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Product Revenue, Net

We sell Auryxia in the United States, primarily to wholesale distributors as well as certain specialty pharmacy providers, collectively, Customers. These Customers resell our product to health care providers and patients. In addition to distribution agreements with Customers, we enter into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks, and discounts with respect to the purchase of our product.

We recognize revenue on product sales when the Customer obtains control of our product, which occurs at a point in time, typically upon delivery to the Customer. We expense incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that we would have recognized is one year or less.

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and are based on various incentives that are offered within contracts between us and our Customers, health care providers, payors and other indirect customers relating to sales of our products. These reserves are based on the amounts earned or to be claimed on the related sales. These reserves include:

- Trade Discounts and Allowances: Discounts that include incentive fees that are explicitly stated in our contracts. In addition, we compensate (through trade discounts and allowances) our Customers for sales order management, data, and distribution services.
- Product Returns: Consistent with industry practice, we generally offer Customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window, when the quantity delivered is different than quantity ordered, the product is damaged in transit prior to receipt by the customer, or is subject to a recall. This right of return generally lapses once the product is provided to a patient. We estimate the amount of our product sales that may be returned for credit by our Customers. We currently estimate product return reserve using available industry data and our own historical sales information, including our visibility into the inventory remaining in the distribution channel.
- Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel at each reporting period end that we expect will be sold to qualified healthcare providers, and chargebacks that Customers have claimed but for which we have not yet issued a credit.
- Commercial and Medicare Part D Rebates: We contract with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of our products. We estimate the rebates for commercial and Medicare Part D payors based upon (i) our contracts with the payors and (ii) information obtained from our Customers and other third parties regarding the payor mix for Auryxia.
- Other Government Rebates: We are subject to discount obligations under state Medicaid programs and other government programs. We estimate Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.
- Other Incentives: Other incentives that we offer include voluntary patient assistance programs such as our co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount we expect to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as our historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The preceding estimates and judgments materially affect our recognition of net product revenues. Changes in our estimates of net product revenues could have a material effect on net product revenues recorded in the period in which we determine that change occurs.

Collaboration Revenues

We enter into out-license and collaboration agreements which are within the scope of ASC 606, under which we license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services we provide through our contract manufacturers; and royalties on net sales of licensed products. Each of these payments may result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

For elements of our collaboration agreements that are accounted for pursuant to ASC 606, we must develop assumptions that require judgment to determine whether the individual promises should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in an out-license and collaboration arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. With regard to the Otsuka collaboration agreements, we recognized revenue related to amounts allocated to the identified performance obligation on a proportional performance basis as the underlying services are performed.

The preceding estimates and judgments materially affect our recognition of collaboration revenues. Changes in our estimates of forecasted development costs could impact proportional performance percentages and could have a material effect on collaboration revenue recorded in the period in which we determine that change occurs.

Refund Liability to Customer

We treat the refund liability to customer as a zero-coupon debt financing, which is recorded at net present value. We recorded an initial discount on the refund liability to the customer and a corresponding deferred gain to the refund liability to customer on the consolidated balance sheet as of the date the funds were received from CSL Vifor, which was March 18, 2022. The discount on the note payable is being amortized to interest expense using the effective interest method over the expected term of the refund liability. The deferred gain is being amortized to interest income on a straight-line basis over the expected term of the refund liability.

Inventory

We value our inventories at the lower-of-cost or net realizable value. We determine the cost of our inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. We classify inventory costs as long-term, in other assets in our consolidated balance sheets, when we expect to utilize the inventory beyond our normal operating cycle.

We perform an assessment of the recoverability of capitalized inventory during each reporting period, and write down any excess and obsolete inventory to our net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required. Additionally, our product is subject to strict quality control and monitoring that we perform throughout the manufacturing process. In the event that certain batches or units of product do not meet quality specifications, we will record a charge to cost of product sales, to write-down any unmarketable inventory to its estimated net realizable value. In all cases, product inventory is carried at the lower of cost or its estimated net realizable value.

Excess Purchase Commitment Liability

We identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, we recorded a liability in purchase accounting. We re-evaluate the excess purchase commitments each reporting period to assess whether any adjustments to the excess purchase commitment liability are necessary. This evaluation includes reviewing the contractual minimums, expiration and utilization assumptions, and sales forecasts. Inventory receipts that have been previously identified as excess are recorded as a reduction to the excess purchase commitment liability.

Liability Related to Sale of Future Royalties

We treat the liability related to sale of future royalties as a debt financing, amortized under the effective interest rate method over the estimated life of the related expected royalty stream. The liability related to sale of future royalties and the debt amortization are based on our current estimates of future royalties expected to be paid over the life of the arrangement. We will periodically assess the expected royalty payments. To the extent our estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, we will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. Changes in our estimates of future royalty payments could have a material effect on the liability related to sale of future royalties balance recorded in the period in which we determine that change occurs.

Intangible Assets

We maintain a definite-lived intangible asset related to developed product rights for Auryxia, which was acquired on December 12, 2018 as part of the Merger.

Intangible assets are initially recorded at fair value and stated net of accumulated amortization and impairments. We amortize our intangible assets that have finite lives using either the straight-line method, or if reliably determinable, based on the pattern in which the economic benefit of the asset is expected to be utilized. Amortization for our intangible asset is recorded over its remaining estimated useful life, which as of December 31, 2022 is estimated to be six years.

We review intangible assets subject to amortization to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment or a change in the remaining useful life. If an impairment indicator exists, we perform a recoverability test by comparing the sum of the estimated undiscounted cash flows of the intangible asset group to its carrying value on the consolidated balance sheet. If the carrying value of the intangible asset group exceeds the undiscounted cash flows used in the recoverability test, we will write the carrying value of the intangible asset group down to the fair value in the period identified. We calculate the fair value of the intangible asset group as the present value of estimated future cash flows expected to be generated from the intangible asset group using a risk-adjusted discount rate. In determining estimated future cash flows associated with the intangible asset group, we use market participant assumptions pursuant to ASC Topic 820, *Fair Value Measurements and Disclosures* (ASC 820). During the second quarter of 2020, we identified indicators of impairment related to the developed product rights for Auryxia and recorded an impairment charge of $115.5 million (see Note 9 contained in this Annual Report on Form 10-K for additional information).

Income Taxes

Income taxes are recorded in accordance with FASB Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. All deferred taxes as of December 31, 2022 and 2021 are classified as noncurrent within the income tax provision (see Note 13 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data).

Recent Accounting Pronouncements

For additional discussion of recent accounting pronouncements, please refer to *New Accounting Pronouncements – Recently Adopted* and *New Accounting Pronouncements – Not Yet Adopted* included within Note 2 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2022 and 2021, we had cash and cash equivalents of $90.5 million and $149.8 million, respectively, consisting primarily of money market mutual funds consisting of

certificates of deposit and corporate debt securities. Interest rate sensitivity is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our investments are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

In addition, we are exposed to market risk related to exchange rates. A substantial portion of our revenues for the year ended December 31, 2022 was received in U.S. dollars, including revenues we receive from royalty payments converted to U.S. dollars based on the net sales of Riona(R) and Vafseo™, in Japanese yen. Our exchange rate risk arises from such foreign currency net sales. As a result, we are exposed to movements in the exchange rates of the Japanese yen against the U.S. dollar.

For the royalty payments we received based on net sales of Riona and Vafseo in Japan during the year ended December 31, 2022, a 5.0% appreciation or depreciation of the Japanese yen against the U.S. dollar would have increased or decreased, respectively, our revenues in the year ended December 31, 2022 by approximately $0.4 million.

We have generally accepted the exposure to exchange rate movements without using derivative financial instruments to manage this foreign currency risk.

Item 8. Financial Statements and Supplementary Data

Akebia Therapeutics, Inc.

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Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Akebia Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Akebia Therapeutics, Inc. (the Company) as of December 31, 2022, and 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 10, 2023, expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue recognition - Payor Mix Impact on Measuring Variable Consideration, specifically payor rebates

Description of the Matter

As of December 31, 2022, the Company recorded accrued product revenue allowances of $29.0 million, which includes payor rebates. As discussed in Note 2 to the Company's consolidated financial statements, the Company recognizes revenue from product sales at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. The Company contracts with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates the rebates for payors based upon (i) its contracts with the payors and (ii) information obtained from its customers and other third parties regarding the payor mix. The Company estimates these payor rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Auditing the measurement of the Company's net product revenues was complex and judgmental due to the significant estimation required in determining the amount of consideration that will be collected net of estimates for payor rebates. In particular, the payor rebate is affected by assumptions in payor behavior such as changes in payor mix, payor collections and current customer contractual requirements.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the Company's revenue recognition process, including controls over the underlying assumptions and inputs used by management to estimate the payor rebates. Specifically, this included controls to assess the completeness and accuracy of the current and historical data used in calculating the estimate.

Our audit procedures to test the Company's recognition of net product revenues and specifically the variable consideration component of payor rebates included, among others, assessing the methodology used to determine the estimate and testing the significant assumptions and the underlying data used by the Company in its analysis. This included testing the reasonableness of management's estimates to other inputs into their calculations such as contract terms, product in the distribution channel, and actual invoices received. We assessed the historical accuracy of management's estimates by comparing actual activity to previous estimates and performed analytical procedures to evaluate the completeness of the payor rebate reserves.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts
March 10, 2023

AKEBIA THERAPEUTICS, INC.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 90,466	$ 149,800
Inventory	21,762	38,195
Accounts receivable, net	39,180	50,875
Prepaid expenses and other current assets	33,541	33,140
Total current assets	184,949	272,010
Property and equipment, net	5,214	6,754
Operating lease assets	29,158	33,852
Goodwill	55,053	55,053
Other intangible assets, net	72,084	108,127
Other assets	5,372	49,754
Total assets	$ 351,830	$ 525,550
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 18,021	$ 33,588
Accrued expenses and other current liabilities	70,997	104,456
Short-term deferred revenue	3,738	20,906
Current portion of long-term debt	32,000	97,543
Total current liabilities	124,756	256,493
Deferred revenue, net of current portion	43,296	21,474
Operating lease liabilities, net of current portion	28,961	33,703
Derivative liability	760	1,820
Long-term debt, net	34,078	—
Liability related to sale of future royalties, net	57,484	53,079
Refund liability to customer	40,992	—
Other non-current liabilities	12,161	82,525
Total liabilities	342,488	449,094
Commitments and contingencies (Note 15)		
Stockholders' equity:		
Preferred stock $0.00001 par value, 25,000,000 shares authorized at December 31, 2022 and 2021; 0 shares issued and outstanding at December 31, 2022 and 2021	—	—
Common stock: $0.00001 par value; 350,000,000 shares authorized at December 31, 2022 and 2021, respectively; 184,135,714 and 177,000,963 shares issued and outstanding at December 31, 2022 and 2021, respectively	2	1
Additional paid-in capital	1,562,247	1,536,800
Accumulated other comprehensive gain	6	6
Accumulated deficit	(1,552,913)	(1,460,351)
Total stockholders' equity	9,342	76,456
Total liabilities and stockholders' equity	$ 351,830	$ 525,550

See accompanying notes to consolidated financial statements.

AKEBIA THERAPEUTICS, INC.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	Year Ended December 31,		
	2022	2021	2020
Revenues:			
Product revenue, net	$ 177,067	$ 142,216	$ 128,901
License, collaboration and other revenue	115,535	71,362	166,406
Total revenues	292,602	213,578	295,307
Cost of goods sold:			
Product	48,754	117,352	148,866
Amortization of intangibles	36,042	36,042	31,515
Impairment of intangible asset	—	—	115,527
Total cost of goods sold	84,796	153,394	295,908
Operating expenses:			
Research and development	129,114	147,852	218,485
Selling, general and administrative	138,699	174,161	153,947
License expense	3,175	3,489	3,409
Restructuring	15,933	—	—
Total operating expenses	286,921	325,502	375,841
Operating loss	(79,115)	(265,318)	(376,442)
Other income (expense):			
Interest income (expense)	(15,687)	(19,936)	(8,871)
Other income (expense)	3,146	2,414	1,856
Loss on extinguishment of debt	(906)	—	—
Net loss before income taxes	(92,562)	(282,840)	(383,457)
Benefit from income taxes	—	—	—
Net loss	$ (92,562)	$ (282,840)	$ (383,457)
Net loss per share - basic and diluted	$ (0.51)	$ (1.70)	$ (2.77)
Weighted-average number of common shares - basic and diluted	182,782,680	165,949,695	138,463,152
Comprehensive loss:			
Net loss	$ (92,562)	$ (282,840)	$ (383,457)
Other comprehensive (loss) gain - unrealized (loss) gain on securities	—	(7)	13
Total comprehensive loss	$ (92,562)	$ (282,847)	$ (383,444)

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.

Consolidated Statements of Stockholders' Equity

(in thousands, except share and per share data)

	Common Stock		Additional Paid-In Capital	Unrealized Gain/Loss	Accumulated Deficit	Total Stockholders' Equity
	Number of Shares	$0.00001 Par Value				
Balance at December 31, 2019	121,674,568	$ 1	$ 1,188,810	$ —	$ (794,054)	$ 394,757
Issuance of common stock, net of issuance costs	24,133,348	—	209,519	—	—	209,519
Proceeds from sale of stock under employee stock purchase plan	235,658	—	1,100	—	—	1,100
Exercise of options	166,633	—	1,226	—	—	1,226
Share-based compensation expense	—	—	24,460	—	—	24,460
Restricted stock unit vesting	1,863,878	—	—	—	—	—
Unrealized gain	—	—	—	13	—	13
Net loss	—	—	—	—	(383,457)	(383,457)
Balance at December 31, 2020	148,074,085	$ 1	$ 1,425,115	$ 13	$ (1,177,511)	$ 247,618
Issuance of common stock, net of issuance costs	26,352,343	—	88,204	—	—	88,204
Proceeds from sale of stock under employee stock purchase plan	307,193	—	746	—	—	746
Share-based compensation expense	—	—	22,735	—	—	22,735
Restricted stock unit vesting	2,267,342	—	—	—	—	—
Unrealized loss	—	—	—	(7)	—	(7)
Net loss	—	—	—	—	(282,840)	(282,840)
Balance at December 31, 2021	177,000,963	$ 1	$ 1,536,800	$ 6	$ (1,460,351)	$ 76,456
Issuance of common stock, net of issuance costs	4,404,600	1	7,121	—	—	7,122
Proceeds from sale of stock under employee stock purchase plan	335,146	—	410	—	—	410
Share-based compensation expense	—	—	17,849	—	—	17,849
Restricted stock unit vesting	2,252,565	—	—	—	—	—
Exercise of options	142,440	—	67	—	—	67
Net loss	—	—	—	—	(92,562)	(92,562)
Balance at December 31, 2022	184,135,714	$ 2	$ 1,562,247	$ 6	$ (1,552,913)	$ 9,342

See accompanying notes to consolidated financial statements.

Akebia Therapeutics, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2022	2021	2020
Operating activities:			
Net loss	$ (92,562)	$ (282,840)	$ (383,457)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,654	1,927	2,075
Amortization of intangibles	36,043	36,043	31,515
Intangible asset impairment charge	—	—	115,527
Non-cash interest expense related to sale of future royalties	6,182	9,117	—
Non-cash royalty revenue related to sale of future royalties	(1,777)	(821)	—
Amortization of premium/discount on investments	—	(15)	(47)
Non-cash collaboration revenue	(9,550)	—	—
Non-cash research and development expense	8,768	—	—
Non-cash interest expense	2,121	1,165	1,534
Non-cash operating lease expense	(2,417)	(1,842)	(2,037)
Non-cash loss on extinguishment of debt	406	—	—
Fair value step-up of inventory sold or written off	—	21,575	68,240
Write-down of inventory	30,242	15,618	20,072
Change in excess inventory purchase commitments	(67,618)	33,391	25,114
Stock-based compensation	17,849	22,735	24,460
Change in fair value of derivative liability	(1,060)	(600)	286
Changes in operating assets and liabilities:			
Accounts receivable	11,695	(24,022)	12,011
Inventory	19,793	(25,847)	6,163
Prepaid expenses and other current assets	381	(18,658)	(8,119)
Operating lease assets	—	(13,888)	—
Other long-term assets	(5,623)	5,674	(2,779)
Accounts payable	1,501	(11,735)	3,678
Accrued expense	(38,227)	(24,680)	6,356
Operating lease liabilities	2,311	15,398	1,411
Deferred revenue	4,654	1,821	(32,391)
Other non-current liabilities	2,080	(12,481)	—
Net cash used in operating activities	(73,154)	(252,965)	(110,388)
Investing activities:			
Purchase of property and equipment	(114)	(59)	(317)
Purchase of available for sale securities	—	—	(99,932)
Proceeds from the maturities of available for sale securities	—	40,000	60,245
Net cash provided by (used in) investing activities	(114)	39,941	(40,004)
Financing activities:			
Proceeds from sale of future royalties, net	—	44,783	—
Proceeds from refund liabilities to customers	40,000	—	—
Proceeds from the issuance of common stock, net of issuance costs	7,121	88,202	209,419
Proceeds from the sale of stock under employee stock purchase plan	410	746	1,100
Proceeds from the exercise of stock options	67	—	1,226
Proceeds from the issuance of debt, net	—	—	19,975
Payments on debt	(33,000)	—	—
Net cash provided by financing activities	14,598	133,731	231,720
Increase (decrease) in cash, cash equivalents, and restricted cash	(58,670)	(79,293)	81,328
Cash, cash equivalents, and restricted cash at beginning of the period	151,839	231,132	149,804
Cash, cash equivalents, and restricted cash at end of the period	$ 93,169	$ 151,839	$ 231,132
Non-cash financing activities			
Unpaid offering costs	$ —	$ 2	$ 100
Cash paid for:			
Interest	6,755	9,632	7,843

See accompanying notes to consolidated financial statements.

1. Nature of Organization and Operations

Akebia Therapeutics, Inc., referred to as Akebia or the Company, was incorporated in the State of Delaware in 2007. Akebia is a fully integrated biopharmaceutical company with the purpose of bettering the lives of people impacted by kidney disease. The Company has one commercial product, Auryxia® (ferric citrate), which is approved by the U.S. Food and Drug Administration, or FDA, and marketed for two indications in the United States: the control of serum phosphorus levels in adult patients with chronic kidney disease, or CKD, on dialysis, or DD-CKD, and the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or NDD-CKD. Ferric citrate is also approved and marketed in Japan as an oral treatment for IDA in adult patients for the improvement of hyperphosphatemia in such patients with DD-CKD and NDD-CKD under the trade name Riona (ferric citrate hydrate).

Vadadustat, the Company's lead investigational product candidate, is an investigational oral hypoxia-inducible factor prolyl hydroxylase, or HIF-PH, inhibitor designed to mimic the physiologic effect of altitude on oxygen availability. On March 29, 2022, the Company received a complete response letter, or CRL, from the FDA. The CRL provided that the FDA had completed its review of the Company's new drug application, or NDA, for vadadustat for the treatment of anemia due to CKD in adult patients and had determined that it could not approve the NDA in its present form. In October 2022, the Company submitted a Formal Dispute Resolution Request, or FDRR, with the FDA. The FDRR focused on the favorable balance between the benefits and risks of vadadustat for the treatment of anemia due to CKD in adult DD-CKD patients in light of safety concerns expressed by the FDA in the CRL for dialysis patients related to the rate of adjudicated thromboembolic events driven by vascular access thrombosis for vadadustat compared to the active comparator and the risk of drug-induced liver injury. In February 2023, we received a second interim response from the FDA to our FDRR. On May 12, 2022, the Company received notice from its former collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, that Otsuka had elected to terminate the Collaboration and License Agreement dated December 18, 2016, or the Otsuka U.S. Agreement, and the Collaboration and License Agreement dated April 25, 2017, or the Otsuka International Agreement. On June 30, 2022, the Company and Otsuka entered into a Termination and Settlement Agreement, or the Termination Agreement, pursuant to which, among other things, the Company and Otsuka agreed to terminate the Otsuka U.S. Agreement and the Otsuka International Agreement as of June 30, 2022 (see Note 4 for further details). In October 2021, Otsuka submitted a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in adult patients with DD-CKD and NDD-CKD to the European Medicines Agency, or EMA. In connection with the Termination Agreement, Otsuka transferred the MAA for vadadustat with the EMA to the Company. Vadadustat is approved in Japan as a treatment for anemia due to CKD in both DD-CKD and NDD-CKD patients under the trade name Vafseo™, and marketed and sold in Japan by Mitsubishi Tanabe Pharma Corporation, or MTPC.

In addition, the Company continues to explore additional development opportunities to expand its pipeline and portfolio of novel therapeutics.

Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities, commercializing Auryxia, and providing general and administrative support for these operations. The Company began recording revenue from the U.S. sales of Auryxia and revenue from sublicensing rights to Auryxia in Japan from the Company's Japanese partners, Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively JT and Torii, in December 2018. Additionally, following regulatory approval of vadadustat in Japan, the Company began recognizing royalty revenues from MTPC from the sale of Vafseo in August 2020. In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or HCR, or the Royalty Agreement, whereby the Company sold its right to receive royalties and sales milestones under its Collaboration Agreement with MTPC, or the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 6 for additional information). The Company has not generated a profit to date, and may never generate profits, from product sales. Vadadustat and the Company's other potential product candidates are subject to long development cycles, and the Company may be unsuccessful in its efforts to develop, obtain marketing approval for or market vadadustat and its other potential product candidates. If the Company does not successfully commercialize Auryxia, vadadustat, if approved, or any other potential product candidate, it may be unable to achieve profitability.

Going Concern

The Company's management completed its going concern assessment in accordance with Accounting Standards Codification, or ASC, 205-40, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern, or ASC 205-40. Pursuant to the requirements of ASC 205-40, the Company's management must evaluate whether there are conditions or events considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one

year after the date the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued.

The Company's operating plan during 2022 included the planned completion of several operating changes that the Company implemented over the course of the year. These assumptions pertained to cost avoidance measures and the reduction of overhead costs that would result from the planned amendment of contractual arrangements with certain supply and collaboration partners, and the reduction of operating expenses, which were outside of the Company's control. Over the course of 2022, and completing in the fourth quarter, the Company executed on certain of these cost avoidance measures and reduction of overhead costs from the amendment or termination of contractual arrangements with certain supply partners as well as the reduction of future operating expenses, which is consistent with the Company's plan to fund operations with existing cash resources and cash from operations.

Examples of these reductions include the amendment, assignment and termination of certain supply agreements for both vadadustat and Auryxia. For example, on December 22, 2022, the Company and BioVectra Inc., or BioVectra, entered into a Termination Agreement, or the BioVectra Termination Agreement, pursuant to which the parties agreed, among other things, to terminate, effective immediately, any and all existing agreements entered into between the parties in connection with the manufacture and supply, by BioVectra to the Company, of Auryxia drug substance. Under the terms of the BioVectra Termination Agreement, the Company agreed to pay BioVectra a total of $32.5 million consisting of (i) an upfront payment of $17.5 million and (ii) six quarterly payments of $2.5 million commencing in April 2024, totaling $15.0 million. Pursuant to the BioVectra Termination Agreement, each of the Company and BioVectra have released one another from all existing and future claims and liabilities and the return of certain materials and documents. Furthermore, as it relates to all open purchase orders, BioVectra is relieved from any obligations to manufacture any product or perform services under any such open purchase orders, and the Company is relieved from any obligations to purchase any product under such open purchase orders. The Company is also relieved from any obligations to pay any outstanding invoices related to performance by BioVectra of services and all other obligations under the agreements.

Additionally, on December 16, 2022, the Company, Mitsubishi Tanabe Pharma Corporation, or MTPC, and Esteve Química, S.A., or Esteve, executed the Assignment Agreement, pursuant to which the Supply Agreement between the Company and Esteve was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Supply Agreement to MTPC, specifically including the obligations under certain purchase orders issued by the Company and accepted by Esteve. As such, the transferred purchase orders will continue to have a binding effect on MTPC to take delivery of the product from Esteve in accordance with the terms of the Supply Agreement. The Company will have no further obligation to take delivery of or pay for product delivered by Esteve under the transferred purchase orders.

In relation to cost avoidance measures, in November 2022, the Board of Directors approved a reduction of the Company's workforce by approximately 14% consisting solely of individuals within the commercial organization as a result of the Company's decision to shift to a strategic account management focused model for its commercial efforts. This shift is due to multiple factors, including the maturity of Auryxia®, the continued impact of the COVID-19 pandemic on dialysis centers and the phosphate binder market and that, if the Company is successful in its appeal of the complete response letter for vadadustat with the U.S. Food and Drug Administration, the Company's commercial focus for vadadustat will be limited to the dialysis patient population for the foreseeable future.

As of December 31, 2022, the Company had cash and cash equivalents of approximately $90.5 million. Based on its current operating plan, the Company believes that its cash resources will be sufficient to allow the Company to fund its current operating plan through at least the next twelve months from the filing of the Company's 2022 Annual Report on Form 10-K. If the Company's operating performance deteriorates significantly from the levels achieved in 2022, it could have an effect on the Company's liquidity and its ability to continue as a going concern in the future. The Company expects to finance future cash needs through product revenue, potential strategic transactions, public or private equity or debt transactions, operating expense management, or a combination of these approaches. Assuming the Company is successful in executing its operating plan, the Company will require additional funding to fund its strategic growth beyond Auryxia or to pursue later stage development and commercial activities for its product candidates and any additional product or product candidates, including those that may be in-licensed or acquired. There can be no assurance that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund our operating plan for the period anticipated by the Company, or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. These consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting

Standards Codification, or ASC, and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB.

New Accounting Pronouncements – Recently Adopted

In March 2020, the FASB issued ASU 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting*. The amendments provide optional guidance for a limited time to ease the potential burden in accounting for reference rate reform. The new guidance provides optional expedients and exceptions for applying U.S. GAAP to contracts, hedging relationships and other transactions affected by reference rate reform if certain criteria are met. The amendments apply only to contracts and hedging relationships that reference LIBOR or another reference rate expected to be discontinued due to reference rate reform. These amendments are effective immediately and may be applied prospectively to contract modifications made and hedging relationships entered into or evaluated on or before December 31, 2022. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing novel therapeutics for people with kidney disease.

Derivative Financial Instruments

The Company accounts for warrants and other derivative financial instruments as either equity or liabilities in accordance with ASC Topic 815, *Derivatives and Hedging*, or ASC 815, based upon the characteristics and provisions of each instrument. Warrants classified as equity are recorded at fair value as of the date of issuance on the Company's consolidated balance sheets and no further adjustments to their valuation are made. Warrants classified as derivative liabilities and other derivative financial instruments that require separate accounting as liabilities are recorded on the Company's consolidated balance sheets at their fair value on the date of issuance and will be revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. The warrant, or the Warrant, to purchase shares of the Company's common stock issued by the Company in connection with the Janssen Pharmaceutica NV Research and License Agreement, or the Janssen Agreement, expired on February 9, 2022. The derivative liability recorded in connection with the Company's Loan Agreement with Pharmakon is classified as a liability in the Company's consolidated balance sheet (see Note 11).

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: prepaid and accrued research and development expense, operating lease assets and liabilities, derivative liabilities, refund liabilities to customers, other non-current liabilities, the excess purchase commitment liability, stock-based compensation expense, product and collaboration revenues including various rebates and reserves related to product sales, non-cash interest expense on the liability related to sale of future royalties, inventories, income taxes, intangible assets and goodwill.

Although the Company regularly assesses these estimates, actual results could differ materially from these estimates. Changes in estimates are recorded in the period they become known. The Company bases its estimates on historical experience and various other assumptions that it believes to be reasonable under the circumstances.

Cash, Cash Equivalents, and Restricted Cash

Cash and cash equivalents consist of all cash on hand, deposits and funds invested in available for sale securities with original maturities of three months or less at the time of purchase. Cash equivalents are reported at fair value. At December 31, 2022, the Company's cash is primarily in money market funds. The Company may maintain balances with its banks in excess of federally insured limits.

Restricted cash represents amounts required for security deposits under the Company's office and lab space lease agreements. Restricted cash is included in "prepaid expenses and other current assets" and "other assets" in the consolidated balance sheets.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported in the consolidated balance sheet that sum to the total of the amounts reported in the consolidated statement of cash flows (in thousands):

	December 31, 2022	December 31, 2021	December 31, 2020
Cash and cash equivalents	$ 90,466	$ 149,800	$ 228,698
Prepaid expenses and other current assets	—	—	395
Other assets	2,703	2,039	2,039
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$ 93,169	$ 151,839	$ 231,132

Accounts Receivable

The Company's accounts receivable represent amounts due to the Company from product sales (see Note 3) and from its collaboration agreement with MTPC (see Note 4). Reimbursable costs that have not been invoiced as of the balance sheet date are recorded as unbilled accounts receivable. Accounts receivable arising from product sales primarily represent amounts due from wholesale distributors as well as certain specialty pharmacy providers, or collectively, Customers. The Company deducts trade allowances for prompt payment, among other discounts, from its accounts receivable based on its experience that the Company's Customers will earn these discounts and fees.

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed as well as historical payment patterns and existing economic factors. The Company believes that credit risks associated with its customers and collaboration partners are not significant. The Company did not have a material allowance for doubtful accounts as of December 31, 2022 and 2021.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash, cash equivalents, and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash and cash equivalents with high quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Accounts receivable represent amounts due from the Company's customers and collaboration partners. As part of its credit management policy, the Company performs ongoing credit evaluations of its Customers and generally does not require collateral from any customer. The Company also monitors economic conditions of its collaboration partners to identify facts or circumstances that may indicate that any of its accounts receivable are at risk of collection.

Gross revenues and accounts receivable from each of the Company's Customers or collaboration partners who individually accounted for 10% or more of total gross revenues and/or 10% or more of total gross accounts receivable consisted of the following:

	Percent of Total Gross Revenues		
	Years Ended December 31,		
	2022	2021	2020
Fresenius Medical Care Rx	34 %	33 %	29 %
Otsuka Pharmaceutical Co. Ltd.	20 %	14 %	29 %
AmerisourceBergen Drug Corporation	15 %	16 %	12 %
McKesson Corporation	— %	13 %	11 %
Cardinal Health, Inc.	— %	11 %	— %

	Percent of Gross Accounts Receivable	
	As of December 31,	
	2022	2021
Fresenius Medical Care Rx	44 %	16 %
AmerisourceBergen Drug Corporation	16 %	15 %
Cardinal Health, Inc.	13 %	10 %
McKesson Corporation	10 %	— %
Otsuka Pharmaceutical Co. Ltd.	— %	22 %
MTPC	— %	20 %

Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Assets under capital lease are included in property and equipment. Property and equipment is depreciated using the straight-line method over the estimated useful lives of the assets, generally three years to seven years. Such costs are periodically reviewed for recoverability when impairment indicators are present. Such indicators include, among other factors, unused capacity, market value declines and technological obsolescence. Recorded values of asset groups of equipment that are not expected to be recovered through undiscounted future net cash flows are written down to current fair value, which generally is determined from estimated discounted future net cash flows (assets held for use) or net realizable value (assets held for sale).

The following is the summary of property and equipment and related accumulated depreciation as of December 31, 2022 and 2021.

	Useful Life	December 31, 2022	December 31, 2021
		(in thousands)	
Computer equipment and software	3	$ 1,010	$ 1,010
Furniture and fixtures	5 - 7	2,086	2,086
Equipment	7	2,750	2,750
Leasehold improvements	Shorter of the useful life or remaining lease term	8,687	8,573
		14,533	14,419
Less accumulated depreciation		(9,319)	(7,665)
Net property and equipment		$ 5,214	$ 6,754

Depreciation expense was approximately $1.7 million, $1.9 million and $2.1 million for the years ended December 31, 2022, 2021 and 2020, respectively.

Leases

In February 2016, the FASB issued ASU 2016-02, *Leases* (Topic 842), which supersedes the existing guidance for lease accounting, Leases (Topic 840). ASU 2016-02 requires entities to recognize right-of-use assets and lease liabilities for leases with lease terms of more than 12 months on their balance sheets and provide enhanced disclosures. In 2018, the FASB issued

additional ASUs related to Topic 842, or ASC 842, that clarified various aspects of the new lease guidance, including how to record certain transition adjustments, as well as other improvements and practical expedients.

The Company made an accounting policy election not to recognize leases with an initial term of 12 months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations. The Company also made the accounting policy election not to separate the non-lease components from the lease components for its building leases and, rather, account for each non-lease component and lease component as a single component.

The Company determines if an arrangement is a lease at inception. An arrangement is determined to contain a lease if the contract conveys the right to control the use of an identified property, plant, or equipment for a period of time in exchange for consideration. If the Company can benefit from the various underlying assets of a lease on their own or together with other resources that are readily available, or if the various underlying assets are neither highly dependent on nor highly interrelated with other underlying assets in the arrangement, they are considered to be a separate lease component. In the event multiple underlying assets are identified, the lease consideration is allocated to the various components based on each of the component's relative fair value.

Operating lease assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent its obligation to make lease payments arising from the leasing arrangement. Operating lease assets and operating lease liabilities are recognized at the commencement date based on the present value of lease payments over the lease term. The Company uses the implicit rate when readily determinable and uses an estimate of its incremental borrowing rate when the implicit rate is not readily determinable based upon the available information at the commencement date of lease inception. The incremental borrowing rate is determined using a credit rating scoring model to estimate the Company's credit rating, adjusted for collateralization. The calculation of the operating lease assets includes any lease payments made and excludes any lease incentives. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option.

The Company's operating leases are reflected in prepaid expenses and other current assets, operating lease assets, accrued expenses and operating lease liabilities, net of current portion in its consolidated balance sheets. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

Inventory

The Company values its inventories at the lower-of-cost or net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company classifies its inventory costs as long-term, in other assets in its consolidated balance sheets, when it expects to utilize the inventory beyond their normal operating cycle.

Prior to the regulatory approval of a product candidate, the Company incurs expenses for the manufacture of material that could potentially be available to support the commercial launch of its products upon approval. Until the first reporting period when regulatory approval has been received or is otherwise considered probable and the future economic benefit is expected to be realized, the Company records all such costs as research and development expense. Inventory used in clinical trials is also expensed as research and development expense, when selected for such use. Inventory that can be used in either the production of clinical or commercial products is expensed as research and development costs when identified for use in a clinical manufacturing campaign.

The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and writes down any excess and obsolete inventory to its net realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded as a component of cost of product sales in the consolidated statements of operations and comprehensive loss. The determination of whether inventory costs will be realizable requires the use of estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required. Additionally, the Company's product is subject to strict quality control and monitoring that it performs throughout the manufacturing process. In the event that certain batches or units of product do not meet quality specifications, the Company will record a charge to cost of product sales, to write-down any unmarketable inventory to its estimated net realizable value. In all cases, product inventory is carried at the lower of cost or its estimated net realizable value.

Debt

The Company performs an assessment of all embedded features of a debt instrument to determine if (1) such features should be bifurcated and separately accounted for, and (2) if bifurcation requirements are met, whether such features should be classified and accounted for as equity or liability instruments. If the embedded feature meets the requirements to be bifurcated and accounted for as a liability, the fair value of the embedded feature is measured initially, included as a liability on the consolidated balance sheet, and re-measured to fair value at each reporting period. Any changes in fair value are recorded in the consolidated statement of operations. The Company monitors, on an ongoing basis, whether events or circumstances could give rise to a change in the classification of embedded features.

Liability Related to Sale of Future Royalties

The Company treats the liability related to sale of future royalties (see Note 6) as a debt financing, amortized under the effective interest rate method over the estimated life of the related expected royalty stream. The liability related to sale of future royalties and the debt amortization are based on the Company's current estimates of future royalties expected to be paid over the life of the arrangement. The Company will periodically assess the expected royalty payments. To the extent the Company's estimates of future royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than previous estimates, the Company will adjust the effective interest rate and recognize related non-cash interest expense on a prospective basis. Non-cash royalty revenue is reflected as royalty revenue within license, collaboration and other revenue, and non-cash amortization of debt is reflected as interest expense in the consolidated statements of operations and comprehensive loss.

Refund Liability to Customer

The Company treats the refund liability to customer as a zero-coupon debt financing, which is recorded at net present value. The Company recorded an initial discount on the refund liability to the customer and a corresponding deferred gain to the refund liability to customer on the consolidated balance sheet as of the date the funds were received from CSL Vifor, which was March 18, 2022. The discount on the note payable is being amortized to interest expense using the effective interest method over the expected term of the refund liability. The deferred gain is being amortized to interest income on a straight-line basis over the expected term of the refund liability.

Restructuring

Restructuring charges principally consist of one-time termination benefits and contractual termination benefits for severance, healthcare, and related benefits as well as non-cash share-based compensation expense. The Company records restructuring charges based on whether the termination benefits are provided under an on-going benefit arrangement or under a one-time benefit arrangement. The Company accounts for on-going benefit arrangements, such as those documented by employment agreements, in accordance with Accounting Standards Codification 712, or ASC 712, Nonretirement Postemployment Benefits. Under ASC 712, liabilities for postemployment benefits are recorded at the time the obligations are probable of being incurred and can be reasonably estimated. The Company accounts for one-time employment benefit arrangements in accordance with ASC 420 Exit or Disposal Cost Obligations. When applicable, the Company records such costs into operating expense.

Excess Purchase Commitment Liability

The Company identified executory contracts in the commercial supply agreements between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast and as such, the Company recorded a liability in purchase accounting. The Company re-evaluates the excess purchase commitments each reporting period to assess whether any adjustments to the excess purchase commitment liability are necessary. This evaluation includes reviewing the contractual minimums, expiration and utilization assumptions, and sales forecasts. Inventory receipts that have been previously identified as excess are recorded as a reduction to the excess purchase commitment liability.

Revenue Recognition

The Company generates revenues primarily from sales of Auryxia, see Note 3, from its collaboration with MTPC and its prior collaboration agreements with Otsuka, see Note 4. The Company recognizes revenue in accordance with ASC 606, which applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, it performs the following five steps:

(i) identify the contract(s) with a customer;
(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;
(iv) allocate the transaction price to the performance obligations in the contract; and
(v) recognize revenue when (or as) the entity satisfies a performance obligation.

The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company does not include a financing component to its estimated transaction price at contract inception unless it estimates that certain performance obligations will not be satisfied within one year. Additionally, the Company recognizes the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that the Company otherwise would have recognized is one year or less.

Product Revenue, Net

The Company sells Auryxia in the United States, or U.S., primarily to wholesale distributors as well as certain specialty pharmacy providers, collectively, Customers. These Customers resell the Company's product to health care providers and patients. In addition to distribution agreements with Customers, the Company enters into arrangements with health care providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks, and discounts with respect to the purchase of the Company's product.

The Company recognizes revenue on product sales when the Customer obtains control of the Company's product, which occurs at a point in time, typically upon delivery to the Customer. The Company expenses incremental costs of obtaining a contract as and when incurred if the expected amortization period of the asset that it would have recognized is one year or less.

Reserves for Variable Consideration

Revenue from product sales is recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established and which result from discounts, returns, chargebacks, rebates, co-pay assistance and other allowances that are offered within contracts between the Company and its Customers, health care providers, payors and other indirect customers relating to the Company's sales of its products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amount will be credited to the Customer) or as a current liability (if the amount is payable to a Customer or a party other than a Customer). When appropriate, these estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in ASC 606 for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Trade Discounts and Allowances: The Company generally provides Customers with discounts that include incentive fees that are explicitly stated in the Company's contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, the Company compensates (through trade discounts and allowances) its Customers for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company's sale of products to the Customer and, therefore, these payments have been recorded as a reduction of revenue within the consolidated statement of operations and comprehensive loss through December 31, 2022. The Company records a corresponding reduction to accounts receivable (if the trade discount and/or allowance will be credited to the Customer) or an increase to accrued expense (if the trade discount and/or allowance is payable to a Customer) on the consolidated balance sheets.

Product Returns: Consistent with industry practice, the Company generally offers Customers a limited right of return which allows for the product to be returned when the product expiry is within an allowable window, when the quantity delivered is different than quantity ordered, the product is damaged in transit prior to receipt by the customer, or is subject to a recall. This right of return generally lapses once the product is provided to a patient. The Company estimates the amount of its product sales that may be returned for credit by its Customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized. The Company currently estimates product return reserve using available industry data and its own historical sales information, including its visibility into the inventory remaining in the distribution channel.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by Customers, and the Company generally issues credits for such amounts within a few weeks of the Customer's resale of the product. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel at each reporting period end that the Company expects will be sold to qualified healthcare providers, and chargebacks that Customers have claimed but for which the Company has not yet issued a credit.

Commercial and Medicare Part D Rebates: The Company contracts with various commercial payor organizations, primarily health insurance companies and pharmacy benefit managers, for the payment of rebates with respect to utilization of its products. The Company estimates the rebates for commercial and Medicare Part D payors based upon (i) its contracts with the payors and (ii) information obtained from its Customers and other third parties regarding the payor mix for Auryxia. The Company estimates these rebates and records such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Government Rebates: The Company is subject to discount obligations under state Medicaid programs and other government programs. The Company estimates its Medicaid and other government programs rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel at the end of each reporting period.

Other Incentives: Other incentives that the Company offers include voluntary patient assistance programs such as the Company's co-pay assistance program, which are intended to provide financial assistance to qualified commercially insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on actual claims processed during a given period, as well as historical utilization data to estimate the amount the Company expects to receive associated with product that has been recognized as revenue, but remains in in the distribution channel at the end of each reporting period.

Collaboration Revenues

The Company enters into out-license and collaboration agreements which are within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services the Company provides through its contract manufacturers; and royalties on net sales of licensed products. Each of these payments may result in license, collaboration and other revenue, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as the Company fulfills its obligations under each of its agreements, the Company implements the five-step model noted above. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine whether the individual promises should be accounted for as separate performance obligations or as a combined performance obligation, and to determine the stand-alone selling price for each performance obligation identified in the contract. A deliverable represents a separate performance obligation if both of the following criteria are met: (i) the customer can benefit from the good or service either on its own or together with other

resources that are readily available to the customer, and (ii) the entity's promise to transfer the good or service to the customer is separately identifiable from other promises in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success. With regard to the MTPC and former Otsuka collaboration agreements, the Company recognizes revenue related to amounts allocated to the identified performance obligation on a proportional performance basis as the underlying services are performed.

Licenses of Intellectual Property

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in an out-license and collaboration arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to assess the milestone as probable of being achieved. There is considerable judgment involved in determining whether a milestone is probable of being reached at each specific reporting period. Milestone payments that are not within the control of the Company or the customer, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenues as, or when, the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect collaboration revenue in the period of adjustment.

Manufacturing Supply Services

Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the licensee exercises these options, any additional payments are recorded in license, collaboration and other revenues when the licensee obtains control of the goods, which is upon delivery.

Royalties

The Company will recognize sales-based royalties, including milestone payments based on the level of sales, at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). The Company receives royalty payments from JT and Torii based on net sales of Riona and MTPC based on net sales of Vafseo in Japan.

Collaborative Arrangements

The Company records the elements of its collaboration agreements that represent joint operating activities in accordance with ASC Topic 808, *Collaborative Arrangements* (ASC 808). Accordingly, the elements of the collaboration agreements that represent activities in which both parties are active participants and to which both parties are exposed to the significant risks and rewards that are dependent on the commercial success of the activities are recorded as collaborative arrangements. The Company considers the guidance in ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*, in determining the appropriate treatment for the transactions between the Company and its collaborative partners and the transactions between the Company and third parties. Generally, the classification of transactions under the collaborative arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the

operations of the participants. Therefore, the Company recognized its allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the former Otsuka U.S. Agreement, as defined below in Note 4, as a component of the related expense in the period incurred. To the extent product revenue is generated from the collaboration, the Company recognizes its share of the net sales on a gross basis if the Company is deemed to be the principal in the transactions with customers, or on a net basis if the Company is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

Intangible Assets

The Company maintains a definite-lived intangible asset related to developed product rights for Auryxia. Intangible assets are initially recorded at fair value and stated net of accumulated amortization and impairments. The Company amortizes its intangible assets that have finite lives using either the straight-line method, or if reliably determinable, based on the pattern in which the economic benefit of the asset is expected to be utilized. Amortization for the Company's intangible asset is recorded over its remaining estimated useful life, which as of December 31, 2022 is estimated to be six years.

The Company reviews intangible assets subject to amortization to determine if any adverse conditions exist or a change in circumstances has occurred that would indicate impairment or a change in the remaining useful life. If an impairment indicator exists, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of the intangible asset group to its carrying value on the consolidated balance sheet. If the carrying value of the intangible asset group exceeds the undiscounted cash flows used in the recoverability test, the Company will write the carrying value of the intangible asset group down to the fair value in the period identified. The Company calculates the fair value of the intangible asset group as the present value of estimated future cash flows expected to be generated from the intangible asset group using a risk-adjusted discount rate. In determining estimated future cash flows associated with its intangible asset group, the Company uses market participant assumptions pursuant to ASC Topic 820, *Fair Value Measurements and Disclosures* (ASC 820). During the second quarter of 2020, the Company identified indicators of impairment related to the developed product rights for Auryxia and recorded an impairment charge of $115.5 million (see Note 9).

Goodwill

The Company allocates any excess purchase price over the fair value of the net tangible and intangible assets acquired in a business combination to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

The Company compares the fair value of its reporting unit to its carrying value. If the carrying value of the net assets assigned to the reporting unit exceeds the fair value of its reporting unit, the Company would record an impairment loss equal to the difference. As described above, the Company operates in one operating segment which the Company considers to be the only reporting unit.

Fair Value of Financial Instruments

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. ASC 820 establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available.

Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments, and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1 – Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.
- Level 2 – Valuations based on quoted prices for similar assets or liabilities in markets that are not active, or for which all significant inputs are observable, either directly or indirectly.
- Level 3 – Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Items measured at fair value on a recurring basis include derivative liabilities (see Note 7). The carrying amounts of prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to their short-term maturities.

Items measured at fair value on a nonrecurring basis include property and equipment, intangible assets and goodwill. The Company remeasures the fair value of these assets upon the occurrence of certain events. There were no impairments to assets measured using Level 3 inputs during the years ended December 31, 2022 and 2021.

The Company's other financial instruments mainly consists of debt (see Note 11). The carrying amount for the Company's Loan Agreement with Pharmakon approximates fair value because the interest rate is variable and reflects current market rates.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses are comprised of costs incurred in providing research and development activities, including salaries and benefits, facilities costs, overhead costs, contract research and development services, and other outside costs. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

External research and development expenses associated with the Company's programs include clinical trial site costs, research compounds and clinical manufacturing costs, costs incurred for consultants and other outside services, such as data management and statistical analysis support, and materials and supplies used in support of the clinical and preclinical programs. Internal costs of the Company's clinical program include salaries, benefits, stock-based compensation, and an allocation of the Company's facility costs. When third-party service providers' billing terms do not coincide with the Company's period-end, the Company is required to make estimates of its obligations to those third parties, including clinical trial and pharmaceutical development costs, contractual services costs and supply costs, incurred in a given accounting period and record accruals at the end of the period. The Company bases its estimates on its knowledge of the research and development programs, services performed for the period, past history for related activities and the expected duration of the third-party service contract, where applicable.

Advertising Expenses

The costs of advertising are expensed as incurred and included in selling, general and administrative expenses in the consolidated statements of operations and comprehensive loss. For the years ended December 31, 2022, 2021 and 2020, advertising expenses totaled $6.7 million, $8.2 million and $5.0 million, respectively, all related to Auryxia.

Income Taxes

Income taxes are recorded in accordance with FASB Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. All deferred taxes as of December 31, 2022 and 2021 are classified as noncurrent within the income tax provision (see Note 13).

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. As of December 31, 2022 and 2021, the Company does not have any significant uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees and non-employees, including grants of stock options, restricted stock, restricted stock units, or RSUs, performance-based restricted stock units, or PSUs, and modifications to existing stock awards, to be recognized in the statements of operations and comprehensive loss based on their fair values. The Company's stock-based awards are comprised of stock options, RSUs and PSUs. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses the market price at the time of grant to determine the fair value of restricted stock awards and performance-based restricted stock awards.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Prior to 2017, due to the lack of company-specific historical and implied volatility data for trading the Company's stock in the public market, the Company had based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility was calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility was based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. During 2017, the Company began to estimate its volatility by using a blend of its stock price history for the length of time it has market data for its stock and the historical volatility of similar public companies for the expected term of each grant. The Company is a commercial-stage biopharmaceutical company and the representative group of companies has certain similar characteristics to the Company. The Company believes the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of the Company. The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock, which is similar to the Company's peer group.

The Company's stock-based awards are subject to either service- or performance-based vesting conditions. Compensation expense related to awards to employees and non-employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term, and is adjusted for pre-vesting forfeitures in the period in which the forfeitures occur. Compensation expense related to awards to employees and non-employees with performance-based vesting conditions is recognized based on the grant date fair value over the requisite service period using the accelerated attribution method to the extent achievement of the performance condition is probable.

For awards with performance conditions in which the award does not vest unless the performance condition is met, the Company recognizes expense if, and to the extent that, the Company estimates that achievement of the performance condition is probable. If the Company concludes that vesting is probable, it recognizes expense from the date it reaches this conclusion through the estimated vesting date.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted-average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the diluted net loss per share calculation, preferred stock, stock options, warrants, restricted stock and RSUs are considered to be common stock equivalents, but have been excluded from the calculation of diluted net loss per share, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented. Diluted net income per share is calculated by dividing the net income by the weighted-average common shares outstanding for the period, including any dilutive effect from outstanding options, warrants, restricted stock and RSUs using the treasury stock method.

3. Product Revenue, Net

To date, the Company's only source of product revenue has been from the U.S. sales of Auryxia. Total net product revenue was $177.1 million, $142.2 million, and $128.9 million for the years ended December 31, 2022, 2021 and 2020, respectively. The following table summarizes activity in each of the product revenue allowance and reserve categories for the years ended December 31, 2020, 2021, and 2022 (in thousands):

	Chargebacks and Discounts	Rebates, Fees and other Deductions	Returns	Total
Balance at December 31, 2019	$ 738	$ 30,552	$ 253	$ 31,543
Provisions related to sales in current year	10,559	149,472	7,238	167,269
Adjustments related to prior year sales	—	377	—	$ 377
Credits/payments made	(10,495)	(140,489)	(6,842)	$ (157,826)
Balance at December 31, 2020	802	39,912	649	41,363
Current provisions related to sales in current year	11,759	133,297	5,852	150,908
Adjustments related to prior year sales	(1)	(1,790)	—	(1,791)
Credits/payments made	(11,282)	(144,794)	(6,026)	(162,102)
Balance at December 31, 2021	$ 1,278	$ 26,625	$ 475	$ 28,378
Current provisions related to sales in current year	11,398	89,686	5,131	106,215
Adjustments related to prior year sales	(9)	401	—	392
Credits/payments made	(11,191)	(87,722)	(4,719)	(103,632)
Balance at December 31, 2022	$ 1,476	$ 28,990	$ 887	$ 31,353

Chargebacks, discounts and returns are recorded as a direct reduction of revenue on the consolidated statement of operations with a corresponding reduction to accounts receivable on the consolidated balance sheets. Rebates, distribution-related fees, and other sales-related deductions are recorded as a reduction in revenue on the consolidated statement of operations with a corresponding increase to accrued liabilities or accounts payable on the consolidated balance sheets.

Accounts receivable, net related to product sales was approximately $36.2 million and $24.6 million as of December 31, 2022 and 2021, respectively.

4. License, Collaboration and Other Significant Agreements

During the years ended December 31, 2022, 2021 and 2020, the Company recognized the following revenues from its license, collaboration and other significant agreements and had the following deferred revenue balances as of December 31, 2022:

	For the Year Ended December 31,		
	2022	2021	2020
License, Collaboration and Other Revenue:		(in thousands)	
MTPC Agreement	$ 17,968	$ 12,438	$ 15,405
Otsuka U.S. Agreement	86,773	36,588	93,446
Otsuka International Agreement	5,503	16,449	45,451
Total Proportional Performance Revenue	$ 110,244	$ 65,475	$ 154,302
JT and Torii	5,291	5,814	5,681
MTPC Other Revenue	—	73	6,423
Total License, Collaboration and Other Revenue	$ 115,535	$ 71,362	$ 166,406

	December 31, 2022		
	Short-Term	Long-Term	Total
Deferred Revenue:		(in thousands)	
MTPC	$ 3,738	$ —	$ 3,738
Vifor Agreement	—	43,296	43,296
Total	$ 3,738	$ 43,296	$ 47,034

The following table presents changes in the Company's contract assets and liabilities during the years ended December 31, 2022 and 2021 (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Twelve Months Ended December 31, 2022				
Contract assets:				
Accounts receivable (1)	$ 19,094	$ 94,515	$ (111,708)	$ 1,901
Prepaid expenses and other current assets	$ 4,309	$ 9,550	$ (13,078)	$ 781
Contract liabilities:				
Deferred revenue	$ 42,380	$ 70,044	$ (65,390)	$ 47,034
Accounts payable	$ 3,171	$ —	$ (3,171)	$ —
Twelve Months Ended December 31, 2021				
Contract assets:				
Accounts receivable (1)	$ 3,045	$ 64,676	$ (48,627)	$ 19,094
Prepaid expenses and other current assets	$ 1,722	$ 2,592	$ (5)	$ 4,309
Contract liabilities:				
Deferred revenue	$ 40,559	$ 83,491	$ (81,670)	$ 42,380
Accounts payable	$ 7,227	$ 3,171	$ (7,227)	$ 3,171
Accrued expenses and other current liabilities	$ 10,000	$ —	$ (10,000)	$ —

(1) Excludes accounts receivable from other services related to clinical and regulatory activities performed by the Company on behalf of MTPC that are not included in the performance obligations identified under the MTPC Agreement as of December 31, 2022 and 2021. Also excludes accounts receivable related to amounts due to the Company from product sales which are included in the accompanying consolidated balance sheets as of December 31, 2022 and 2021.

During the years ended December 31, 2022, 2021 and 2020, the Company recognized the following revenues as a result of changes in the contract asset and contract liability balances in the respective periods (in thousands):

	For the Year Ended December 31,		
Revenue Recognized in the Period from:	**2022**	**2021**	**2020**
Amounts included in deferred revenue at the beginning of the period	$ 29,574	$ 23,364	$ 36,032
Performance obligations satisfied in previous periods	$ —	$ 81	$ 25,964

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC entered into a collaboration agreement, or the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat in Japan and certain other Asian countries, collectively, the MTPC Territory, which was amended effective as of December 2, 2022. In addition, the Company supplies vadadustat to MTPC for both clinical and commercial use in the MTPC Territory.

The Company and MTPC agreed that, instead of including Japanese patients in the Company's global Phase 3 program for vadadustat, MTPC would be the sponsor of a Phase 3 program for vadadustat in Japan. MTPC was responsible for the costs of the Phase 3 program in Japan and other studies required in Japan, and made no funding payments for the global Phase 3 program for vadadustat. In June 2020, vadadustat was approved in Japan for the treatment of anemia due to CKD, which triggered a $15.0 million regulatory milestone payment to the Company that was received in the third quarter of 2020. In August 2020, MTPC launched vadadustat commercially in Japan under the trade name Vafseo™ as a treatment of anemia due to CKD for adult patients on dialysis and not on dialysis. MTPC filed a new drug application for vadadustat for the treatment of anemia due to CKD in adult patients in Taiwan in January 2022 and in Korea in March 2022.

The Company and MTPC have established a joint steering committee pursuant to the MTPC Agreement to oversee development and commercialization of vadadustat in the MTPC Territory, including approval of any development or

commercialization plans. Unless earlier terminated, the MTPC Agreement will continue in effect on a country-by-country basis until the later of the following: expiration of the last-to-expire patent covering vadadustat in such country in the MTPC Territory; expiration of marketing or regulatory exclusivity in such country in the MTPC Territory; or ten years after the first commercial sale of vadadustat in such country in the MTPC Territory. MTPC may terminate the MTPC Agreement upon twelve months' notice at any time after the second anniversary of the effective date of the MTPC Agreement. Either party may terminate the MTPC Agreement upon the material breach of the other party that is not cured within a specified time period or upon the insolvency of the other party.

MTPC is required to make certain milestone payments to the Company aggregating up to approximately $225.0 million upon the achievement of specified development, regulatory and commercial events. More specifically, the Company received $10.0 million in development milestone payments and is eligible to receive up to $40.0 million in regulatory milestone payments, of which the Company received $10.0 million in relation to the Japanese NDA, or JNDA, filing in the third quarter of 2019 and earned an additional $15.0 million following regulatory approval of vadadustat in Japan in the second quarter of 2020, which the Company received in the third quarter of 2020, and up to $175.0 million in commercial milestone payments associated with aggregate sales of all products. In consideration for the exclusive license and other rights contained in the MTPC Agreement, MTPC also made a $20.0 million upfront payment as well as a payment of $20.5 million for Phase 2 studies in Japanese patients completed by the Company and reimbursed by MTPC. The Company is also entitled to receive tiered royalty payments ranging from 13% to 20% on annual net sales of vadadustat in the MTPC Territory. Royalty payments are subject to certain reductions, including upon the introduction of competitive products in certain instances. Royalties are due on a country-by-country basis from the date of first commercial sale of a licensed product in a country until the last to occur of: (i) the expiration of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the expiration of marketing or regulatory exclusivity in such country, or (iii) the tenth anniversary of the first commercial sale of such licensed product in such country. Due to the uncertainty of drug development and commercialization and the high historical failure rates associated therewith, although the Company has received $10.0 million in development milestones and $25.0 million in regulatory milestones, no additional milestone may ever be received from MTPC. The Company recognizes any revenue from MTPC royalties in the period in which the sales occur.

In February 2021, the Company entered into a royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P., or the Royalty Agreement, whereby the Company sold its right to receive royalties and sales milestones under the MTPC Agreement, subject to certain caps and other terms and conditions (see Note 6).

Revenue Recognition

The Company evaluated the elements of the MTPC Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, MTPC, is a customer. The Company's arrangement with MTPC contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize vadadustat in the MTPC Territory (the License Deliverable), (ii) clinical supply of vadadustat (the Clinical Supply Deliverable), (iii) knowledge transfer, (iv) Phase 2 dosing study research services (the Research Deliverable), and (v) rights to future know-how.

The Company identified two performance obligations in connection with its material promises under the MTPC Agreement as follows: (i) License, Research and Clinical Supply Performance Obligation and (ii) Rights to Future Know-How Performance Obligation. Factors considered in making the assessment of which material promises will be accounted for as separate performance obligations included, among other things, the capabilities of the collaboration partner, whether any other vendor sells the item separately, whether the good or service is highly interdependent or highly interrelated to the other elements in the arrangement, and whether there are other vendors that can provide the items. Additionally, the MTPC Agreement does not include a general right of return.

The Company allocates the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it is immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License, Research and Clinical Supply Performance Obligation and allocated the entire transaction price to this performance obligation. The deliverables associated with the License, Research and Clinical Supply Performance Obligation were satisfied as of June 30, 2018.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the estimated cost for the Phase 2 studies, (iii) a non-substantive milestone associated with the first patient enrolled in the NDD-CKD Phase 3 study, and (iv) the cost of all clinical supply provided to MTPC for the Phase 3 studies. No other development and no regulatory milestones were included in

the transaction price at inception, as all other milestone amounts were fully constrained. Subsequent to inception, the transaction price also included certain development and regulatory milestones, as described below. As part of its evaluation of the constraint, the Company considers numerous factors, including that receipt of the milestones is outside the control of the Company and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to MTPC and therefore have also been excluded from the transaction price. The Company re-evaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur. The Company determined that the remaining consideration that may be payable to the Company subsequent to MTPC's commercial launch of Vafseo™, in the third quarter of 2020 is quarterly royalties on net sales, sales milestones, and certain regulatory milestones.

As of December 31, 2022, the transaction price was comprised of: (i) the up-front payment of $20.0 million, (ii) the cost for the Phase 2 studies of $20.5 million, (iii) the cost of all clinical supply provided to MTPC for the Phase 3 studies, (iv) $10.0 million in development milestones received, (v) $25.0 million in regulatory milestones received, comprised of $10.0 million relating to the JNDA filing and $15.0 million relating to regulatory approval of vadadustat in Japan, and (vi) $3.0 million in royalties from net sales of Vafseo. As of December 31, 2022, all development milestones and $25.0 million in regulatory milestones have been achieved. No other regulatory milestones have been assessed as probable of being achieved and as a result have been fully constrained. Revenue for the License, Research and Clinical Supply Performance Obligation for the MTPC Agreement is being recognized using a proportional performance method, for which all deliverables have been completed. Accordingly, the Company recognized the $15.0 million regulatory milestone relating to regulatory approval of vadadustat in Japan as revenue during the year ended December 31, 2020 and the $10.0 million regulatory milestone for the filing of the JNDA as revenue during the year ended December 31, 2019, as the regulatory milestones were both deemed probable of being achieved and the required performance obligations had been satisfied as of December 31, 2020 and 2019, respectively. The Company recognized $1.8 million, $0.8 million, and $0.4 million of revenue for royalties from the net sales of Vafseo during the years ended December 31, 2022, 2021, and 2020, respectively. As noted above, in February 2021, the Company entered into the Royalty Agreement, whereby the Company sold its right to receive these royalties and sales milestones under the MTPC Agreement, subject to certain caps and other conditions (see Note 6). The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2022, there is $0.6 million in accounts receivable, no deferred revenue, and no contract assets. There were no asset or liability balances related to the MTPC Agreement classified as long-term in the consolidated balance sheet as of December 31, 2022.

Supply of Drug Product to MTPC

In March 2020, in connection with the MTPC Agreement, the Company and MTPC executed an amendment to the MTPC Agreement pursuant to which the Company agreed to supply MTPC with certain vadadustat process validation drug product for commercial use, and MTPC agreed to reimburse the Company for certain manufacturing-related expenses. In connection with this arrangement, the Company invoiced the upfront payment of $10.4 million, which it received during the three months ended June 30, 2020. The Company does not recognize revenue under this arrangement until risk of loss on the drug product passes to MTPC and delivery has occurred and MTPC has accepted the product. During the years ended December 31, 2022, 2021 and 2020, the Company recognized $0 million, $0 million, and $6.2 million, respectively, in revenue for drug product that was delivered during the applicable period. As of December 31, 2022, the Company recorded no accounts receivable, no deferred revenue, no other current liabilities and no other non-current liabilities for drug product that is subject to return by MTPC.

On July 15, 2020, the Company and its collaboration partner MTPC entered into a supply agreement, or the MTPC Supply Agreement, which was amended effective as of December 5, 2022. The MTPC Supply Agreement includes the terms and conditions under which the Company supplies vadadustat drug product to MTPC for commercial use in Japan and certain other Asian countries, as contemplated by the MTPC Agreement.

Pursuant to the MTPC Supply Agreement, MTPC provides a rolling forecast, or the MTPC Forecast, to the Company on a quarterly basis. The MTPC Forecast reflects MTPC's needs for vadadustat drug product over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. MTPC makes an up-front payment for a certain percentage of each batch of vadadustat drug product ordered. The term of the MTPC Supply Agreement extends throughout the term of the MTPC Agreement, and the termination provisions of the MTPC Agreement govern termination of the MTPC Supply Agreement.

On December 16, 2022, the Company, MTPC, and Esteve Química, S.A., or Esteve, executed an Assignment of Supply Agreement, or the Assignment Agreement, pursuant to which the Supply Agreement between the Company and Esteve (see Note 15), or the Esteve Agreement, was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Esteve Agreement to MTPC, including the obligations under certain purchase orders issued by the Company and

accepted by Esteve. As such, the transferred purchase orders will continue to have a binding effect on MTPC to take delivery of the product from Esteve in accordance with the terms of the Esteve Agreement. The Company will have no further obligation to take delivery of or pay for product delivered by Esteve under the transferred purchase orders.

During the years ended December 31, 2022, 2021, and 2020, the Company recognized $16.2 million, $11.6 million, and 0 million, respectively, of revenue under the MTPC Supply Agreement. As of December 31, 2022, the Company recorded $2.1 million in accounts receivable and $3.7 million in deferred revenues.

U.S. Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On December 18, 2016, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka U.S. Agreement. The collaboration was focused on the development and commercialization of vadadustat in the United States. Under the terms of the Otsuka U.S. Agreement, the Company was responsible for leading the development of vadadustat, for which it submitted an NDA to the FDA in March 2021, and for which it received the CRL in March 2022. On May 12, 2022, the Company received notice from Otsuka that Otsuka had elected to terminate the Otsuka U.S. Agreement and the Otsuka International Agreement. On June 30, 2022, the Company and Otsuka entered into the Termination Agreement, pursuant to which, among other things, the Company and Otsuka agreed to terminate the Otsuka U.S. Agreement and the Otsuka International Agreement as of June 30, 2022.

Under the terms of the Otsuka U.S. Agreement, the Company granted to Otsuka a co-exclusive, non-sublicensable license under certain intellectual property controlled by the Company solely to perform medical affairs activities and to conduct non-promotional and commercialization activities related to vadadustat in accordance with the associated plans. The co-exclusive license related to activities that would be jointly conducted by the Company and Otsuka pursuant to the terms of the Otsuka U.S. Agreement. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the Otsuka U.S. Agreement.

Revenue Recognition

The Company evaluated the elements of the Otsuka U.S. Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, was a customer. The Company identified three performance obligations in connection with its obligations under the Otsuka U.S. Agreement as follows: (i) License and Development Services Combined (License Performance Obligation); (ii) Rights to Future Intellectual Property (Future IP Performance Obligation) and (iii) Joint Committee Services (Committee Performance Obligation). The Company allocated the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed would be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar.

The Company re-evaluated the transaction price in each reporting period and as uncertain events were resolved or other changes in circumstances occurred. The Company determined that under ASC 606, the contract was modified in the second quarter of 2019, when the Company elected to require Otsuka to increase the aggregate percentage of current global development costs it funds under the Otsuka U.S. Agreement and the Otsuka International Agreement from 52.5% to 80%, or the Otsuka Funding Option, and the Company became eligible to receive the amount from the Otsuka Funding Option. In connection with the modification, the Company adjusted the transaction price to include the amount from the Otsuka Funding Option as additional variable consideration. The Company constrained the variable consideration to an amount for which a significant revenue reversal is not probable.

Pursuant to the Otsuka U.S. Agreement, the Company received: (i) the up-front payment of $125.0 million, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016 of $33.8 million, and (iii) the net cost share consideration received with respect to amounts incurred by the Company under the global development plan of approximately $319.2 million with respect to amounts incurred by the Company subsequent to December 31, 2016.

Pursuant to the Termination Agreement, in July 2022, the Company received a nonrefundable and non-creditable payment of $55.0 million in consideration for the covenants and agreements set forth in the Termination Agreement, including the settlement and release of all disputes and claims as provided therein. The Company determined that the Termination Agreement met the definition of a contract modification and was accounted for as a cumulative catch-up adjustment at the time of modification under ASC 606.

During the year ended December 31, 2022, the Company recognized $92.3 million of collaboration revenue from the Otsuka U.S. Agreement and the Otsuka International Agreement combined in its consolidated statement of operations and comprehensive loss. The collaboration revenue for the year ended December 31, 2022 is primarily comprised of the $55.0 million payment received pursuant to the Termination Agreement, $15.5 million related to previously deferred revenue as of the date of termination and $9.6 million of non-cash consideration related to Otsuka's obligations to complete certain agreed upon clinical activities related to the Phase 3b clinical trial of vadadustat Otsuka is conducting. During the years ended December 31, 2021 and 2020, the Company recognized collaboration revenue totaling approximately $36.6 million and $93.4 million, respectively, with respect to the Otsuka U.S. Agreement.

The Company determined that the medical affairs, commercialization and non-promotional activities elements of the Otsuka U.S. Agreement represented joint operating activities in which both parties were active participants and of which both parties were exposed to significant risks and rewards that were dependent on the success of the activities. Accordingly, the Company accounted for the joint medical affairs, commercialization and non-promotional activities in accordance with ASC No. 808, *Collaborative Arrangements* (ASC 808). Additionally, the Company determined that in the context of the medical affairs, commercialization and non-promotional activities, Otsuka did not represent a customer as contemplated by ASC 606-10-15, *Revenue from Contracts with Customers – Scope and Scope Exceptions*. As a result, the activities conducted pursuant to the medical affairs, commercialization and non-promotional activities plans were accounted for as a component of the related expense in the period incurred. During the years ended December 31, 2022, 2021 and 2020, the Company incurred approximately $7.6 million, $17.5 million and $5.1 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement of which approximately $3.8 million, $8.6 million and $2.2 million were reimbursable by Otsuka and recorded as a reduction to research and development expense during each of the years ended December 31, 2022, 2021 and 2020, respectively. During the year ended December 31, 2022, Otsuka incurred no costs related to the cost-sharing provisions of the Otsuka U.S. Agreement. During the years ended December 31, 2021 and 2020, Otsuka incurred $0.9 million and $2.1 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of which approximately $0.4 million and $1.1 million were reimbursable by the Company and recorded as an increase to research and development expense during the years ended December 31, 2021 and 2020, respectively.

International Collaboration and License Agreement with Otsuka Pharmaceutical Co. Ltd.

Summary of Agreement

On April 25, 2017, the Company entered into a collaboration and license agreement with Otsuka, or the Otsuka International Agreement. The collaboration was focused on the development and commercialization of vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories, collectively, the Otsuka International Territory.

Under the terms of the Otsuka International Agreement, the Company granted to Otsuka an exclusive, sublicensable license under certain intellectual property controlled by the Company to develop and commercialize vadadustat and products containing or comprising vadadustat in the Otsuka International Territory. Additionally, under the terms of this agreement, the Company was responsible for leading the development of vadadustat. Otsuka had the sole responsibility, at its own cost, for the commercialization of vadadustat in the Otsuka International Territory, subject to the approval by the relevant regulatory authorities.

Revenue Recognition

The Company has accounted for the Otsuka International Agreement separately from the collaboration arrangement with Otsuka with respect to the U.S. due to the lack of interrelationship and interdependence of the elements and payment terms within each of the contracts as they related to the respective territories. Accordingly, the Company applied the guidance in ASC 606 solely in reference to the terms and conditions of the Otsuka International Agreement, while the Otsuka U.S. Agreement continued to be accounted for as a discrete agreement in its own right. The Company evaluated the Otsuka International Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, Otsuka, was a customer. The Company identified three performance obligations in connection with its obligations under the Otsuka International Agreement as follows: (i) License and Development Services Combined (License Performance Obligation); (ii) Rights to Future Intellectual Property (Future IP Performance Obligation) and (iii) Joint Committee Services (Committee Performance Obligation). The Company allocated the transaction price to each performance obligation based on the Company’s

best estimate of the relative standalone selling price. The Company developed a best estimate of standalone selling price for the Committee Performance Obligation after considering the nature of the services to be performed and estimates of the associated effort and rates applicable to such services that would be expected to be realized under similar contracts. The Company developed a best estimate of standalone selling price for the Future IP Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement. The Company did not develop a best estimate of standalone selling price for the License Performance Obligation due to the following: (i) the best estimates of standalone selling price associated with the Future IP Performance Obligation was determined to be immaterial and (ii) the period of performance and pattern of recognition for the License Performance Obligation and the Committee Performance Obligation was determined to be similar.

The Company re-evaluated the transaction price in each reporting period and as uncertain events were resolved or other changes in circumstances occurred. Pursuant to the Otsuka International Agreement, the Company received: (i) the up-front payment of $73.0 million, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017 of $0.2 million, and (iii) the net cost share consideration received with respect to amounts incurred by the Company subsequent to March 31, 2017 of $216.7 million.

As discussed above, the Otsuka International Agreement was terminated on June 30, 2022 pursuant to the Termination Agreement. Refer to earlier in this Note 4 for further details of the recognition of this Termination Agreement in the Company's consolidated statement of operations and comprehensive loss.

During the years ended December 31, 2021 and 2020, the Company recognized revenue totaling approximately $16.4 million and $45.5 million, respectively, with respect to the Otsuka International Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2021, there was approximately $0.9 million in contract liabilities (included in accounts payable) and $1.3 million in prepaid expenses and other current assets in the consolidated balance sheet.

Janssen Pharmaceutica NV Research and License Agreement

Summary of Agreement

On February 9, 2017, the Company entered into a Research and License Agreement, the Janssen Agreement, with Janssen Pharmaceutica NV, or Janssen, a subsidiary of Johnson & Johnson, pursuant to which Janssen granted the Company an exclusive license under certain intellectual property rights to develop and commercialize worldwide certain HIF prolyl hydroxylase targeted compounds.

Under the terms of the Janssen Agreement, the Company made an upfront payment of $1.0 million in cash to Janssen and issued a warrant to purchase 509,611 shares of the Company’s common stock, which expired on February 9, 2022. On August 1, 2022, the Company notified Janssen that it was exercising its right to terminate the Janssen Agreement in its entirety, and Janssen agreed to the termination which became effective on August 2, 2022.

Cyclerion Therapeutics License Agreement

Summary of Agreement

On June 4, 2021, the Company entered into a License Agreement, the Cyclerion Agreement, with Cyclerion Therapeutics Inc., or Cyclerion, pursuant to which Cyclerion granted the Company an exclusive global license under certain intellectual property rights to research, develop and commercialize praliciguat, an investigational oral soluble guanylate cyclase stimulator.

Under the terms of the Cyclerion Agreement, the Company made an upfront payment of $3.0 million in cash to Cyclerion, which was paid during the second quarter of 2021. Substantially all of the fair value of the assets acquired in conjunction with the Cyclerion Agreement was concentrated in the acquired license. As a result, the Company accounted for this transaction as an asset acquisition under ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business*. The upfront payment was charged to expense at acquisition, as it relates to a development stage compound with no alternative future use.

In addition, Cyclerion is eligible to receive up to an aggregate of $222.0 million from the Company in specified development and regulatory milestone payments on a product-by-product basis. Cyclerion will also be eligible to receive specified commercial milestones as well as tiered royalties ranging from a low-single-digit to mid-double-digit percentage of net sales, on a product-by-product basis, and subject to reduction upon expiration of patent rights or the launch of a generic product in the

territory. The Company recorded the upfront payment in the amount of $3.0 million to research and development expense in June 2021.

Unless earlier terminated, the Cyclerion Agreement will expire on a product-by-product and country-by-country basis upon the expiration of the last royalty term, which ends upon the longest of (i) the expiration of the patents licensed under the Cyclerion Agreement, (ii) the expiration of regulatory exclusivity for such product, and (iii) 10 years from first commercial sale of such product. The Company may terminate the Cyclerion Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Cyclerion. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Cyclerion Agreement or in the event of certain additional circumstances.

CSL Vifor License Agreement

Summary of Agreement

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd. (now a part of CSL Limited), or CSL Vifor, pursuant to which the Company granted CSL Vifor an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, an affiliate of Fresenius Medical Care North America, or FMCNA, in the United States. On April 8, 2019, the Company and CSL Vifor entered into an Amended and Restated License Agreement, or the Vifor First Amended Agreement, which amended and restated in full the Vifor Agreement. On February 18, 2022, the Company and CSL Vifor entered into a Second Amended and Restated License Agreement, or the Vifor Second Amended Agreement, which amends and restates the Vifor First Amended Agreement.

Pursuant to the Vifor Second Amended Agreement, the Company granted CSL Vifor an exclusive license to sell vadadustat to FMCNA and its affiliates, including Fresenius Kidney Care Group LLC, to certain third party dialysis organizations approved by the Company, to independent dialysis organizations that are members of certain group purchasing organizations, and to certain non-retail specialty pharmacies, or collectively, the Supply Group, in the United States, or the Territory. Pursuant to the Vifor Second Amended Agreement, CSL Vifor agreed that it would not sell or otherwise supply vadadustat until the FDA has granted regulatory approval for vadadustat for the treatment of anemia due to CKD in adult patients with DD-CKD in the Territory and until CSL Vifor has entered a supply agreement with the applicable member of the Supply Group.

Similar to the Vifor First Amended Agreement, the Vifor Second Amended Agreement is structured as a profit share arrangement between the Company and CSL Vifor in which the Company will receive approximately 66% of the profit, net of certain pre-specified costs. Under the Vifor Second Amended Agreement, in February 2022, CSL Vifor made an upfront payment to the Company of $25.0 million in lieu of the previously disclosed milestone payment of $25.0 million that CSL Vifor was to pay the Company following approval of vadadustat by the FDA, as established under the Vifor First Amended Agreement.

Unless earlier terminated, the Vifor Second Amended Agreement will expire upon the later of the expiration of all patents that claim or cover vadadustat or expiration of marketing or regulatory exclusivity for vadadustat in the Territory. CSL Vifor may terminate the Vifor Second Amended Agreement in its entirety upon 30 months' prior written notice after the first anniversary of the receipt of regulatory approval, if approved, from the FDA for vadadustat for dialysis-dependent CKD patients. The Company may terminate the Vifor Second Amended Agreement in its entirety for convenience, following the earlier of a certain period of time elapsing or following certain specified regulatory events, and upon six months' prior written notice. If the Company so terminates for convenience, subject to specified exceptions, the Company will pay a termination fee to CSL Vifor. In addition, either party may, subject to a cure period, terminate the Vifor Second Amended Agreement in the event of the other party's uncured material breach or bankruptcy.

Investment Agreement

In connection with the Vifor Agreement, in May 2017, the Company and CSL Vifor entered into an investment agreement, or the First Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or the 2017 Shares, to CSL Vifor at a price per share of $14.00 for a total of $50.0 million. The amount representing the premium over the closing stock price of $12.69 on the date of the transaction, totaling $4.7 million, was determined by the Company to represent consideration related to the Vifor Agreement.

CSL Vifor agreed to a lock-up restriction such that it agreed not to sell the 2017 Shares for a period of time following the effective date of the First Investment Agreement as well as a customary standstill agreement. The lock-up restriction in place as part of the First Investment Agreement has since expired. In addition, the First Investment Agreement contains voting agreements made by CSL Vifor with respect to the 2017 Shares. The 2017 Shares have not been registered pursuant to the

Securities Act of 1933, as amended, or the Securities Act, and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and Rule 506 promulgated thereunder.

In connection with entering into the Vifor Second Amended Agreement, on February 18, 2022, the Company and CSL Vifor entered into an investment agreement, or the Second Investment Agreement, pursuant to which the Company sold an aggregate of 4,000,000 shares of its common stock, or the 2022 Shares, to CSL Vifor for a total of $20.0 million on February 22, 2022. The amount representing the premium over the grant date fair value on the date of the transaction, $13.6 million, was determined by the Company to represent the consideration related to the Vifor Second Amended Agreement. CSL Vifor has agreed to a lock-up restriction to not sell or otherwise dispose of the 2022 Shares for a period of time following the effective date of the Second Investment Agreement as well as a customary standstill agreement. In addition, the Second Investment Agreement contains voting agreements made by CSL Vifor with respect to the 2022 Shares. The 2022 Shares have not been registered pursuant to the Securities Act and were issued and sold in reliance upon the exemption from registration contained in Section 4(a)(2) of the Securities Act and/or Rule 506 promulgated thereunder, as the transaction did not involve any public offering within the meaning of Section 4(a)(2) of the Securities Act.

Revenue Recognition

The Company evaluated the elements of the Vifor Second Amended Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, CSL Vifor, is a customer. The Company's arrangement with CSL Vifor contains one material promise under the contract at inception, which is the non-sublicensable, non-transferrable license under certain of the Company's intellectual property to (i) sell vadadustat solely to the Supply Group, (ii) sell vadadustat to Designated Wholesalers solely for resale to members of the Supply Group, (iii) conduct medical affairs with respect to vadadustat in the Territory in the field during the term of the Vifor Second Amended Agreement and (iv) use the Akebia Trademark solely in connection with the sale of vadadustat (the License Deliverable).

The Company has identified one performance obligation in connection with its obligations under the Vifor Second Amended Agreement, which is the License Deliverable, or License Performance Obligation. The transaction price at inception was comprised of: (i) the up-front payment of $25.0 million, (ii) the premium paid by CSL Vifor on the First Investment Agreement of $4.7 million, and (iii) the premium paid by CSL Vifor on the Second Investment Agreement of $13.6 million. Pursuant to the terms of the Vifor Second Amended Agreement, these payments from CSL Vifor are non-refundable and non-creditable against any other amount due to the Company. Also pursuant to the Vifor Second Amended Agreement, if the Centers for Medicare & Medicaid Services, or CMS, determines that vadadustat is excluded from the Transitional Drug Add-on Payment Adjustment, or TDAPA, the Company can terminate the Vifor Second Amended Agreement and will be required to repay the up-front payment and the premiums paid by CSL Vifor in the First Investment Agreement and Second Investment Agreement, respectively. The Company considered whether the transaction price was constrained as required per the guidance in ASC 606-10-32-11. As part of its evaluation of the constraint, the Company considered numerous factors, including the CRL received from the FDA for vadadustat, the uncertainty associated with a potential future approval of vadadustat by the FDA, and if approval of vadadustat is received in the future, whether vadadustat would be included in certain reimbursement bundles by CMS, which are all outside of the Company's control. CSL Vifor also agreed that it will not sell or otherwise supply vadadustat until the FDA has granted regulatory approval for vadadustat in the DD-CKD Indication. The Company constrains the variable consideration to an amount for which a significant revenue reversal is not probable. Therefore, the Company determined that the entire transaction price at inception was constrained under ASC 606, and the Company has recorded the transaction price to deferred revenue as of December 31, 2022.

Refund Liability to Customer

Pursuant to the Vifor Second Amended Agreement, CSL Vifor contributed $40.0 million to a working capital fund established to partially fund the Company's costs of purchasing vadadustat from its contract manufacturers, or the Working Capital Fund, which amount of funding will fluctuate, and which funding the Company is required to repay to CSL Vifor over time. The $40 million initial contribution to the Working Capital Fund represented 50% of the amount of purchase orders that the Company had placed with its contract manufacturers for the supply of vadadustat for the Territory already delivered as of the effective date of the Vifor Second Amended Agreement, and to be delivered through the end of 2023. The amount of the Working Capital Fund will be reviewed at specified intervals and is adjusted based on a number of factors including outstanding supply commitments for vadadustat for the Territory and agreed upon vadadustat inventory levels held by the Company for the Territory. Upon termination or expiration of the Vifor Second Amended Agreement for any reason other than convenience by CSL Vifor (including following receipt of the CRL for vadadustat), the Company will be required to refund the outstanding balance of the Working Capital Fund on the date of termination or expiration.

The Company has recorded the Working Capital Fund as a refund liability under ASC 606. The Company has determined that the refund liability itself does not represent an obligation to transfer goods or services to CSL Vifor in the future. The Company has therefore determined that this refund liability is not a contract liability under ASC 606. The Company accounted for the refund liability as a debt arrangement with zero coupon interest. The Company imputed interest on the refund liability to the customer at a rate of 15.0% per annum, which was determined based on certain factors, including the Company's credit rating, comparable securities yield, and the expected repayment period of the Working Capital Fund. The Company recorded an initial discount on the refund liability to the customer and a corresponding deferred gain to the refund liability to customer on the consolidated balance sheet as of the date the funds were received from CSL Vifor, which was March 18, 2022. The discount on the note payable is being amortized to interest expense using the effective interest method over the expected term of the refund liability. The deferred gain is being amortized to interest income on a straight-line basis over the expected term of the refund liability. The amortization of the discount was $3.4 million for the year ended December 31, 2022. The amortization of the deferred gain was $2.4 million for the year ended December 31, 2022. The $41.0 million total refund liability is classified as a long-term refund liability based on management's estimate of potential amounts that could be refundable exceeding a one-year period.

Priority Review Voucher Letter Agreement

On February 14, 2020, the Company entered into a letter agreement, or the Letter Agreement, with CSL Vifor relating to CSL Vifor’s agreement with a third party to purchase a Priority Review Voucher, or the PRV, issued by the FDA, subject to satisfaction of customary closing conditions, or the PRV Purchase. Pursuant to the Letter Agreement, Akebia paid CSL Vifor $10.0 million in connection with the closing of the PRV Purchase. The $10.0 million payment to CSL Vifor was recorded to research and development expense in the consolidated statement of operations and as an operating cash outflow in the unaudited consolidated statement of cash flows during 2020. In March 2021, the Company submitted an NDA for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. The Company's NDA submission did not include a PRV.

On August 21, 2021, the Company and CSL Vifor executed an amendment to the Letter Agreement whereby the parties agreed that CSL Vifor would sell the PRV to a third party, and the Company and CSL Vifor would share the proceeds from the sale based on certain terms. In the fourth quarter of 2021, CSL Vifor sold the PRV to a third party, and CSL Vifor paid the Company $8.6 million in proceeds from the sale, which was recorded as contra research and development expense. These proceeds were subsequently paid to Otsuka as reimbursement for their contribution to the purchase of the PRV, as required under a separate letter agreement executed with Otsuka.

License Agreement with Panion & BF Biotech, Inc.

The Company had a license agreement, which was amended from time to time, with Panion & BF Biotech, Inc., or Panion, under which Keryx, the Company’s wholly owned subsidiary, was the contracting party, or the Panion License Agreement, pursuant to which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, or the Licensor Territory, for the development and commercialization of ferric citrate.

On April 17, 2019, the Company and Panion entered into a second amended and restated license agreement, or the Panion Amended License Agreement, which amends and restates in full the Panion License Agreement. The Panion Amended License Agreement provides Keryx with an exclusive license under Panion-owned know-how and patents covering the rights to sublicense, develop, make, use, sell, offer for sale, import and export ferric citrate worldwide, excluding the Licensor Territory. The Panion Amended License Agreement also provides Panion with an exclusive license under Keryx-owned patents covering the rights to sublicense (with the Company’s written consent), develop, make, use, sell, offer for sale, import and export ferric citrate in certain countries in the Licensor Territory. Under the Panion Amended License Agreement, Panion is eligible to receive from the Company or any sublicensee royalty payments based on a mid-single digit percentage of sales of ferric citrate in the Company’s licensed territories. The Company is eligible to receive from Panion or any sublicensee royalty payments based on a mid-single digit percentage of net sales of ferric citrate in Panion’s licensed territories.

The Panion Amended License Agreement terminates upon the expiration of each of the Company’s and Panion’s obligations to pay royalties thereunder. In addition, the Company may terminate the Panion Amended License Agreement (i) in its entirety or (ii) with respect to one or more countries in the Company’s licensed territory, in either case upon 90 days’ notice. The Company and Panion also each have the right to terminate the Panion Amended License Agreement upon the occurrence of a material breach of the Panion Amended License Agreement by the other party, subject to certain cure provisions, or certain insolvency events. The Panion Amended License Agreement also provides that, on a country-by-country basis, until the second anniversary of the expiration of the obligation of the Company or Panion, as applicable, to pay royalties in a country in which such party has ferric citrate for sale on the date of such expiration, neither the other party nor its affiliates will, directly or

indirectly, sell, distribute or otherwise commercialize or supply or cause to supply ferric citrate to a third party for sale or distribution in such country.

The Panion Amended License Agreement includes customary terms relating to, among others, indemnification, confidentiality, remedies, and representations and warranties. In addition, the Panion Amended License Agreement provides that each of the Company and Panion has the right, but not the obligation, to conduct litigation against any infringer of certain patent rights under the Panion Amended License Agreement in certain territories.

During the years ended December 31, 2022, 2021 and 2020, the Company incurred approximately $13.8 million, $11.8 million and $11.2 million, respectively, in royalty payments due to Panion relating to the Company's sales of Auryxia in the United States and JT and Torii's net sales of Riona in Japan.

Sublicense Agreement with Japan Tobacco, Inc. and its subsidiary, Torii Pharmaceutical Co., Ltd.

Summary of Agreement

The Company has an Amended and Restated Sublicense Agreement, which was amended in June 2013, with JT and Torii, or the JT and Torii Sublicense Agreement, under which Keryx, the Company's wholly owned subsidiary, remains the contracting party. Under the JT and Torii Sublicense Agreement, JT and Torii obtained the exclusive sublicense rights for the development and commercialization of ferric citrate hydrate in Japan. JT and Torii are responsible for the future development and commercialization costs in Japan.

In January 2014, JT and Torii received manufacturing and marketing approval of ferric citrate from the Japanese Ministry of Health, Labour and Welfare. Ferric citrate hydrate, which launched in May 2014 and is being marketed in Japan by Torii under the brand name Riona, is indicated as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including NDD-CKD and DD-CKD. In July 2019, JT and Torii, reported positive top-line results from a pivotal Phase 3 comparative study evaluating Riona for the treatment of IDA in adult patients in Japan, which was approved in March 2021. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan. The Company is eligible to receive royalty payments based on a tiered low double-digit percentage of net sales of Riona in Japan inclusive of amounts that the Company must pay to Panion on JT and Torii's net sales of Riona under the Panion License Agreement subject to certain reductions upon expiration or termination of the Amended and Restated License Agreement between Keryx and Panion, pursuant to which Keryx in-licensed the exclusive worldwide rights, excluding certain Asian-Pacific countries, for the development and commercialization of ferric citrate. The Company is entitled to receive up to an additional $55.0 million upon the achievement of certain annual net sales milestones.

The sublicense under the JT and Torii Sublicense Agreement terminates upon the expiration of all underlying patent rights. Also, JT and Torii may terminate the JT and Torii Sublicense Agreement with or without cause upon at least six months' prior written notice to the Company. Additionally, either party may terminate the JT and Torii Sublicense Agreement for cause upon 60 days' prior written notice after the breach of any uncured material provision of the JT and Torii Sublicense Agreement, or after certain insolvency events.

Revenue Recognition

The Company evaluated the elements of the JT and Torii Sublicense Agreement in accordance with the provisions of ASC 606 and concluded that the contract counterparty, JT and Torii, is a customer. The Company's arrangement with JT and Torii contains the following material promises under the contract at inception: (i) exclusive license to develop and commercialize ferric citrate hydrate in Japan (the License Deliverable), (ii) supply of ferric citrate hydrate until JT and Torii could secure their own source (the Supply Deliverable), (iii) knowledge transfer, and (iv) rights to future know-how.

The Company identified two performance obligations in connection with its obligations under the JT and Torii Sublicense Agreement: (i) *License and Supply Performance Obligation* and (ii) *Rights to Future Know-How Performance Obligation*. The Company allocated the transaction price to each performance obligation based on the Company's best estimate of the relative standalone selling price. The Company developed a best estimate of the standalone selling price for the Rights to Future Know-How Performance Obligation primarily based on the likelihood that additional intellectual property covered by the license conveyed will be developed during the term of the arrangement and determined it immaterial. As such, the Company did not develop a best estimate of standalone selling price for the License and Supply Performance Obligation and allocated the entire transaction price to this performance obligation. Additionally, as of the consummation of the Merger, the services associated with the License and Supply Performance Obligation were completed and JT and Torii had secured their own source to manufacture ferric citrate hydrate. As such, any initial license fees as well as any development-based milestones and manufacturing fee revenue were received and recognized prior to the Merger. The Company determined that the remaining

consideration that may be payable to the Company under the terms of the sublicense agreement are either quarterly royalties on net sales or payments due upon the achievement of sales-based milestones. In accordance with ASC 606, the Company recognizes sales-based royalties and milestone payments based on the level of sales, when the related sales occur as these amounts have been determined to relate predominantly to the license granted to JT and Torii and therefore are recognized at the later of when the performance obligation is satisfied, or the related sales occur.

During the years ended December 31, 2022, 2021 and 2020, the Company recognized $5.3 million, $5.8 million and $5.7 million, respectively, in license revenue related to royalties earned on net sales of Riona in Japan. The Company records the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of Riona, in the same period as the royalty revenue from JT and Torii is recorded.

License Agreement with Averoa SAS

Summary of Agreement

On December 22, 2022, the Company and Averoa SAS, or Averoa, entered into a license agreement, or the Averoa License Agreement, pursuant to which the Company granted to Averoa an exclusive license to develop and commercialize ferric citrate, or the Licensed Product, in the European Economic Area, Turkey, Switzerland and the United Kingdom, or the Territory.

Under the Averoa License Agreement, the Company is entitled to receive tiered, escalating royalties ranging from a mid-single digit percentage to a low double-digit percentage of Averoa's annual net sales in the Territory, including certain minimum royalty amounts in certain years, and subject to reduction in certain circumstances. The royalties will expire on a country-by-country basis upon the last to occur of (a) 10 years following the date of first commercial sale of the Licensed Product in such country; (b) expiration of the last valid claim of Company patent rights and joint patent rights in such country; and (c) the date of expiration of the data, regulatory, or marketing exclusivity period conferred by the applicable regulatory authority in such country with respect to the Licensed Product.

The Company and Averoa will establish a joint steering committee to oversee the development, manufacturing and commercialization of the Licensed Product in the Territory.

The Averoa License Agreement expires on the date of expiration of all royalty obligations due thereunder with respect to the Licensed Product on a country-by-country basis in the Territory, unless earlier terminated in accordance with the agreement. Either party may, subject to a cure period, terminate the Averoa License Agreement in the event of the other party’s uncured material breach. Averoa has the right to terminate the Averoa License Agreement for convenience upon 12 months’ prior written notice delivered on or after the date that is 12 months after the effective date. In addition, Averoa has the right to terminate the Averoa License Agreement upon 30 days’ notice if the EMA rejects Averoa’s marketing authorization application for the Licensed Product, and the parties in good faith agree that submitting a new marketing authorization application to the EMA will not result in approval. The Averoa License Agreement includes customary terms relating to, among others, indemnification, confidentiality, remedies, and representations and warranties.

The Averoa License Agreement provides that the Company and Averoa will enter into a supply agreement pursuant to which the Company will supply the Licensed Product to Averoa for commercial use in the Territory. The Company will have the right to terminate the supply agreement upon 24 months' notice, which may be provided on or after January 1, 2024. The Company did not receive any consideration under this agreement as of December 31, 2022.

5. Restructuring and Other Charges, Net

On April 4, 2022, the Board of Directors of the Company approved a reduction of the Company’s workforce by approximately 42% across all areas of the Company (47% inclusive of the closing of the majority of open positions) following the receipt of the CRL from the FDA to the Company’s NDA for vadadustat for the treatment of anemia due to CKD in adult patients. On May 5, 2022, the Company implemented a further reduction in workforce consisting of several members of management. These actions reflected the Company’s determination to refocus its strategic priorities around its commercial product, Auryxia®, and its development portfolio, and are steps in a cost savings plan to significantly reduce the Company’s expense profile.

The workforce reductions were completed as of December 31, 2022, and the Company has incurred all related charges. During the year ended December 31, 2022, the Company recognized $14.5 million of restructuring charges in the consolidated statement of operations. These charges included $11.3 million of one-time termination benefits and contractual termination benefits for severance, healthcare, and related benefits and $3.2 million of non-cash share-based compensation expense. The

charges were recorded pursuant to ASC 712, *Compensation-Nonretirement Postemployment Benefits* or ASC 420, *Exit or Disposal Cost Obligations*, depending on the employee.

On November 7, 2022, the Board of Directors approved a reduction of the Company's workforce by approximately 14% consisting solely of individuals within the commercial organization as a result of the Company's decision to shift to a strategic account management focused model for its commercial efforts. This shift in approach supports the Company's strategic pillars to drive Auryxia revenue while also continuing to decrease operating costs.

The workforce reduction was completed as of December 31, 2022, and the Company has incurred all related charges. During the year ended December 31, 2022, the Company recognized $1.4 million of restructuring charges in the consolidated statement of operations. These charges included one-time termination benefits and contractual termination benefits for severance, healthcare, and related benefits and non-cash share-based compensation expense. The charges were recorded pursuant to ASC 712, *Compensation-Nonretirement Postemployment Benefits* or ASC 420, *Exit or Disposal Cost Obligations*, depending on the employee.

Details of the restructuring liability activity for the Company's workforce reductions for the period ended December 31, 2022 as recorded in accrued expenses and other current liabilities and other non-current liabilities in the consolidated balance sheet on this Form 10-K are as follows:

	December 31, 2022 (in thousands)
Balance at December 31, 2021	$ —
Restructuring charges	15,933
Stock-based compensation expense	(3,197)
Severance payments and adjustments	(8,977)
Balance at December 31, 2022	$ 3,758

6. Liability Related to Sale of Future Royalties

On February 25, 2021, the Company entered into the Royalty Agreement with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which the Company sold to HCR its right to receive royalties and sales milestones for vadadustat in Japan and certain other Asian countries, such countries, collectively, the MTPC Territory, and such payments collectively the Royalty Interest Payments, in each case, payable to the Company under the MTPC Agreement, subject to an annual maximum "cap" of $13.0 million, or the Annual Cap, and an aggregate maximum "cap" of $150.0 million, or the Aggregate Cap. After HCR receives Royalty Interest Payments equal to the Annual Cap in a given calendar year, the Company will receive 85% of the Royalty Interest Payments for the remainder of that year. After HCR receives Royalty Interest Payments equal to the Aggregate Cap, or the Company pays the Aggregate Cap to HCR (net of the Royalty Interest Payments already received by HCR), the Royalty Interest Payments will revert back to the Company, and HCR would have no further right to any Royalty Interest Payments. The Company received $44.8 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and the Company is eligible to receive an additional $5.0 million in each year from 2021 through 2023 under the Royalty Agreement if specified annual sales milestones are achieved for vadadustat in the MTPC Territory, subject to the satisfaction of certain customary conditions. The sales milestone for vadadustat in the MTPC Territory was not achieved for 2022 or 2021. The Company retains the right to receive all potential future regulatory milestones for vadadustat under the MTPC Agreement. The Royalty Agreement will terminate on the earlier of the date on which HCR has received (i) the last Royalty Interest Payment or (ii) payment by the Company of an amount equal to the Aggregate Cap minus the aggregate amount of all Royalty Interest Payments actually received by HCR.

Although the Company sold its right to receive royalties and sales milestones for vadadustat in the MTPC Territory as described above, as a result of its ongoing involvement in the cash flows related to these royalties, the Company will continue to account for these royalties as revenue. The Company recognized the proceeds received from HCR as a liability that is being amortized using the effective interest method over the life of the arrangement. At the transaction date, the Company recorded the net proceeds of $44.8 million as a liability. In order to determine the amortization of the liability, the Company is required to estimate the total amount of future net royalty payments to be made to HCR over the term of the Royalty Agreement. The total threshold of net royalties to be paid, less the net proceeds received, will be recorded as interest expense over the life of the liability. The Company imputes interest on the unamortized portion of the liability using the effective interest method. The annual effective interest rate as of December 31, 2022 was 0% which is reflected as interest expense in the consolidated

statements of operations and comprehensive loss. Over the course of the Royalty Agreement, the actual interest rate will be affected by the amount and timing of royalty revenue recognized and changes in forecasted royalty revenue. There are a number of factors that could materially affect the amount and timing of royalty payments from MTPC, none of which are within the Company's control. On a quarterly basis, the Company reassesses the effective interest rate and adjusts the rate prospectively as needed.

The following table shows the activity within the liability account for the year ended December 31, 2022:

	December 31, 2022 (in thousands)
Liability related to sale of future royalties, net — beginning balance	$ 53,079
MTPC royalties payable	(1,777)
Non-cash interest expense recognized	6,182
Liability related to sale of future royalties, net — ending balance	$ 57,484

The Royalty Agreement requires the Company to take certain actions, including actions with respect to the Royalty Interest Payments, the MTPC Agreement, the MTPC Supply Agreement, and the Company's intellectual property. The Royalty Agreement also contains certain representations and warranties, covenants, indemnification obligations, events of default and other provisions that are customary for a royalty monetization transaction of this nature. In addition, the Company granted HCR a precautionary security interest in connection with the Royalty Interest Payments.

7. Fair Value of Financial Instruments

The Company utilizes a portfolio management company for the valuation of the majority of its investments. This company is an independent, third-party vendor recognized to be an industry leader with access to market information that obtains or computes fair market values from quoted market prices, pricing for similar securities, recently executed transactions, cash flow models with yield curves and other pricing models. For valuations obtained from the pricing service, the Company performs due diligence to understand how the valuation was calculated or derived, focusing on the valuation technique used and the nature of the inputs.

Based on the fair value hierarchy, the Company classifies its cash equivalents and available for sale securities within Level 1 or Level 2. This is because the Company values its cash equivalents and available for sale securities using quoted market prices or alternative pricing sources and models utilizing market observable inputs.

Assets measured or disclosed at fair value on a recurring basis as of December 31, 2022 and 2021 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2022				
Assets:				
Cash and cash equivalents	$ 90,466	—	—	$ 90,466
	$ 90,466	$ —	$ —	$ 90,466
Liabilities:				
Derivative liability	—	—	$ 760	$ 760
	$ —	$ —	$ 760	$ 760

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
December 31, 2021				
Assets:				
Cash and cash equivalents	$ 149,800	—	—	$ 149,800
	$ 149,800	$ —	$ —	$ 149,800
Liabilities:				
Derivative liability	—	—	$ 1,820	$ 1,820
	$ —	$ —	$ 1,820	$ 1,820

The Company's Loan Agreement with Pharmakon (see Note 11) contains certain provisions that change the underlying cash flows of the debt instrument, including a potential extension to the interest-only period dependent on both (i) no event of default having occurred and continuing and (ii) the Company achieving certain regulatory and revenue conditions. One of the regulatory conditions was approval of vadadustat by August 2022, however, in March 2022, the Company received the CRL from the FDA stating that the FDA had determined that it could not approve the NDA for vadadustat in its present form. Therefore, the Company is no longer eligible for the interest-only extension period and this no longer changes the underlying cash flows of the debt instrument. The Company also assessed the acceleration of the obligations under the Loan Agreement under certain events of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The potential events of default include maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. The Company recorded a derivative liability related to the Company's Loan Agreement with Pharmakon of $0.8 million and $1.8 million as of December 31, 2022 and 2021, respectively. The Company classified the derivative liability as a non-current liability on the balance sheet at December 31, 2022 and 2021. The estimated fair value of the derivative liability on both December 31, 2022 and 2021 was determined using a scenario-based approach and discounted cash flow model that includes principal and interest payments under various scenarios involving clinical development success for vadadustat and various cash flow assumptions. The Company used a 0% probability of clinical development success due to receipt of the CRL from the FDA for vadadustat. Should the Company's assessment of the probabilities around these scenarios change, including for changes in market conditions, there could be a change to the fair value of the derivative liability.

The following table provides a roll-forward of the fair value of the derivative liability (in thousands):

Balance at December 31, 2021	$ 1,820
Change in fair value of derivative liability, recorded as other income	(1,060)
Balance at December 31, 2022	$ 760

The Company had no other assets or liabilities measured at fair value on a recurring basis using significant unobservable inputs (Level 3) at December 31, 2022 and 2021.

8. Inventory

The components of inventory are summarized as follows:

	December 31, 2022	December 31, 2021
	(in thousands)	
Raw materials	$ 610	$ 1,763
Work in process	8,086	62,635
Finished goods	13,676	14,661
Total inventory	$ 22,372	$ 79,059

Long-term inventory, which primarily consists of raw materials and work in process, is included in other assets in the Company's consolidated balance sheets.

	December 31, 2022	December 31, 2021
	(in thousands)	
Balance Sheet Classification:		
Inventory	$ 21,762	$ 38,195
Other assets	610	40,864
Total inventory	$ 22,372	$ 79,059

Inventory amounts written down as a result of excess, obsolescence, scrap or other reasons and charged to cost of goods sold totaled $30.2 million, $15.6 million, and $20.1 million during the years ended December 31, 2022, 2021, and 2020, respectively. The increase in inventory amounts written down for the year ended December 31, 2022 as compared to the year ended December 31, 2021 was primarily due to higher write-downs to inventory reserves related to Auryxia drug substance that will not be forward processed into drug product. In addition, there were $0 million, $8.7 million, and $11.4 million in related step-up charges during the years ended December 31, 2022, 2021, and 2020, respectively.

If future sales of Auryxia are lower than expected, the Company may be required to write-down the value of such inventories. Inventory write-downs and losses on purchase commitments are recorded as a component of cost of sales in the consolidated statement of operations.

9. Intangible Assets and Goodwill

Intangible Assets

The following table presents the Company's intangible assets (in thousands):

	December 31, 2022		
	Gross Carrying Value	Accumulated Amortization	Total
Acquired intangible assets:			
Developed product rights for Auryxia	$ 213,603	$ (141,519)	$ 72,084
Total	$ 213,603	$ (141,519)	$ 72,084

	December 31, 2021		
	Gross Carrying Value	Accumulated Amortization	Total
Acquired intangible assets:			
Developed product rights for Auryxia	$ 213,603	$ (105,476)	$ 108,127
Total	$ 213,603	$ (105,476)	$ 108,127

The Company amortizes its definite-lived intangible assets using the straight-line method, which is considered the best estimate of economic benefit, over its estimated useful life of six years. The Company recorded $36.0 million in amortization expense during the years ended December 31, 2022 and 2021, and $31.5 million in amortization expense during the year ended December 31, 2020 related to the developed product rights for Auryxia. Estimated future amortization expense for the intangible asset as of December 31, 2022 is as follows (in thousands):

	Total
2023	$ 36,042
2024	36,042
	$ 72,084

Auryxia Intangible Asset Impairment

In the second quarter of 2020, in connection with a routine business review, the Company reduced its short-term and long-term Auryxia revenue forecast. This reduction was primarily driven by the compounding impact of the September 2018 CMS decision that rescinded Medicare Part D coverage of Auryxia for the IDA Indication and the related imposition by CMS of a prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. As a result, the Company determined indicators of impairment existed for the developed product rights for Auryxia and performed an undiscounted cash flow analysis pursuant to ASC 360-10, *Impairment or Disposal of Long-lived Assets*, to determine if the cash flows expected to be generated by the Auryxia asset group over the estimated remaining useful life of the primary assets were sufficient to recover the carrying value of the Auryxia asset group. Based on this analysis, the undiscounted cash flows were not sufficient to recover the carrying value of the Auryxia asset group. As a result, the Company was required to perform Step 3 of the impairment test to determine the fair value of the Auryxia asset group.

To estimate the fair value, the Company performed a business enterprise valuation for the Auryxia asset group using the income approach, which is based on a discounted cash flow analysis and calculates the fair value by estimating the after-tax cash flows attributable to the asset group and then discounting the after-tax cash flows to present value using a risk-adjusted discount rate. Key estimates and assumptions used in the valuations included projected revenues and expenses related to the asset, estimated contributory asset charges, and a risk-adjusted discount rate of 9.5% to calculate the present value of the future expected cash inflows. The Company believes its assumptions are consistent with the plans and estimates that a market participant would use to manage the business. The discount rates used are intended to reflect the risks inherent in future cash flow projections and were based on an estimate of the weighted average cost of capital, or WACC, of market participants relative to the Auryxia asset group.

As a result of this analysis, the fair value of the Auryxia asset group was below its carrying value, and the Company recorded an impairment charge of $115.5 million during the three months ended June 30, 2020 and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia from nine years to seven years. The impairment charge has been entirely allocated to the Company’s only intangible asset, the developed product rights for Auryxia, as all other long-lived assets had fair values that were either equal to or greater than their carrying value. Per ASC 360-10, the carrying amount of a long-lived asset of the group would not be reduced below its fair value. The Company believes its assumptions used to determine the fair value of the Auryxia asset group are reasonable. In the event the estimates and assumptions used in the valuation of the Auryxia asset group, including the forecasted projections, change in the future, additional impairment charges could be recorded in the future.

In the fourth quarter of 2020, as part of the Company's routine forecasting process, the Company reassessed and prospectively adjusted the estimated useful life of the developed product rights for Auryxia from seven years to six years. This was not deemed an impairment indicator as of December 31, 2020.

Goodwill

Goodwill was $55.1 million as of December 31, 2022 and 2021. The Company operates in one operating segment which the Company considers to be the only reporting unit. Goodwill is evaluated for impairment at the reporting unit level on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that an impairment may exist. Events that could indicate impairment and trigger an impairment assessment include, but are not limited to, an adverse change in current economic or market conditions, including a significant prolonged decline in market capitalization, a significant adverse change in legal factors, unexpected adverse business conditions, and an adverse action by a regulator. During the year ended December 31, 2022, the Company evaluated business factors, including the receipt of the CRL from the FDA for vadadustat, the Company's market capitalization as impacted by a recent decline in the Company's stock price, the impact of the Otsuka Termination Agreement on the Company's future cash flows, and the impact of the BioVectra Termination Agreement to the Company's excess purchase commitment liability to determine if there were events or changes in circumstance to indicate that the fair value of the reporting unit was less than its carrying value. The Company performed a qualitative impairment assessment of the Company's goodwill balance as the year ended December 31, 2022. The Company determined that it was not more likely than not that the fair value of the reporting unit was less than its carrying value and, therefore, did not perform a further quantitative impairment test.

The Company's qualitative assessments were based on the Company's estimates and assumptions, a number of which are dependent on external factors and actual results may differ materially from these estimates. In addition, the future occurrence of events including, but not limited to, an adverse change in current economic and market conditions, including a significant prolonged decline in market capitalization, a significant adverse change in legal factors, unexpected adverse business conditions and an adverse action or assessment by a regulator could indicate potential impairment and trigger an impairment assessment of goodwill, which could result in an impairment of goodwill. As a result of the significance of goodwill, the Company's results of

operations and financial position in a future period could be negatively impacted should an impairment test be triggered that results in an impairment of goodwill.

There were no impairments of goodwill during the years ended December 31, 2021 and 2020.

10. Accrued Expenses

Accrued expenses are as follows:

	December 31, 2022	December 31, 2021
	(in thousands)	
Product revenue allowances	$ 29,005	$ 26,624
Accrued clinical	5,755	14,036
Amounts due to collaboration partners	—	22,654
Accrued payroll and related	11,481	15,863
Lease liability	4,744	4,802
Royalties	3,804	3,472
Professional fees	1,734	1,899
Accrued commercial manufacturing	4,310	3,843
Accrued restructuring	2,751	—
Accrued other	7,413	11,263
Total accrued expenses	$ 70,997	$ 104,456

11. Debt

Term Loans

On November 11, 2019, the Company, with Keryx as guarantor, entered into a loan agreement, or the Loan Agreement, with BioPharma Credit PLC as collateral agent and a lender, or the Collateral Agent, and BioPharma Credit Investments V (Master) LP as a lender, pursuant to which term loans in an aggregate principal amount of $100.0 million were made available to the Company in two tranches, subject to certain terms and conditions, or the Term Loans. BioPharma Credit PLC subsequently transferred its interest in the Term Loans, solely in its capacity as a lender, to its affiliate, BPCR Limited Partnership. The Collateral Agent and the lenders are collectively referred to as Pharmakon. The first tranche of $80.0 million, or Tranche A, was drawn on November 25, 2019, or the Tranche A Funding Date, and the second tranche of $20.0 million, or Tranche B, was drawn on December 10, 2020, or the Tranche B Funding Date. Each of the Tranche A Funding Date and the Tranche B Funding Date, a Funding Date.

Proceeds from the Term Loans may be used for general corporate purposes. The Company and Keryx entered into a Guaranty and Security Agreement with the Collateral Agent, or the Guaranty and Security Agreement, on the Tranche A Funding Date. Pursuant to the Guaranty and Security Agreement, the Company's obligations under the Term Loans are unconditionally guaranteed by Keryx, or the Guarantee. Additionally, the obligations of the Company and Keryx under the Term Loans and the Guarantee are secured by a first priority lien on certain assets of the Company and Keryx, including Auryxia and certain related assets, cash, and certain equity interests held by the Company and Keryx, collectively the Collateral.

The Term Loans bear interest at a floating rate per annum equal to the three-month LIBOR rate plus 7.50%, subject to a 2.00% LIBOR floor and a 3.35% LIBOR cap, payable quarterly in arrears. The Term Loans will mature on the fifth anniversary of the Tranche A Funding Date, or the Maturity Date. The Company will repay the principal under the Term Loans in equal quarterly payments starting on the 33rd-month anniversary of the applicable Funding Date, or the Amortization Schedule. If certain conditions were met, it would have had the option to repay the principal in equal quarterly payments starting on the 48th-month anniversary of the applicable Funding Date. One of these conditions was approval of vadadustat; however, the Company received the CRL from the FDA in March 2022 stating that the FDA had determined that it could not approve the NDA in its present form. Therefore, the Company is no longer eligible for this option to delay repayment of the principal under the Loan Agreement. During the year ended December 31, 2022, the Company made its first quarterly principal payment under the Term

Loans of $8.0 million. Under certain circumstances, unless certain liquidity conditions are met, the Maturity Date may decrease by up to one year, and the Amortization Schedule may correspondingly commence up to one year earlier.

On the Tranche A Funding Date, the Company paid to Pharmakon a facility fee equal to 2.00% of the aggregate principal amount of the Term Loans, or $2.0 million, in addition to other expenses incurred by Pharmakon and reimbursed by the Company, or Lender Expenses. The Tranche A draw was $77.3 million, net of facility fee, Lender Expenses and issuance costs. The Tranche B draw was $20.0 million, net of immaterial Lender Expenses and issuance costs. The Loan Agreement permits voluntary prepayment at any time in whole or in part, subject to a prepayment premium. The prepayment premium would be 2.00% of the principal amount being prepaid prior to the third anniversary of the applicable Funding Date, 1.00% on or after the third anniversary, but prior to the fourth anniversary, of the applicable Funding Date, and 0.50% on or after the fourth anniversary of the applicable Funding Date but prior to the Maturity Date, and a make-whole premium on or prior to the second anniversary of the applicable Funding Date in an amount equal to foregone interest through the second anniversary of the applicable Funding Date. A change of control triggers a mandatory prepayment of the Term Loans.

The Loan Agreement contains customary representations, warranties, events of default and covenants of the Company and its subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold which started in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. On February 18, 2022, the Loan Agreement was amended pursuant to a First Amendment and Waiver, or the First Amendment and Waiver, which waived the provision under the Loan Agreement that required the Company to not be subject to any qualification as a going concern within the Company's 2021 Annual Report on Form 10-K. Pursuant to the First Amendment and Waiver, the Company’s filings of Form 10-Q for fiscal quarters ending June 30, 2022 and September 30, 2022, and its future Annual Reports on Form 10-K, must not be subject to any qualification as to going concern, which requirement as to the Company's filings on Form 10-Q was waived in the Second Amendment and Waiver. If the Company does not satisfy the covenant as to going concern, in any of these filings, the Company will be in default under the Loan Agreement. If an event of default occurs and is continuing under the Loan Agreement, the Collateral Agent is entitled to take enforcement action, including acceleration of amounts due under the Loan Agreement. Under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. As of December 31, 2022, the Company determined that no events of default had occurred.

On July 15, 2022, or the Effective Date, the Company and Pharmakon entered into the Second Amendment and Waiver, or the Second Amendment and Waiver, which amended and waived certain provisions of the Loan Agreement, as amended by the First Amendment and Waiver.

Pursuant to the Second Amendment and Waiver, on the Effective Date, the Company made a $5.0 million prepayment of the principal of the Tranche A loan, or the Second Amendment Effective Date Tranche A Prepayment, and a $20.0 million prepayment of principal of the Tranche B loan, or the Second Amendment Effective Date Tranche B Prepayment, in each case, together with any and all accrued and unpaid interest on such prepayments of principal to the Effective Date. In connection therewith, the Company also paid $0.5 million in prepayment premiums under the Loan Agreement. During the year ended December 31, 2022, the Company recorded a debt extinguishment loss of $0.9 million. Subject to the payment in full of the Second Amendment Effective Date Tranche A Prepayment and the Second Amendment Effective Date Tranche B Prepayment, Pharmakon agreed to, among other things, (1) increase the amount of the working capital facility established in connection with the Company’s Second Amended and Restated License Agreement with CSL Vifor, which facility is part of the definition of Permitted Indebtedness (as such term is defined in the Loan Agreement) under the Loan Agreement, that the Company is permitted to repay to CSL Vifor without causing an acceleration of the liabilities under the Loan Agreement, (2) waive the requirement that the Company’s Quarterly Reports on Form 10-Q for the fiscal quarters ending June 30, 2022 and September 30, 2022 not be subject to any qualification as to going concern, and (3) waive certain amounts payable under the Loan Agreement in connection with the Second Amendment Effective Date Tranche B Prepayment. Future principal payments pursuant to the contractual terms of the Loan Agreement, as amended, as of December 31, 2022 are as follows (in thousands):

	Principal Payments (in thousands)
2023	$ 32,000
2024	35,000
Total before unamortized discount and issuance costs	67,000
Less: unamortized discount and issuance costs	(922)
Total term loans	$ 66,078

The Company assessed the terms and features of the Loan Agreement in order to identify any potential embedded features that would require bifurcation or any beneficial conversion feature. As part of this analysis, the Company assessed the economic characteristics and risks of the Loan Agreement, including put and call features. The terms and features assessed include a potential extension to the interest-only period dependent on both no event of default having occurred and continuing and on the Company achieving certain regulatory and revenue conditions. The Company also assessed the acceleration of the obligations under the Loan Agreement under an event of default. In addition, under certain circumstances, a default interest rate will apply on all outstanding obligations during the occurrence and continuance of an event of default. In accordance with ASC 815, the Company concluded that these features are not clearly and closely related to the host instrument, and represent a single compound derivative that is required to be re-measured at fair value on a quarterly basis.

The fair value of the derivative liability related to the Company's Loan Agreement was $0.8 million and $1.8 million as of December 31, 2022 and 2021, respectively. The Company classified the derivative liability as a non-current liability on the balance sheet at December 31, 2022.

The Company recognized approximately $9.5 million, $10.9 million, and $8.9 million of interest expense related to the Loan Agreement during the years ended December 31, 2022, 2021, and 2020, respectively.

12. Stockholders' Equity

Authorized and Outstanding Capital Stock

On June 5, 2020, the Company filed a Certificate of Amendment to its Ninth Amended and Restated Certificate of Incorporation, or its Charter, to increase the number of authorized shares of common stock from 175,000,000 to 350,000,000. As of December 31, 2022, the authorized capital stock of the Company included 350,000,000 shares of common stock, par value $0.00001 per share, of which 184,135,714 and 177,000,963 shares were issued and outstanding at December 31, 2022 and 2021, respectively; and 25,000,000 shares of undesignated preferred stock, par value $0.00001 per share, of which no shares were issued and outstanding at December 31, 2022 and 2021.

At-the-Market Facility

On March 12, 2020, the Company filed a prospectus supplement relating to the Company's sales agreement with Cantor Fitzgerald & Co., or the Prior Sales Agreement, pursuant to which it was able to offer and sell up to $65.0 million of its common stock at current market prices from time to time. Through December 31, 2020, the Company sold 3,509,381 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $10.6 million. During the three months ended March 31, 2021, the Company sold 5,224,278 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $15.9 million.

On February 25, 2021, the Company filed a prospectus relating to the sales agreement with its new shelf registration statement (which replaced the prior shelf registration statement), pursuant to which it was able to offer and sell up to $100.0 million of its common stock at current market prices from time to time. Through December 31, 2021, the Company sold 21,128,065 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $72.4 million. On March 1, 2022, the Company filed a prospectus relating to the Prior Sales Agreement, pursuant to which it was authorized to offer and sell up to $25.3 million of its common stock at current market prices from time to time. On March 16, 2022, the Company terminated the Prior Sales Agreement. During the three months ended March 31, 2022, the Company sold 404,600 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of $0.8 million.

On April 7, 2022, the Company entered into an Open Market Sale Agreement[SM], or the Sales Agreement, with Jefferies LLC, or Jefferies, as agent, for the offer and sale of common stock at current market prices in amounts to be determined from time to time. Also, on April 7, 2022, the Company filed a prospectus supplement relating to the Sales Agreement, pursuant to which it

is able to offer and sell under the Sales Agreement up to $26.0 million of its common stock at current market prices from time to time. From the date of filing of the prospectus supplement through the date of the filing of this Annual Report on Form 10-K, the Company has not sold any shares of its common stock under this program.

Equity Plans

The Company maintains one stock incentive plan, the 2014 Incentive Plan, or the 2014 Plan, as well as the 2014 Employee Stock Purchase Plan, or the 2014 ESPP. The 2014 Plan replaced the Company's Amended and Restated 2008 Equity Incentive Plan, or the 2008 Plan, however, options or other awards granted under the 2008 Plan prior to the adoption of the 2014 Plan that have not been settled or forfeited remain outstanding and effective. On June 6, 2019, the Company's stockholders approved the Amended and Restated 2014 Employee Stock Purchase Plan, or the ESPP. In May 2016, the Company's Board of Directors approved an inducement award program that was separate from the Company's equity plans and which, consistent with Nasdaq Listing Rule 5635(c)(4), did not require stockholder approval, or the Inducement Award Program. During the year ended December 31, 2022, the Company granted 435,000 options to purchase shares of the Company's common stock to new hires under the Inducement Award Program, of which 258,000 options to purchase shares of the Company's common stock remained outstanding at December 31, 2022.

The 2014 Plan allows for the granting of stock options, stock appreciation rights, or SARs, restricted stock, unrestricted stock, restricted stock units, or RSUs, performance awards and other awards convertible into or otherwise based on shares of the Company's common stock. Dividend equivalents may also be provided in connection with an award under the 2014 Plan. The Company's employees, officers, directors and consultants and advisors are eligible to receive awards under the 2014 Plan. The Company initially reserved 1,785,000 shares of its common stock for the issuance of awards under the 2014 Plan. The 2014 Plan provides that the number of shares reserved and available for issuance under the 2014 Plan will automatically increase annually on January 1 of each calendar year, by an amount equal to three percent (3%) of the number of the Company's shares outstanding on a fully diluted basis as of the close of business on the immediately preceding December 31, or the 2014 Plan Evergreen Provision. The Company's Board of Directors may act prior to January 1 of any year to provide that there will be no automatic increase in the number of Akebia Shares available for grant under the 2014 Plan for that year (or that the increase will be less than the amount that would otherwise have automatically been made). On December 12, 2018, in connection with the consummation of the Merger, the Company assumed outstanding and unexercised options to purchase Keryx's stock, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, under the following Keryx equity plans, or the Keryx Equity Plans: the Keryx 1999 Share Option Plan, the Keryx 2004 Long-Term Incentive Plan, the Keryx 2007 Incentive Plan, the Keryx Amended and Restated 2013 Incentive Plan, and the Keryx 2018 Equity Incentive Plan, or the Keryx 2018 Plan. In addition, the number of Keryx shares available for issuance under the Keryx 2018 Plan, as adjusted by the Exchange Multiplier pursuant to the terms of the Merger Agreement, may be used for awards granted by the Company under its 2014 Plan, or the Assumed Shares, provided that the Company uses the Assumed Shares for individuals who were not employees or directors of the Company prior to the consummation of the Merger. During the year ended December 31, 2022, the Company granted 3,233,500 options to purchase Akebia Shares to employees under the 2014 Plan, 435,000 options to purchase Akebia Shares to employees under the Inducement Award Program, 5,219,908 Akebia RSUs to employees under the 2014 Plan, 800,000 performance stock units, or PSUs, to employees under the 2014 Plan, 140,700 options to purchase Akebia Shares to directors under the 2014 Plan, and 95,900 RSUs to directors under the 2014 Plan.

The ESPP provides for the issuance of shares of the Company's common stock to participating employees at a discount to their fair market value. The maximum aggregate number of shares at December 31, 2022 of the Company's common stock available for future issuance under the ESPP is 4,837,995. Under the ESPP, each offering period is six months, at the end of which employees may purchase shares of the Company's common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of each offering period is equal to the lesser of eighty-five percent (85%) of the closing price of the Company's common stock at the beginning or end of the offering period.

Shares Reserved for Future Issuance

The Company has reserved for future issuance the following number of shares of common stock:

	December 31, 2022	December 31, 2021
Common stock options, RSUs and PSUs outstanding (1)	17,407,227	16,065,218
Shares available for issuance under Akebia equity plans (2)	5,498,984	4,675,734
Warrant to purchase common stock	—	509,611
Shares available for issuance under the ESPP	4,837,995	5,173,141
Total	27,744,206	26,423,704

(1) Includes awards granted under the 2014 Plan and the Inducement Award Program and awards issued in connection with the Merger.
(2) On January 1, 2023, January 1, 2022 and January 1, 2021, the shares reserved for future grants under the 2014 Plan increased by 6,046,288, 5,807,270 and 4,880,775 shares, respectively, pursuant to the 2014 Plan Evergreen Provision.

Stock-Based Compensation

Stock Options

Service-Based Stock Options

On February 28, 2022, as part of the Company's annual grant of equity, the Company issued 2,833,500 stock options to employees. In addition, the Company issues stock options to directors, new hires and occasionally to other employees not in connection with the annual grant process. Options granted by the Company generally vest over periods of between 12 and 48 months, subject, in each case, to the individual's continued service through the applicable vesting date. Options generally vest either 100% on the first anniversary of the grant date or in installments of (i) 25% at the one year anniversary and (ii) 12 equal quarterly installments beginning after the one year anniversary of the grant date, subject to the individual's continuous service with the Company. Options generally expire ten years after the date of grant. The Company recorded approximately $6.8 million, $8.9 million and $8.5 million of stock-based compensation expense related to stock options granted during the years ended December 31, 2022, 2021 and 2020, respectively.

The assumptions used in the Black-Scholes pricing model to estimate the grant date fair value of options granted under the 2014 Plan are as follows:

	Year ended December 31,								
	2022			2021			2020		
Risk-free interest rate	1.69%	-	4.17%	0.66%	-	1.37%	0.32%	-	1.38%
Dividend yield		—%			—%			—%	
Volatility	79.77%	-	91.57%	77.81%	-	81.79%	69.56%	-	75.91%
Expected term (years)	5.51	-	6.25	5.51	-	6.25	5.51	-	6.25

The following table summarizes the Company's stock option activity, excluding performance-based options, for the year ended December 31, 2022:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2021	11,398,215	$ 7.60		$ 267,830
Granted	3,809,200	$ 1.81		
Exercised	(142,440)	$ 0.47		$ 44,905
Forfeited	(3,331,840)	$ 6.43		$ 3,813
Expired/cancelled	(407,045)	$ 9.52		
Outstanding, December 31, 2022	11,326,090	$ 6.01	7.26	$ 112,709
Options exercisable, December 31, 2022	6,239,437	$ 8.37	6.08	$ 1,904
Vested and expected to vest, December 31, 2022	11,326,090	$ 6.01		

The weighted-average grant date fair values of options granted in the years ended December 31, 2022, 2021, and 2020 were $1.27, $2.29, and $5.63 per share, respectively. There was an immaterial intrinsic value of options exercised during the year ended December 31, 2022 as the value of the options exercised in 2022 was immaterial. There was no intrinsic value of options exercised during the year ended December 31, 2021, as there were no options exercised in 2021. The total intrinsic value of options exercised during the year ended December 31, 2020 was $0.4 million. The fair value of options that vested during the years ended December 31, 2022, 2021, and 2020 were $8.4 million, $10.6 million, and $6.8 million, respectively. As of December 31, 2022, there was approximately $8.1 million of unrecognized compensation cost related to stock options outstanding under the Company's 2014 Plan or made pursuant to the Inducement Award Program, which is expected to be recognized over a weighted average period of 2.04 years.

Performance-Based Stock Options

The Company also grants performance-based stock options to employees under the 2014 Plan. The performance-based stock options granted by the Company generally vest in connection with the achievement of specified commercial, regulatory, and corporate milestones. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of options granted and recognized over time based on the probability of meeting such commercial, regulatory and corporate milestones. The Company issued 400,000 and 99,558 performance-based options during the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, the Company had 400,000 performance-based options outstanding compared to 99,558 performance-based options outstanding at December 31, 2021.

The following table summarizes the Company’s performance-based option activity for the year ended December 31, 2022:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2021	99,558	$ 2.74		$ —
Granted	400,000	$ 0.41		$ 1,120
Exercised	—	$ —		$ —
Forfeited/cancelled	(99,558)	$ 2.74		
Outstanding, December 31, 2022	400,000	$ 0.41	9.4	$ 66,800

The Company did not record any stock-based compensation expense related to performance-based options during 2022, 2021 and 2020. There were no performance-based options that vested during fiscal year 2022, 2021 or 2020. As of December 31, 2022, there were no unrecognized compensation costs related to performance-based stock options under the Company’s 2014 Plan.

Restricted Stock Units

Service-Based Restricted Stock Units

On February 28, 2022, as part of the Company’s annual grant of equity, the Company issued 2,899,008 RSUs to employees. In addition, the Company also occasionally issues RSUs not in connection with the annual grant process to employees. Generally, RSUs granted by the Company vest in one of the following ways: (i) 100% of each RSU grant vests on the first anniversary of the grant date, (ii) one third of each RSU grant vests on the first, second and third anniversaries of the grant date, (iii) 50% of each RSU grant vests on the first anniversary and 25% of each RSU grant vests every six months after the one year anniversary of the grant date, or (iv) one third of each RSU grant vests on the first anniversary of the grant date and the remaining two-thirds vests in eight substantially equal quarterly installments beginning after the one year anniversary, subject, in each case, to the individual’s continued service through the applicable vesting date. The expense recognized for these awards is based on the grant date fair value of the Company’s common stock multiplied by the number of units granted and recognized on a straight-line basis over the vesting period. The Company recorded approximately $7.6 million, $12.9 million and $14.6 million of stock-based compensation expense related to employee RSUs in 2022, 2021 and 2020, respectively.

Performance-Based Restricted Stock Units

During the year ended December 31, 2022, the Company issued 400,000 performance-based restricted stock units, or PSUs, to the Company’s executives. The PSUs granted by the Company vest in connection with the achievement of specified commercial, regulatory, and corporate milestones. The expense recognized for these awards is based on the grant date fair value of the Company’s common stock multiplied by the number of units granted and recognized over time based on the probability of meeting such commercial, regulatory, and corporate milestones. The Company recorded approximately $0.1 million, $0.3 million and $0.5 million of stock-based compensation expense related to employee PSUs in 2022, 2021 and 2020, respectively.

The following table summarizes the Company’s RSU and PSU activity for the year ended December 31, 2022:

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance, December 31, 2021	4,554,343	$ 5.17
Granted	5,715,808	$ 1.30
Vested	(2,252,565)	$ 5.01
Forfeited	(2,349,551)	$ 3.33
Unvested balance, December 31, 2022	5,668,035	$ 2.09

The total fair value of RSUs and PSUs that vested during 2022, 2021 and 2020 (measured on the date of vesting) was $11.2 million, $15.4 million, and $9.4 million, respectively. As of December 31, 2022, there was approximately $5.2 million of unrecognized compensation cost related to RSUs and PSUs, which is expected to be recognized over a weighted average period of 1.44 years.

Employee Stock Purchase Plan

The first offering period under the ESPP opened on January 2, 2015. The Company issued 335,146 shares during the year ended December 31, 2022. The Company recorded approximately $0.1 million, $0.6 million and $0.8 million of stock-based compensation expense related to the ESPP during 2022, 2021 and 2020, respectively.

Compensation Expense Summary

The Company has classified its stock-based compensation expense related to share-based awards as follows:

	Years ended December 31,		
	2022	2021	2020
	(in thousands)		
Research and development	$ 3,683	$ 5,816	$ 6,113
Selling, general and administrative	10,969	16,919	18,347
Total	$ 14,652	$ 22,735	$ 24,460

Compensation expense by type of award:

	Years ended December 31,		
	2022	2021	2020
	(in thousands)		
Stock options	$ 6,839	$ 8,958	$ 8,517
Restricted stock units	7,566	12,927	14,639
Performance RSUs	100	294	464
Employee stock purchase plan	147	556	840
Total	$ 14,652	$ 22,735	$ 24,460

13. Income Taxes

The Company’s income tax provision was computed based on the federal statutory rate and the state statutory rates, net of the related federal benefit. There was no current or deferred income tax expense or benefit for the years ended December 31, 2022 and 2021 due to the Company’s net losses and increases in its valuation allowance against its deferred tax assets.

Our effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2022, 2021 and 2020:

	Year ended December 31,		
	2022	2021	2020
Federal tax at statutory rate	21.0 %	21.0 %	21.0 %
State and local tax at statutory rate	2.4	3.0	3.0
Research and development tax credits	—	—	0.1
Change in valuation allowance	(19.2)	(22.7)	(21.5)
Other permanent differences	(1.0)	(1.0)	(0.4)
Stock Option Cancellations	(2.5)	—	—
Stock Option Shortfalls	(1.6)	—	—
Effect of rate changes	0.6	0.3	0.8
Provision to Return Adjustment	0.3	0.3	(1.5)
Prior Period Adjustment to State NOL DTA	—	—	(1.5)
Other	—	(0.9)	—
Effective tax rate	— %	— %	— %

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. When realization of the deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operations is recognized as a reduction of income tax expense. A valuation allowance is recorded against deferred tax assets if it is more likely than not that some or all of the deferred tax assets will not be realized. The Company cannot be certain that future taxable income will be sufficient to realize its deferred tax assets. Accordingly, the Company has recorded a valuation allowance against the Company's otherwise recognizable net deferred tax assets. The Company continues to maintain the underlying tax benefits to offset future taxable income and to monitor the need for a valuation allowance based on the profitability of its future operations. The valuation allowance increased by approximately $17.8 million and $64.2 million during the years ended December 31, 2022 and 2021, respectively. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
Accrued expenses	$ 2,924	$ 3,306
Deferred revenue	1,250	9,725
Sale of Royalty	13,291	12,037
Stock based compensation	8,317	9,194
Research and development credits	4,827	5,034
Capitalized research and development costs	13,825	—
Other non-current liabilities	2,754	20,424
Net operating loss carryforward	288,147	286,908
ASC 842 lease liability	8,032	9,096
Inventory reserve	17,411	10,281
Refund liability	9,478	—
Other	13,159	10,483
Total deferred tax assets	383,415	376,488
Less valuation allowance	(359,926)	(342,122)
Total deferred tax assets, net of valuation allowance	23,489	34,366
Deferred tax liabilities:		
Fixed assets	—	—
Intangible assets	(15,981)	(25,598)
Inventory	—	—
ASC 842 ROU asset	(7,426)	(8,486)
Other	(82)	(282)
Total deferred tax liabilities	(23,489)	(34,366)
Net deferred tax liability	$ —	$ —

At December 31, 2022 and 2021, the Company had approximately $0.1 million (after amortization of $1.8 million) and $0.3 million (after amortization of $1.7 million), respectively, of start-up expenses capitalized for income tax purposes with amortization available to offset future federal, state and local income tax.

As of December 31, 2022 and 2021, the Company had approximately $1,227.9 million and $1,223.3 million, respectively, of federal NOL carry-forwards which expire through 2037. Included in the $1,227.9 million of federal NOLs are losses of $645.9 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. Additionally, at December 31, 2022 and 2021, the Company had approximately $1,803.6 million and $1,792.1 million, respectively, of state NOL carry-forwards, which expire through 2042. The Company also has approximately $2.5 million of federal research and development tax credit carryforwards which expire through 2040 and $2.9 million of state research and development tax credit carryforwards which expire through 2036.

Under the provisions of the Internal Revenue Code, the net operating losses and tax credit carry-forwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating losses and tax credit carryforwards may become subject to an annual limitation under Internal Revenue Code 382 and 383 if there is more than a 50% change in ownership of the stockholders that own 5% or more of the Company's outstanding stock over a three-year period. The Company completed an evaluation of its ownership changes and concluded that an ownership change did occur on December 12, 2018 for both Akebia and Keryx in connection with the Merger. As a consequence of this ownership change, the Company's NOLs and tax credit carryforwards allocable to the tax periods preceding the ownership change became subject to limitation under Section 382. The Company reduced its associated deferred tax assets by $44.9 million as a result of the limitation.

The Company files income tax returns in the U.S. federal and various state and local jurisdictions. For federal and state income tax purposes, the 2021, 2020 and 2019 tax years remain open for examination under the normal three-year statute of limitations.

The statute of limitations for income tax audits in the United States will commence upon utilization of net operating losses and will expire three years from the filing of the tax return the loss was utilized on.

There was no accrual for uncertain tax positions or for interest and penalties related to uncertain tax positions for 2022, 2021 and 2020. The Company does not believe that there will be a material change in its unrecognized tax positions over the next twelve months. All of the unrecognized tax benefits, if recognized, would be offset by the valuation allowance.

14. Employee Retirement Plan

In 2008, the Company established a retirement plan, or the Plan, authorized by Section 401(k) of the Internal Revenue Code. In accordance with the Plan, all employees who have attained the age of 21 are eligible to participate in the Plan as of the first Entry Date, as defined, following their date of employment. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary and contributions in the amount of approximately $2.6 million, $1.8 million and $1.6 million were made during the years ended December 31, 2022, 2021 and 2020, respectively.

15. Commitments and Contingencies

Leases

The Company leases approximately 65,167 square feet of office and lab space in Cambridge, Massachusetts under a lease which was most recently amended in November 2020, collectively the Cambridge Lease. Under the Third Amendment to the Cambridge Lease, or the Third Amendment, executed in July 2016, total monthly lease payments under the initial base rent were approximately $242,000 and are subject to annual rent escalations. In addition to such annual rent escalations, base rent payments for a portion of said premises commenced on January 1, 2017 in the monthly amount of approximately $22,000. The Fourth Amendment to the Cambridge Lease, executed in May 2017, provided additional storage space to the Company and did not impact rent payments. In April 2018, the Company entered into a Fifth Amendment to the Cambridge Lease, or the Fifth Amendment, for an additional 19,805 square feet of office space on the 12th floor. Monthly lease payments for the existing 45,362 square feet of office and lab space, under the Third Amendment, remain unchanged. The new space leased by the Company was delivered in September 2018 and additional monthly lease payments of approximately $135,000 commenced in February 2019 and are subject to annual rent escalations, which commenced in September 2019. In November 2020, the Company entered into a Sixth Amendment to the Cambridge Lease, or the Sixth Amendment, to extend the term of the Cambridge Lease with respect to the lab space from November 30, 2021 to January 31, 2025. The Sixth Amendment includes two months of free rent starting in December 2020 and additional monthly lease payments of approximately $48,000, which commenced in December 2021, and is subject to annual rent escalations, which commenced in December 2022.

Additionally, the Company has a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease. The total monthly lease payments under the base rent are approximately $136,000 and are subject to annual rent escalations. In February 2022, the Company entered into the First Amendment to the Boston Lease, or the First Lease Amendment, to extend the term of the Boston Lease from February 2023 to July 2031. The First Lease Amendment includes five months of free rent starting in March 2023 and monthly lease payments of $200,122 commencing on August 1, 2023, with an annual rent escalation of approximately 2% commencing on August 1, 2024. The First Lease Amendment also includes a landlord's allowance for certain leasehold improvements to the premises in an amount of up to $1,954,680, provided that such allowance must be used prior to August 1, 2024.

The term of the Cambridge Lease with respect to the office space expires on September 11, 2026, with one five-year extension option available. The term of the Boston Lease office space expires on July 31, 2031, with an extension option for one additional five-year extension option available. The renewal options in these real estate leases were not included in the calculation of the operating lease assets and operating lease liabilities as the renewal is not reasonably certain. The term of the Cambridge Lease with respect to the lab space expires on January 31, 2025, with an extension option for one additional period through September 11, 2026. The renewal options in this real estate lease were included in the calculation of the operating lease assets and operating lease liabilities as the renewal is reasonably certain. The lease agreements do not contain residual value guarantees. Operating lease costs were $7.1 million, $6.7 million and $6.7 million for the years ended December 31, 2022, 2021and 2020, respectively. Cash paid for amounts included in the measurement of operating lease liabilities were $7.2 million, $7.1 million and $7.0 million for the years ended December 31, 2022, 2021 and 2020, respectively.

In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc., or Foundation. The sublease is subject and subordinate to the Boston Lease between Keryx and the landlord. The term of the sublease commenced on October 16, 2019, upon receipt of the required consent from the landlord for the sublease agreement,

and expired on February 27, 2023. Foundation is obligated to pay Keryx rent that approximates the rent due from Keryx to its landlord with respect to the Boston Lease. Sublease rental income is recorded to other income. Keryx continues to be obligated for all payment terms pursuant to the Boston Lease, and the Company will guaranty Keryx's obligations under the sublease. Keryx recorded $1.8 million in sublease rental income from Foundation during each of the years ended December 31, 2022, 2021 and 2020.

The Company has not entered into any material short-term leases or financing leases as of December 31, 2022.

The total security deposit in connection with the Cambridge Lease is $1.6 million as of December 31, 2022. Additionally, the Company recorded $1.1 million for the security deposit under the Boston Lease. Both the Cambridge Lease and the Boston Lease have their security deposits in the form of a letter of credit, all of which are included as restricted cash in prepaid expenses and other current assets in the Company's consolidated balance sheet as of December 31, 2022.

As of December 31, 2022, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter are as follows:

	Operating Leases	Lease Payments to be Received from Sublease	Net Operating Lease Payments
	(in thousands)		
2023	$ 6,950	$ 307	$ 6,643
2024	8,162	—	8,162
2025	8,289	—	8,289
2026	6,132	—	6,132
2027	2,570	—	2,570
Thereafter	9,631	—	9,631
Total	$ 41,734	$ 307	$ 41,427

In arriving at the operating lease liabilities, the Company applied incremental borrowing rates ranging from 6.65% to 7.25%, which were based on the remaining lease term at either the date of adoption of ASC 842 or the effective date of any subsequent lease term extensions. As of December 31, 2022, the remaining lease terms ranged from 3.70 years to 8.59 years. As of December 31, 2022, the following represents the difference between the remaining undiscounted minimum rental commitments under non-cancelable leases and the operating lease liabilities:

	Operating Leases
	(in thousands)
	Total
Undiscounted minimum rental commitments	$ 41,734
Present value adjustment using incremental borrowing rate	(8,030)
Operating lease liabilities	$ 33,704

Manufacturing Agreements

As a result of the Merger, the Company's contractual obligations include Keryx's commercial supply agreements with BioVectra and Siegfried to supply commercial drug substance for Auryxia.

Pursuant to the Manufacture and Supply Agreement with BioVectra and the Product Manufacture and Supply and Facility Construction Agreement with BioVectra, the Company agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices. On September 4, 2020, the Company and BioVectra entered into an Amended and Restated Product Manufacture and Supply and Facility Construction Agreement, which provided for reduced minimum quantity commitments and revised the predetermined prices. The price per kilogram decreased with an increase in quantity above the predetermined purchase quantity tiers. In addition, the Manufacture and Supply Agreement with BioVectra and the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement with BioVectra required the Company to reimburse BioVectra for certain costs in connection with construction of a new facility for the manufacture and supply of

Auryxia drug substance. These construction costs were recorded in other assets and amortized into drug substance as inventory was released to the Company from BioVectra.

On December 22, 2022, the Company and BioVectra entered into the BioVectra Termination Agreement, pursuant to which the parties agreed, among other things, to terminate, effective immediately, any and all existing agreements entered into between the parties in connection with the manufacture and supply, by BioVectra to the Company, of Auryxia drug substance. Under the terms of the BioVectra Termination Agreement, the Company agreed to pay BioVectra a total of $32.5 million consisting of (i) an upfront payment of $17.5 million and (ii) six quarterly payments of $2.5 million commencing in April 2024, totaling $15.0 million. The upfront payment of $17.5 million was made during the quarter ended December 31, 2022 and was recognized to cost of goods sold. In accordance with ASC 420, *Exit or Disposal Cost Obligations*, the Company recognized a liability and corresponding expense for the remaining termination fees based on estimated fair value as of December 22, 2022, or the BioVectra Effective Date. The Company imputed interest on the liability for the remaining termination fees at a rate of 17.0% per annum, which was determined based on certain factors, including the Company's credit rating, comparable securities yield, and expected repayment period of the remaining termination fees. The Company recorded an initial discount on the remaining termination fees on the consolidated balance sheet as of the BioVectra Effective Date. This resulted in the recording of a liability and corresponding charge to cost of goods sold of $11.2 million during the quarter ended December 31, 2022. The discount on the liability balance is being amortized to interest expense using the effective interest rate method over the term of the liability. In addition, each of the Company and BioVectra have released one another from all existing and future claims and liabilities and the return of certain materials and documents. Furthermore, as it relates to all open purchase orders, BioVectra is relieved from any obligations to manufacture any product or perform services under any such open purchase orders, and the Company is relieved from any obligations to purchase any product under such open purchase orders. The Company is also relieved from any obligations to pay any outstanding invoices related to performance by BioVectra of services and all other obligations under the agreements.

Pursuant to the Master Manufacturing Services and Supply Agreement between the Company and Siegfried, as amended through December 31, 2022, or the Siegfried Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The term of the Siegfried Agreement was to expire on December 31, 2022, but was automatically extended into 2023 as a result of Siegfried’s updated production schedule for delivery of product originally scheduled for delivery in 2022. The Siegfried Agreement provides the Company and Siegfried with certain termination rights. As of December 31, 2022, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately $8.4 million through the third quarter of 2023. As of the date of the filing of this Annual Report on Form 10-K, the Company has amended the Siegfried Agreement pursuant to which, the Company agreed to extend the term and purchase a minimum quantity of drug substance of Auryxia at a predetermined price as further described in Note 17 to the Company's consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data of this Annual Report.

Certain of the Company's commercial supply agreements are executory contracts between Keryx and its contract manufacturers for Auryxia, which include future firm purchase commitments. These executory contracts were deemed to have an off-market element related to the amount of purchase commitments that exceed the current forecast. The Company regularly reviews its estimate of the excess purchase commitment liability including review of assumptions of expected future demand, estimates of anticipated expiry of inventory under firm purchase commitments that are estimated to expire before they could be sold as well as any modifications to supply agreements during each reporting period. The excess purchase commitment liability relating to these executory contracts was $0 million and $76.7 million as of December 31, 2022 and 2021, respectively. During the quarter ended December 31, 2022, the Company recorded a $74.3 million reduction to the excess purchase commitments liability within cost of goods sold driven by the reduction in purchase commitments due to execution of the BioVectra Termination Agreement.

On April 9, 2019, the Company entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement included the terms and conditions under which Esteve would manufacture vadadustat drug substance for commercial use. Pursuant to the Esteve Agreement, the Company provided rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflected the Company’s needs for vadadustat drug substance produced by Esteve over a certain number of months, represented as a quantity of vadadustat drug substance per calendar quarter. The parties agreed to a volume-based pricing structure under the Esteve Agreement. On December 16, 2022, the Company, MTPC, and Esteve executed the Assignment Agreement, pursuant to which the Supply Agreement between the Company and Esteve was assigned to MTPC. The Assignment Agreement transferred the rights and obligations of the Supply Agreement to MTPC, specifically including the obligations under certain purchase orders issued by the Company and accepted by Esteve. As such, the Company will have no further obligation to take delivery of or pay for product delivered by Esteve under the transferred purchase orders.

On March 11, 2020, the Company entered into a Supply Agreement with Patheon Inc., or Patheon, or the Patheon Agreement. The Patheon Agreement includes the terms and conditions under which Patheon will manufacture vadadustat drug product for commercial use. Pursuant to the Patheon Agreement, the Company provides Patheon a long-term forecast on an annual basis, as well as short-term forecasts on a quarterly basis, or the Patheon Forecast. The Patheon Forecast reflects the Company’s needs

for commercial supply of vadadustat drug product produced by Patheon, represented as a quantity of drug product per calendar quarter. The parties have agreed to a volume-based pricing structure under the Patheon Agreement. The Patheon Agreement has an initial term beginning March 11, 2020 and ending June 30, 2023 and automatically renews for successive one-year terms unless either party gives the other party eighteen months' prior written notice. The current term of the Patheon Agreement ends June 30, 2025. Pursuant to the Patheon Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug product from Patheon. As of December 31, 2022, the Company had a minimum commitment with Patheon for $3.1 million through the third quarter of 2023.

On April 2, 2020, the Company entered into a Supply Agreement with STA Pharmaceutical Hong Kong Limited, a subsidiary of WuXi AppTec, or WuXi STA, or the WuXi STA DS Agreement. The WuXi STA DS Agreement includes the terms and conditions under which WuXi STA will manufacture vadadustat drug substance for commercial use. Pursuant to the WuXi STA DS Agreement, the Company provides rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DS Forecast. The WuXi STA DS Forecast reflects the Company's needs for vadadustat drug substance produced by WuXi STA over a certain number of quarters. The parties have agreed to a volume-based pricing structure under the WuXi STA DS Agreement. The WuXi STA DS Agreement has an initial term of four years, beginning April 2, 2020 and ending April 2, 2024. Pursuant to the WuXi STA DS Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from WuXi STA. As of December 31, 2022, the Company has committed to purchase $15.3 million of vadadustat drug substance from WuXi STA through the end of 2023.

On February 10, 2021, the Company entered into a Supply Agreement with WuXi STA, or the WuXi STA DP Agreement. The WuXi STA DP Agreement includes the terms and conditions under which WuXi STA will manufacture and supply vadadustat drug product for commercial purposes. Pursuant to the WuXi STA DP Agreement, the Company will provide rolling forecasts to WuXi STA on a quarterly basis, or the WuXi STA DP Forecast. Each WuXi STA DP Forecast will reflect the quantities of vadadustat drug product that the Company expects to order from WuXi STA over a certain number of months, represented as a quantity of vadadustat drug product per calendar quarter. Pursuant to the WuXi STA DP Agreement, the Company has agreed to purchase a certain percentage of global demand for vadadustat drug product from WuXi STA. The parties have agreed to a volume-based pricing structure under the WuXi STA DP Agreement. The vadadustat drug product price will remain fixed for the first 12 months and thereafter shall be annually reviewed by the Company and WuXi STA. The Company will also reimburse WuXi STA for certain reasonable expenses. The WuXi STA DP Agreement has an initial term of four years, beginning February 10, 2021 and ending February 10, 2025. The WuXi STA DP Agreement may be renewed or extended by mutual agreement of the Company and WuXi STA with at least 18 months' prior written notice. The WuXi STA DP Agreement allows the Company to terminate the relationship on 180 calendar days' prior written notice to WuXi STA for any reason. In addition, each party has the ability to terminate the WuXi STA DP Agreement upon the occurrence of certain conditions.

Other Third Party Contracts

The Company contracts with various organizations to conduct research and development activities with remaining contract costs to the Company of approximately $90.2 million at December 31, 2022. The scope of the services under these research and development contracts can be modified and the contracts cancelled by the Company upon written notice. In some instances, the contracts may be cancelled by the third party upon written notice.

Litigation and Related Matters

From time to time, the Company may become subject to legal proceedings and claims which arise in the ordinary course of its business. Consistent with ASC 450, *Contingencies*, the Company's policy is to record a liability if a loss in a significant legal dispute is considered probable and an amount can be reasonably estimated. The Company provides disclosure when a loss in excess of any reserve is reasonably possible, and if estimable, the Company discloses the potential loss or range of possible loss. Significant judgment is required to assess the likelihood of various potential outcomes and the quantification of loss in those scenarios. The Company's estimates change as litigation progresses and new information comes to light. Changes in Company estimates could have a material impact on the Company's results and financial position. As of December 31, 2022, the Company does not have any significant legal disputes that require a loss liability to be recorded. The Company continually monitors the need for a loss liability for litigation and related matters.

16. Net Loss per Share

The shares in the table below were excluded from the calculation of diluted net loss per share, prior to the use of the treasury stock method, due to their anti-dilutive effect:

	Year ended December 31,		
	2022	2021	2020
Warrants	—	509,611	509,611
Outstanding stock options	11,326,090	11,398,215	9,386,517
Unvested restricted stock units	6,081,137	4,667,003	4,722,311
Total	17,407,227	16,574,829	14,618,439

17 Subsequent Events

On February 28, 2023, the Company and Siegfried entered into Amendment No. 5 to the Siegfried Agreement, or the Amendment. Pursuant to the Amendment, the Company has agreed to purchase a minimum quantity of drug substance for Auryxia at a predetermined price. As a result of the Amendment, the term of the Siegfried Agreement expires on December 31, 2024, subject to the Company's option to extend through December 31, 2026 by providing 12 months' prior written notice to Siegfried.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Management's Evaluation of our Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding required disclosure.

As of December 31, 2022, our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our Chief Executive Officer and Chief Financial Officer have concluded based upon the evaluation described below that, as of December 31, 2022, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Securities Exchange Act of 1934 as a process designed by, or under the supervision of, the Company's Chief Executive Officer and Chief Financial Officer and effected by the Company's board of directors, management and other personnel to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America and includes those policies and procedures that:

(1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets;

(2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the issuer are being made only in accordance with authorizations of management and directors; and

(3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the Company's consolidated financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

Management conducted an assessment of the effectiveness of our internal control over financial reporting as of December 31, 2022 based on the criteria set forth in *Internal Control - Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on the assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2022.

Remediation of Previously Identified Material Weakness

As disclosed in our 2021 Annual Report on Form 10-K, management identified a material weakness in our internal control over financial reporting relating to our inventory process. Management is committed to maintaining a strong internal control environment. In response to the material weakness identified, management, with the oversight of the Audit Committee of the Board of Directors, took comprehensive actions to remediate the material weakness in internal control over financial reporting relating to our inventory process, including; (i) designing and implementing more robust controls throughout 2022, including through increased training of individuals within the supply chain, manufacturing, quality and inventory processes, including review documentation requirements, (ii) designing controls to address the completeness and accuracy of key reports utilized in the execution of internal controls, (iii) implementing an inventory count policy and standard operating procedures to ensure consistency and accuracy of the inventory count process and adherence to these policies at facilities managed by third party logistics and contract manufacturing organizations, and (iv) continuing to engage an outside firm in 2022 to assist management with performing sufficient testing throughout the year to validate the operating effectiveness of certain controls over financial reporting. The remediation efforts addressed the material weakness and also enhanced our overall financial reporting control environment. As of December 31, 2022, we have determined that our previously reported material weakness has been remediated.

Changes in Internal Control over Financial Reporting

Except for the remediation efforts as noted in the preceding paragraphs, there have been no changes in the Company's internal control over financial reporting during the fourth quarter of 2022, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Ernst & Young, LLP, the Company's independent registered public accounting firm, has issued an auditor's report on management's assessment of the effectiveness of the Company's internal control over financial reporting as of December 31, 2022. This report is included below.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Akebia Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting

We have audited Akebia Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Akebia Therapeutics, Inc. (the "Company") maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2022, and the related notes and our report dated March 10, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual

Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 10, 2023

Item 9B. Other Information

We confirm that we do not hold any deposits or securities or maintain any accounts at Silicon Valley Bank.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Director, Executive Officers and Corporate Governance

The information required by this Item 10 will be included in our Definitive Proxy Statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and, other than the information required by Item 402(v) of Regulation S-K, is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) Documents filed as part of this Annual Report on Form 10-K.
(b) Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Stockholders' Equity

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed below are filed as part of this Annual Report on Form 10-K.

Exhibit Number	Description of Exhibit
2.1**	Agreement and Plan of Merger, dated as of June 28, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc., and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K (001-36352), filed on June 28, 2018)
2.2	First Amendment to Agreement and Plan of Merger, dated as of October 1, 2018, by and among Akebia Therapeutics, Inc., Alpha Therapeutics Merger Sub, Inc. and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K (001-36352), filed on October 1, 2018)
3.1	Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (001-36352), filed on March 28, 2014)
3.2	Certificate of Amendment of Ninth Amended and Restated Certificate of Incorporation of Akebia Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (001-36352), filed on June 9, 2020)
3.3	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (001-36352), filed on March 28, 2014)
4.1	Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
4.2	Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014 (incorporated by reference to Exhibit 4.4 to the Company's Annual Report on Form 10-K (001-36352), filed on March 4, 2015)
4.3#	Amendment No. 1 to Fourth Amended and Restated Investors' Rights Agreement, dated June 28, 2017 (incorporated by reference to Exhibit 4.5 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
4.4#	Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated May 12, 2017 (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2017)
4.5!	Investment Agreement between Akebia Therapeutics, Inc. and Vifor (International) Ltd., dated February 18, 2022 (incorporated by reference to Exhibit 4.5 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
4.6	Description of Registrant's Securities (incorporated by reference to Exhibit 4.6 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.1†	Form of Director and Officer Indemnification Agreement (incorporated by reference to Exhibit 10.1 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
10.2	Office Lease Agreement Between MA-Riverview/245 First Street, L.L.C. and Akebia Therapeutics, Inc., dated December 3, 2013 (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.3	First Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated December 15, 2014 (incorporated by reference to Exhibit 10.3 to the Company's Annual Report on Form 10-K (001-36352), filed on March 4, 2015)
10.4	Second Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated November 23, 2015 (incorporated by reference to Exhibit 10.4 to the Company's Annual Report on Form 10-K (001-36352), filed on March 14, 2016)
10.5	Third Amendment to Office Lease Agreement Between Jamestown Premier 245 First, LLC and Akebia Therapeutics, Inc., dated July 25, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 9, 2016)

Exhibit Number	Description of Exhibit
10.6	Fourth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc., dated May 1, 2017 (incorporated by reference to Exhibit 10.6 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
10.7	Fifth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated April 9, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2018)
10.8	Sixth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated November 30, 2020 (incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.9	One Marina Park Drive Office Lease dated April 29, 2015, by and between Keryx Biopharmaceuticals, Inc. and Fallon Cornerstone One MPD LLC (incorporated by reference to Exhibit 10.29 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K (000-30929), filed on March 1, 2017)
10.10	First Amendment to One Marina Park Drive Office Lease, dated February 24, 2022, by and between Keryx Biopharmaceuticals, Inc. and CLPF One Marina Park Drive LLC (successor-in-interest to Fallon Cornerstone One MPD LLC) (incorporated by reference to Exhibit 10.10 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.11	Assignment and Assumption Agreement, dated February 24, 2022, by and between Keryx Biopharmaceuticals, Inc. and Akebia Therapeutics, Inc. (incorporated by reference to Exhibit 10.11 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.12	Sublease, dated as of September 9, 2019, by and between Keryx Biopharmaceuticals, Inc. and Foundation Medicine, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 12, 2019)
10.13†	Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.14†	Amendment No. 1 to Amended and Restated 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.15†	Executive Employment Agreement with John P. Butler, dated September 16, 2013 (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (333-193969), filed on February 14, 2014)
10.16†	Offer Letter to David Spellman, dated as of June 13, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 10, 2020)
10.17†	Form of Non-Statutory Stock Option Agreement for officers (incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.18†	Form of Non-Statutory Stock Option Agreement for Non-Employee Directors (incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.19†	Non-Employee Director Compensation Program, effective January 26, 2021 (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.20†	Form of Executive Severance Agreement for officers (incorporated by reference to Exhibit 10.27 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.21†	2014 Incentive Plan (incorporated by reference to Exhibit 10.29 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)
10.22†	Amendment No. 1 to the Akebia Therapeutics, Inc. 2014 Incentive Plan (incorporated by reference to Exhibit 4.4 to the Company's Registration Statement on Form S-8 (333-229366), filed on January 25, 2019)

Exhibit Number	Description of Exhibit
10.23†	Amended and Restated 2014 Employee Stock Purchase Plan (incorporated by reference to Appendix A to the Company's Definitive Proxy Statement on Schedule 14A (001-36352), filed with the Securities and Exchange Commission on April 26, 2019)
10.24†	Amended and Restated Cash Incentive Plan, effective January 19, 2022 (incorporated by reference to Exhibit 10.28 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.25†	Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2018)
10.26†	Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (incorporated by reference to Exhibit 10.29 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.27†	Form of Officer Inducement Award Non-Statutory Stock Option Agreement (incorporated by reference to Exhibit 4.4 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018)
10.28†	Form of Inducement Award Non-Statutory Stock Option Agreement for non-officers (incorporated by reference to Exhibit 4.5 to the Company's Registration Statement on Form S-8 (333-222728), filed on January 26, 2018)
10.29†	Form of Officer Performance-Based Stock Option Award, under the Company's 2014 Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 4, 2021)
10.30†	Form of Officer Performance-Based Stock Restricted Stock Unit Award, under the Company's 2014 Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 4, 2021)
10.31†	Form of Officer Restricted Stock Unit Award Agreement under 2014 Incentive Plan (Retention Awards) (incorporated by reference to Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 4, 2022)
10.32†	Form of Officer Non-Statutory Stock Option Agreement under 2014 Incentive Plan (Retention Awards) (incorporated by reference to Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 4, 2022)
10.33†!	Form of Officer Cash Bonus Letter Agreement (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 4, 2021)
10.34†	Keryx Biopharmaceuticals, Inc. 1999 Stock Option Plan (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (001-30929), filed on March 21, 2003)
10.35†	Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan (incorporated by reference to Annex C to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A (000-30929), filed on April 29, 2004)
10.36†	Amendment to the Keryx Biopharmaceuticals, Inc. 2004 Long-Term Incentive Plan dated April 11, 2006 (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on August 9, 2006)
10.37†	Keryx Biopharmaceuticals, Inc. 2007 Incentive Plan, (incorporated by reference to Annex D to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A (000-30929), filed on April 30, 2007)

Exhibit Number	Description of Exhibit
10.38†	Keryx Biopharmaceuticals, Inc. Amended and Restated 2013 Incentive Plan (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K (000-30929), filed on May 27, 2016)
10.39†	Keryx Biopharmaceuticals, Inc. 2018 Equity Incentive Plan (incorporated by reference to Exhibit 99.1 to Keryx Biopharmaceuticals, Inc.'s Registration Statement on Form S-8 (333-226005), filed on June 29, 2018)
10.40†	Form of Indemnification Agreement between Keryx Biopharmaceuticals, Inc. and its directors and officers (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on November 9, 2016)
10.41†	Form of Employee Agreement (Confidentiality, Non-Competition, Non-Solicitation and Development Agreement) applicable to officers (incorporated by reference to Exhibit 10.56 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.42†	Keryx Biopharmaceuticals, Inc. Fourth Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Current Report on Form 8-K (000-30929), filed on May 27, 2016)
10.43†	Keryx Biopharmaceuticals, Inc. Third Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on August 7, 2014)
10.44†	Keryx Biopharmaceuticals, Inc. Director Non-Statutory Stock Option Award Terms and Conditions under the Third Amended and Restated Directors Equity Compensation Plan (incorporated by reference to Exhibit 10.59 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.45†	Form of Officer Retention Letter Agreement (incorporated by reference to Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 9, 2022)
10.46†!	Form of Retention and Separation Agreement for Michel Dahan and Nicole R. Hadas (incorporated by reference to Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 9, 2022)
10.47†!	Form of Amendment to Retention and Separation Agreement for Michel Dahan and Nicole R. Hadas (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 3, 2022)
10.48†	Separation Agreement with Dell Faulkingham, dated May 5, 2022 (incorporated by reference to Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 9, 2022)
10.49†	Retention Agreement with David Spellman, dated June 22, 2022 (incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 4, 2022)
10.50#	Master Services Agreement, between Akebia Therapeutics, Inc., and Quintiles, Inc., dated as of June 8, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 11, 2015)
10.51!	Collaboration Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated December 11, 2015 (incorporated by reference to Exhibit 10.49 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.52#	Letter Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated September 26, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on November 8, 2017)
10.53!*	Amendment No. 1 to Collaboration Agreement, dated December 2, 2022, by and between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation

Exhibit Number	Description of Exhibit
10.54#	Collaboration and License Agreement, between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated December 18, 2016 (incorporated by reference to Exhibit 10.26 to the Company's Annual Report on Form 10-K (001-36352) and filed on March 6, 2017)
10.55#	Collaboration and License Agreement between Akebia Therapeutics, Inc. and Otsuka Pharmaceutical Co. Ltd., dated April 25, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2017)
10.56!	Termination and Settlement Agreement, dated June 30, 2022, by and between the Company and Otsuka Pharmaceutical Co. Ltd (incorporated by reference to Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 4, 2022)
10.57!	Second Amended and Restated License Agreement, dated February 18, 2022, by and between Akebia Therapeutics, Inc. and Vifor (International) Ltd. (incorporated by reference to Exhibit 10.54 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.58	Open Market Sale Agreement℠, dated April 7, 2022, by and between Akebia Therapeutics, Inc. and Jefferies LLC (incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K (001-36352), filed on April 7, 2022)
10.59!	Second Amended and Restated License Agreement dated April 17, 2019, by and between Akebia Therapeutics, Inc. and Panion & BF Biotech, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 8, 2019)
10.60#	Amended and Restated Sub-License Agreement, dated June 8, 2009, as amended by the First Amendment thereto, dated June 12, 2013, by and between Keryx Biopharmaceuticals, Inc., Japan Tobacco, Inc. and Torii Pharmaceutical Co., Ltd (incorporated by reference to Exhibit 10.1 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on November 7, 2017)
10.61!	Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates, dated September 27, 2016, and related Product Agreement dated September 27, 2016, and related Product Agreement dated October 12, 2016 (incorporated by reference to Exhibit 10.58 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.62#	Product Agreement, dated August 29, 2017, by and between Keryx Biopharmaceuticals, Inc. and Patheon Inc. (an affiliate of Patheon Manufacturing Services LLC) related to the Master Manufacturing Services Agreement by and between Keryx Biopharmaceuticals, Inc. and Patheon Manufacturing Services LLC and certain of its affiliates dated November 12, 2016 (incorporated by reference to Exhibit 10.2 to Keryx Biopharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (000-30929), filed on November 7, 2017)
10.63#	Master Manufacturing Services and Supply Agreement, dated December 20, 2017, by and between Keryx Biopharmaceuticals, Inc. and Siegfried Evionnaz SA (incorporated by reference to Exhibit 10.13 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K (000-30929), filed on February 21, 2018)
10.64	Amendment No. 1 to Master Manufacturing Services and Supply Agreement, dated as of December 21, 2020, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.58 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.65	Amendment No. 2 to Master Manufacturing Services and Supply Agreement, dated as of January 29, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.58 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.66!	Amendment No. 3 to Master Manufacturing Services and Supply Agreement, dated as of February 11, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.59 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)
10.67	Amendment No. 4 to Master Manufacturing Services and Supply Agreement, dated as of December 17, 2021, by and between Siegfried Evionnaz SA and Keryx Biopharmaceuticals, Inc. (incorporated by reference to Exhibit 10.64 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)

Exhibit Number	Description of Exhibit
10.68#	Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated October 16, 2014 and First Amendment to Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated April 14, 2015 (incorporated by reference to Exhibit 10.60 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.69#	Manufacture and Supply Agreement between Keryx Biopharmaceuticals, Inc. and BioVectra Inc., dated May 26, 2017 and Amendment to Manufacture and Supply Agreement between Keryx Biopharmaceuticals, Inc. and BioVectra Inc., dated December 11, 2017 (incorporated by reference to Exhibit 10.61 to the Company's Annual Report on Form 10-K (001-36352), filed on March 26, 2019)
10.70!*	Termination and Settlement Agreement, dated December 22, 2022, by and between Keryx Biopharmaceuticals, Inc. and BioVectra Inc.
10.71!	Loan Agreement, dated November 11, 2019, by and among the Company, Keryx Biopharmaceuticals, Inc., Biopharma Credit plc and Biopharma Credit Investments V (Master) LP (incorporated by reference to Exhibit 10.62 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2020)
10.72!	First Amendment and Waiver, dated February 18, 2022, by and among the Company, Biopharma Credit plc, BCPR Limited Partnership and Biopharma Credit Investments V (Master) LP (incorporated by reference to Exhibit 10.69 to the Company's Annual Report on Form 10-K (001-36352), filed on March 1, 2022)
10.73!	Second Amendment and Waiver, dated July 15, 2022, by and among the Company, Biopharma Credit plc, BCPR Limited Partnership and Biopharma Credit Investments V (Master) LP (incorporated by reference to Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 4, 2022)
10.74!	Guaranty and Security Agreement, dated November 25, 2019, by and between the Company, Keryx Biopharmaceuticals, Inc. and Biopharma Credit plc (incorporated by reference to Exhibit 10.63 to the Company's Annual Report on Form 10-K (001-36352), filed on March 12, 2020)
10.75!	Supply Agreement, dated as of March 11, 2020, by and between Akebia Therapeutics, Inc. and Patheon, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 5, 2020)
10.76!	Supply Agreement, dated as of April 2, 2020, by and between Akebia Therapeutics, Inc. and STA Pharmaceutical Hong Kong Limited (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 10, 2020)
10.77!	Amendment #1 to the Supply Agreement, dated as of April 15, 2021, by and between Akebia Therapeutics, Inc. and STA Pharmaceutical Hong Kong Limited (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on August 5, 2021)
10.78!	Amended and Restated Product Manufacture and Supply and Facility Construction Agreement between BioVectra, Inc. and Keryx Biopharmaceuticals, Inc., dated September 4, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (001-36352), filed on September 11, 2020)
10.79!	Supply Agreement, dated February 10, 2021, by and between the Company and STA Pharmaceutical Hong Kong Limited (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 10, 2021)
10.80!	Royalty Interest Acquisition Agreement, dated February 25, 2021, by and between the Company and HealthCare Royalty Partners IV, L.P. (incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q (001-36352), filed on May 10, 2021)
10.81!*	License Agreement, dated December 22, 2022, by and among Akebia Therapeutics, Inc., Keryx Biopharmaceuticals, Inc. and Averoa SAS
21.1	List of Subsidiaries (incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K (001-36352), filed on February 25, 2021)

Exhibit Number	Description of Exhibit
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of Principal Executive Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. 1350
101.INS*	Inline XBRL Instance Document (the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document)
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

* Filed, or submitted electronically, herewith
† Indicates management contract or compensatory plan
# Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment
! Indicates portions of the exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K
** The schedules to the Agreement and Plan of Merger have been omitted pursuant to Item 601(b)(2) of Regulation S-K. The Company will furnish copies of such schedules to the Securities and Exchange Commission upon request by the Commission

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

AKEBIA THERAPEUTICS, INC.

Date: March 10, 2023	By:	/s/ John P. Butler
		John P. Butler
		President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report was signed by the following persons on behalf of the registrant and in the capacities and on the date indicated.

Date: March 10, 2023	By:	/s/ John P. Butler
		John P. Butler
		Director, President and Chief Executive Officer (Principal Executive Officer)
Date: March 10, 2023	By:	/s/ David A. Spellman
		David A. Spellman
		Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)
Date: March 10, 2023	By:	/s/ Adrian Adams
		Adrian Adams
		Chairperson and Director
Date: March 10, 2023	By:	/s/ Ron Frieson
		Ron Frieson
		Director
Date: March 10, 2023	By:	/s/ Steven C. Gilman
		Steven C. Gilman
		Director
Date: March 10, 2023	By:	/s/ Michael Rogers
		Michael Rogers
		Director
Date: March 10, 2023	By:	/s/ Cynthia Smith
		Cynthia Smith
		Director
Date: March 10, 2023	By:	/s/ Myles Wolf
		Myles Wolf
		Director
Date: March 10, 2023	By:	/s/ LeAnne M. Zumwalt
		LeAnne M. Zumwalt
		Director

Exhibit 10.53

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

AMENDMENT NO.1 TO COLLABORATION AGREEMENT

THIS AMENDMENT NO.1 TO COLLABORATION AGREEMENT (this "**Amendment No. 1**") is effective as of December 2, 2022 (the "**Effective Date**") and made by and between:

Akebia Therapeutics, Inc., a company organized and existing under the laws of the State of Delaware, United States of America, with its principal offices at 245 First Street, Cambridge, MA 02142, U.S.A. ("**Akebia**"),

and

Mitsubishi Tanabe Pharma Corporation, a company organized and existing under the laws of Japan, with its principal offices at 3-2-10, Dosho-machi, Chuo-ku, Osaka 541-8505, Japan ("**Licensee**"), on the other hand.

Akebia and Licensee may be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, the Parties entered into the Collaboration Agreement dated December 11, 2015 (the "**Collaboration Agreement** "); and

WHEREAS, the Parties wish to revise, amend or supplement certain provisions of the Collaboration Agreement to provide that Licensee may procure API of the Licensed Product by contracting with specific contract manufacturing organizations, for the use of Licensee's activities permitted under the Collaboration Agreement in the Territory; and

NOW THEREFORE, in consideration of the mutual promises and benefits made and contained herein, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1. Unless otherwise expressly provided in this Amendment No.1, all capitalized terms used in this Amendment No.1 have the meaning respectively as defined in the Collaboration Agreement.

2. **Section 7.01 (Manufacture and Supply of Licensed Products) of the Collaboration Agreement** is hereby amended in its entity and replaced as follows:

(a) Subject to the terms and conditions of this Agreement (as amended) and the associated Supply Agreement made and entered into as of July 15, 2020 (as amended), Akebia shall continue to manufacture or have manufactured and supply Licensed Product for clinical and commercial use in the Territory in accordance with GCP and GMP at the same level of diligence [**].

(b) After First Commercial Sale of the Licensed Product in the Territory, Licensee shall have the right, but not the obligation, to manufacture (or have its Affiliates manufacture) Licensed Products inside or outside the Territory in tablet form (for clarity, not API) for use in the Territory; provided, however, that if Licensee chooses to exercise its manufacturing right it shall also [**]. If Licensee wishes to exercise this right, it shall so notify Akebia, and Licensee and Akebia shall promptly enter into a supply agreement for Akebia's supply of API to Licensee, as well as Licensee's supply of tablets to Akebia. For the avoidance of doubt, Licensee shall not be permitted to manufacture API of the Licensed Product in or outside the Territory. Upon the execution of a supply agreement, the Parties will enter into mutually acceptable technology transfer agreement, which shall include the Parties' respective obligations and responsibilities relating to matters of technology transfer to enable Licensee to manufacture the tablet form of the Licensed Product from API, which technology transfer and all costs associated therewith shall be [**]. If Licensee wishes to engage a Third Party to manufacture Licensed Products pursuant to

this Section 7.01(b), Licensee may do so only with Akebia's prior written consent, not to be unreasonably withheld or delayed, and all other terms of this Section 7.01(b) shall apply.

(c) If, at any time during the Term, Licensee reasonably expects that Akebia will be [**], Licensee may request a discussion with Akebia and the Parties shall promptly discuss a potential resolution, which may include a [**].

(d) Licensee shall have the right, but not the obligation, to manufacture (or have its Affiliates manufacture) the API of the Licensed Product at the following location:

[**]; and

For clarity, the foregoing right granted to Licensee under this **Section 7.01(b)** is limited to the foregoing manufacturing organization, and Licensee may not manufacture (or have its Affiliates manufacture) the API of the Licensed Product outside of this organization; *provided*, that, this **Section 7.01(d)** shall have not have, or shall not revise, amend, restrict or render ineffective any part of Licensee's rights and performance of activities permitted under the provisions of **Section 7.01(a) through (c)**.

(e) Licensee shall have the right, but not the obligation, to develop (or have its Affiliates develop) an alternate manufacturing pathway [**] for the API of the Licensed Product Vadadustat at the following [**] sites; *provided*, that, the following list of the permitted [**] Third Party contractors may be amended to incorporate any additional Third Party contractor upon written agreement of the Parties:

[**].

For clarity, the treatment of any Inventions or Know-How relating to or arising from Licensee's activities as provided for under the provisions of Section 7.01(d) and (e) shall be governed by Article IX of this Agreement, as applicable.

3. Except as expressly set forth in this Amendment No. 1, nothing in this Amendment No. 1 shall be construed to revise, amend or supplement any of terms, conditions, or obligations set forth in the Collaboration Agreement or in any way effect its enforceability.

4. This Amendment No. 1 and the rights of the Parties hereunder shall be construed under and governed by the laws of the State of New York, United States, exclusive of its conflicts of laws principles.

5. This Amendment No. 1 may be executed in counterparts, all of which taken together shall be regarded as one and the same instrument.

[*Signature Page Follows:*]

IN WITNESS WHEREOF, the Parties have freely executed this Amendment No.1 through their duly authorized representatives to be effective as of the Effective Date.

For and on behalf of:

Akebia Therapeutics, Inc.

By: /s/ David Spellman
Name: David Spellman

Title: SVP, Chief Financial Officer and Treasurer

Date: 03-Dec-2022 | 9:53 AM EST

For and on behalf of:

Mitsubishi Tanabe Pharma Corporation

By: /s/ Atsushi Hashimoto
Name: Atsushi Hashimoto

Title: Vice President, Head of Business Development Department

Date: 02-Dec-2022 | 12:30 PM JST

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

TERMINATION AND SETTLEMENT AGREEMENT

This termination and settlement agreement (the "**Termination Agreement**") shall be effective as of December 22, 2022 (the "**Termination Effective Date**") between Keryx Biopharmaceuticals, Inc. ("**Keryx**"), a wholly-owned subsidiary of Akebia Therapeutics, Inc. ("**Akebia**"), with a place of business at 245 First Street, Cambridge, Massachusetts, 02142, USA, and BIOVECTRA Inc., with a place of business at 11 Aviation Avenue, Charlottetown, Prince Edward Island, C1E0A1, Canada ("**BIOVECTRA**") to terminate any and all existing agreements entered into by the parties in connection with the manufacture and supply, by BIOVECTRA to Akebia, of Akebia's proprietary active pharmaceutical ingredient, ferric citrate drug substance (the "**Product**"). Akebia (on behalf of itself and Keryx) and BIOVECTRA are each referred to individually as a "**Party,**" and collectively as the "**Parties**" to this Termination Agreement.

RECITALS

Whereas, Keryx and BIOVECTRA are parties to certain agreements, including but not limited to that certain Manufacture and Supply Agreement, as amended, dated as of May 26, 2017, that certain Product Manufacture and Supply and Facility Construction Agreement, dated December 11, 2017, as amended and restated by the First Amendment No. 1 to Product Manufacture and Supply and Facility Construction Agreement, dated April 20, 2018, as further amended and restated by that certain Amended and Restated Product Manufacture and Supply and Facility Construction Agreement, dated September 4, 2020, and that certain Quality Agreement, dated February 22, 2021, pursuant to which BIOVECTRA manufactures and supplies the Product to Akebia and builds a facility for the manufacture of Product (collectively, the "**Agreements**");

Whereas, on December 12, 2018, Keryx became a wholly-owned subsidiary of Akebia;

Whereas, Akebia has authority to act on behalf of Keryx;

Whereas, due to business considerations, the Parties have decided to discontinue the manufacture of the Product by BIOVECTRA and to terminate the Agreements; and

Whereas, the Parties have agreed to terminate all agreements and contracts between the Parties, including but not limited to the Agreements, and resolve their disputes with each other concerning the Agreements under the terms and conditions set forth herein.

AGREEMENT

In consideration of the mutual covenants, terms and conditions set forth below, BIOVECTRA and Akebia (on behalf of itself and Keryx) agree as follows:

1. **Recitals**. The recitals set forth above are incorporated by reference and are explicitly made a part of this Termination Agreement.

2. **Defined Terms**. Capitalized terms used and not otherwise defined in this Termination Agreement shall have the meanings assigned to them in the Agreements.

3. **Termination**. As consideration for the termination of all Agreements between them, the Parties shall perform the following obligations:

A. Termination Fees. The Parties have agreed that, in connection with the termination of the Agreements, Akebia shall pay BIOVECTRA certain fees, which shall be paid in full by Akebia as set out in Annex No. 1 hereto (together the "**Termination Fees**" and each a "**Termination Fee Payment**"). This payment of Termination Fees shall be in full satisfaction of all payments and

other obligations of Akebia to BIOVECTRA relating to or arising out of, under, or in connection with the Agreements.

B. Akebia Materials. BIOVECTRA disclaims any ownership interest in the lots and retain samples listed in Annex No. 2 hereto (the "**Akebia Materials**"). Within [**] after the Termination Effective Date, BIOVECTRA will return the Akebia Materials to Akebia, at Akebia's expense, to the location and in a manner as directed by Akebia. Until the Akebia Materials have been transferred to Akebia, BioVectra will maintain such Akebia Materials in the manner proscribed under the Agreements. With respect to the Transferring Stability Studies (as defined on Annex No. 2), until such transfer to Akebia is effectuated, BioVectra will maintain the ICH compliant stability programs, including [**].

C. BIOVECTRA Ownership of Equipment, Work in Progress and Raw Materials: Akebia represents and warrants that, other than the Akebia Materials, Akebia has no ownership interest in any equipment, work in progress, raw materials, consumables, non-consumables, or materials obtained for the development and manufacture of the Product that are currently in the possession of BIOVECTRA (the **"BIOVECTRA Equipment and Materials")**. BIOVECTRA may use or dispose of all such BIOVECTRA Equipment and Materials as it sees fit.

D. Confidential Information, Keryx Technology, and Improvements:

1. Akebia retains its rights and interests in and with respect to all Keryx Technology, Improvements, and Confidential Information of Keryx, as those terms are defined, and as those rights and interests are specified, in the Agreements. BIOVECTRA agrees to abide by all provisions in the Agreements for the return, disposition, or other treatment upon termination of Keryx Technology, Improvements, and Confidential Information of Keryx, and those obligations of BIOVECTRA shall survive the termination of the Agreements. Within [**] of the Termination Effective Date, BIOVECTRA shall transfer to Akebia all Records and Supporting Documentation as defined in the Agreements, as well as all documentation and copies thereof in BIOVECTRA's (or any of its Affiliate's) possession, custody or control relating to the Product, Quality Modules, Specifications or Keryx Technology, Improvements and all other Confidential Information of Keryx with appropriate manifest, including, without limitation, [**]; provided, however, that BIOVECTRA may retain any documentation which it must retain for such period of time as required by Applicable Law, as to which copies shall be provided to Akebia, and which records BIOVECTRA must continue to treat as Confidential Information in accordance with the terms of the Agreements.

2. BIOVECTRA retains its rights and interests with respect to all Confidential Information of BIOVECTRA, as that term is defined, and as those rights and interests are specified, in the Agreements. Akebia agrees to abide by all provisions in the Agreements for the return, disposition, or other treatment upon termination of the Confidential Information of BIOVECTRA.

E. Mutual Release of Claims. Each Party and its direct and indirect parents, subsidiaries, Affiliates, predecessors, successors and assigns and their present and former directors, officers, employees, managers, stockholders, investors, , indemnitees, attorneys, representatives, licensors, licensees, subrogees, and agents, (collectively the "Releasing Parties") hereby release the other Party and its direct and indirect parents, subsidiaries, Affiliates, predecessors, successors and assigns and their present and former directors, officers, employees, managers, stockholders, investors, indemnitees, attorneys, representatives, licensors, licensees, subrogees, and agents (collectively the "Released Parties") from any and all past, present and future claims, demands, obligations, liabilities and

causes of action of any nature whatsoever ("**Claims**"), known or unknown, from the inception of time through the Termination Effective Date, including but not limited to all Claims relating to or arising out of, under, or in connection with the Agreements or their termination; provided, however, that neither Party hereby releases the other from any Claims or obligations arising under this Termination Agreement. The Parties intend for their respective mutual general releases to apply to Claims which they do not presently know to exist at this time. The Parties understand that the facts upon which they have based their decision to enter into this Termination Agreement may hereafter prove to be different from the facts now known or believed by them, and they hereby accept and assume the risk thereof and agree that this Termination Agreement shall be and shall remain, in all respects, effective and not subject to termination or rescission by reason of any such difference in facts.

F. Termination of Obligations. Effective upon the Termination Effective Date, the Parties agree to terminate:

a. all open Purchase Orders; in particular, both Parties acknowledge and agree that BIOVECTRA shall be relieved from any obligations to manufacture any Product or perform any services under any such open Purchase Orders, and Akebia shall be relieved from any obligation to pay balance of any outstanding invoices related to performance by BIOVECTRA of services and obligations under the Agreements;
b. all outstanding invoices; in particular, both Parties acknowledge and agree that Akebia shall be relieved from any obligations to pay any outstanding invoices related to performance by BIOVECTRA of services and obligations under the Agreements;
c. all agreements and contracts between the Parties, including but not limited to the Agreements in their entireties and, more generally, any commercial relationship between the Parties with the exception of (i) the Parties' rights and obligations under this Termination Agreement, and (ii) with respect to those rights and obligations under the Agreements that survive termination as set forth in Section 3.D of this Termination Agreement.

G. Product. After receipt of Termination Fee Payment 1 (as set out in Annex No. 1), BIOVECTRA shall promptly destroy or otherwise dispose of, any remaining inventory of Product, stability lots and retain samples not included in the Akebia Material. BIOVECTRA is responsible for expenses related to disposal of inventory located at BIOVECTRA's Facility, and Akebia will reimburse BIOVECTRA for costs related to the disposal of inventory located at LSU.

H. Covenant Not to Sue. The Releasing Parties covenant and agree not to commence, aid, prosecute, or cause to be commenced or prosecuted any action or other proceeding, based upon any Claims relating to, arising out of, under, or in connection with the matters subject to the mutual releases as set forth herein, and the Releasing Parties further covenant and agree to hold harmless and indemnify the other Released Parties in respect of all Claims (including, but not limited to, all court costs and reasonable attorneys' fees), suffered, sustained, incurred, or required to be paid by such other Released Parties from or in connection with any such action or proceeding.

I. Compromise Agreement. This Termination Agreement is a compromise and settlement of claims and is not intended to be, nor shall be construed as, any admission of liability or wrongdoing by any Party hereto or any other person or entity.

J. Confidentiality. No public disclosures about the termination of the Agreements, the contents of this Termination Agreement, or the relationship between the Parties or their predecessors shall be made by either Party without the prior written approval of the other Party, which approval shall not be unreasonably withheld or delayed, provided; however, that each of the Parties may disclose such information to its attorneys, accountants, insurers, and auditors who have a need to

know such information and who are otherwise bound by an agreement or a professional duty of confidentiality to keep such information confidential to the same degree as are the Parties. Further, each of the Parties may disclose such information to the extent necessary to comply with applicable law, or the rules of a stock exchange on which the securities of the disclosing Party are listed (or to which an application for listing has been submitted). In the event a Party is required by Applicable Law or the rules of a stock exchange on which its securities are listed (or to which an application for listing has been submitted) to make such a public disclosure, such Party will submit the proposed disclosure in writing to the other Party with sufficient opportunity (to the extent practicable) for the other Party to review and comment on such required disclosure and request confidential treatment thereof or a protective order therefor if appropriate. Neither Party will be required to seek the permission of the other Party to repeat any information regarding the terms of this Termination Agreement or any amendment hereto or other information of the other Party that has already been publicly disclosed by such Party or by the other Party, in accordance with this Section, *provided* that such information remains accurate as of such time.

K. Successors and Assigns. The provisions of this Termination Agreement shall be binding upon and inure to the benefit of the Parties hereto and their respective successors and assigns.

L. Entire Agreement. This Termination Agreement constitutes the entire agreement between the Parties with respect to the subject matter of the Termination Agreement. This Termination Agreement supersedes all prior agreements, whether written or oral, with respect to the subject matter of the Termination Agreement. Each Party confirms that it is not relying on any statements, representations, warranties or covenants of any person (whether a Party to this Agreement or not) except as specifically set out in this Termination Agreement. Nothing in this Termination Agreement is intended to limit or exclude any liability for fraud.

M. Counterparts. This Termination Agreement may be executed in two or more counterparts, each of which shall be deemed an original and all of which shall together be deemed to constitute one agreement. The Parties agree that execution of this Termination Agreement by industry standard electronic signature software or by exchanging PDF signatures shall have the same legal force and effect as the exchange of original signatures, and that in any proceeding arising under or relating to this Termination Agreement, each party hereby waives any right to raise any defense or waiver based upon execution of this Termination Agreement by means of such electronic signatures or maintenance of the executed agreement electronically.

N. Jointly Drafted. The terms, provisions and language of this Termination Agreement have been jointly negotiated and drafted by the Parties and their respective legal counsel. Nothing in this Termination Agreement should be construed or interpreted against any of the Parties as the drafting Parties, or for any other reason by operation of similar rules of construction.

O. Headings. The headings of the sections, paragraphs and subsections of this Termination Agreement are inserted for convenience of reference and are not a part of and are not intended to govern, limit, or aid in the construction or interpretation of any term or provision hereof.

P. Tax Consequences. Each of the Parties are solely responsible for any tax consequences of this Termination Agreement, and none of the Parties or their representatives has made any representations regarding such tax consequences, if any.

Q. No Waiver. Failure to insist on compliance with any term, covenant or condition contained in this Termination Agreement shall not be deemed a waiver of that term, covenant or condition, nor

shall any waiver or relinquishment of any right or power contained in this Termination Agreement at any one time or more times be deemed a waiver or relinquishment of any right or power at any other time or times.

R. Amendment. This Termination Agreement may not be modified or terminated orally and no modification termination or waiver shall be valid unless in writing and signed by all of the Parties hereto.

4. **Choice of Law; Jurisdiction and Venue**. This Termination Agreement and any claim or controversy directly or indirectly based upon or arising out of this Termination Agreement (whether based on contract, tort or any other theory), including all matters of construction, validity and performance, shall in all respects be governed by and interpreted, construed and determined in accordance with, the internal laws of the State of Delaware (without regard to any conflicts of law provision thereof that would require the application of the laws of any other jurisdiction). Each of the Parties, to the extent permitted by the applicable laws and regulations irrevocably (i) submits itself to the personal jurisdiction of the State and Federal Courts of the State of Delaware, as well as to the jurisdiction of all courts to which an appeal may be taken, in any suit, action, or proceeding arising out of or relating to this Termination Agreement, or any of the transactions contemplated by this Settlement Agreement, including; (ii) agrees that all claims in respect of such suit, action or proceeding shall be brought, heard and determined exclusively in the State and Federal Courts in the State of Delaware; and (iii) agrees not to bring any action or proceeding arising out of or relating to this Termination Agreement or any of the transactions contemplated by this Termination Agreement in any other court.

5. Jury Trial Waiver. THE PARTIES HEREBY KNOWINGLY, VOLUNTARILY, INTENTIONALLY, IRREVOCABLY, AND UNCONDITIONALLY WAIVE TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW ANY RIGHT THEY MAY HAVE TO A TRIAL BY JURY WITH RESPECT TO ANY ACTION, SUIT OR PROCEEDING DIRECTLY OR INDIRECTLY ARISING OUT OF, UNDER OR IN CONNECTION WITH THIS SETTLEMENT AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY. THE PARTIES EACH HEREBY (I) CERTIFY THAT NO REPRESENTATIVE, AGENT OR ATTORNEY OF THE OTHERS HAS REPRESENTED, EXPRESSLY OR OTHERWISE, THAT SUCH OTHER PERSON WOULD NOT, IN THE EVENT OF ANY ACTION, SUIT OR PROCEEDING, SEEK TO ENFORCE THE FOREGOING WAIVER AND (II) ACKNOWLEDGES THAT IT HAS BEEN INDUCED TO ENTER INTO THIS AGREEMENT BY, AMONG OTHER THINGS, THE MUTUAL WAIVERS AND CERTIFICATIONS CONTAINED IN THIS SECTION 5.

[Remainder of page intentionally left blank.]

IN WITNESS WHEREOF, the parties have caused their respective duly authorized representatives to execute this Termination Agreement effective as of the Termination Effective Date.

BIOVECTRA INC.

By: /s/ Valana Deighan

Name: Valana Deighan

Title: General Counsel

KERYX BIOPHARMACEUTICALS, INC., a wholly-owned subsidiary of AKEBIA THERAPEUTICS, INC.

By: /s/ David Spellman

Name: David Spellman

Title: SVP, Chief Financial Officer and Treasurer

ANNEX No. 1 – Termination Fees

Termination Fee Payment	Amount (USD)	Payment Due Date
1.	$17,500,000.00	On the Termination Effective Date
2.	$2,500,000.00	April 5, 2024
3.	$2,500,000.00	July 5, 2024
4.	$2,500,000.00	October 5, 2024
5.	$2,500,000.00	January 5, 2025
6.	$2,500,000.00	April 5, 2025
7.	$2,500,000.00	July 5, 2025

Payment Terms and Conditions:

1. With the exception of Termination Fee Payment 1, at least [**] prior to each Payment Due Date listed above, BIOVECTRA will issue invoices with payment instructions to Akebia. Payment of each Termination Fee Payment is due on the corresponding Payment Due Date listed above.

2. In addition, for each Termination Fee Payment that Akebia is [**] late to pay ("Late Payment"), Akebia will pay a late fee of [**] percent ([**]%) of the payment, being [**] US dollars ($[**]USD). BIOVECTRA will issue an invoice to Akebia for the late fee and payment for late fee is due upon receipt of the invoice.

3. The first Late Payment will also trigger a one-time additional Termination Fee by Akebia to BIOVECTRA of [**] US dollars ($[**]USD). This one-time additional Termination Fee Payment, if triggered, will be due [**].

4. Akebia shall be entitled to a [**] percent ([**]%) discount for prepayment of any of Termination Fees 2-7 listed above in the Termination Fees table. The prepayment will be applied to the last Termination Fee Payment first. For example, should Akebia communicate its intention prior to [**] to prepay a Termination Fee Payment that has yet to be paid, Akebia will receive a discount of [**] percent ([**]%) off the prepayment of Termination Fee Payment 7. The discounted Termination Fee payment would be [**] US dollars ($[**]USD). Akebia can elect to prepay multiple Termination Fee Payments at once, up to and including all Termination Fee Payments 2-7 listed above.

5. On a quarterly basis commencing [**], BIOVECTRA has the right to a [**] teleconference with Akebia's Chief Financial Officer (or then current Akebia representative with financial responsibility within Akebia) to inquire and confirm ability of Akebia to make remaining Termination Fee payments. The teleconference will take place within [**] following Akebia's quarterly earnings call but not later than [**] after the end of the quarter, except that such call shall occur not later than [**] after the end of each calendar year.

ANNEX No. 2 – Akebia Materials

[**]

Exhibit 10.81

CONFIDENTIAL ***Execution Version***

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

LICENSE AGREEMENT

by and among

Akebia Therapeutics, Inc.,

Keryx Biopharmaceuticals, Inc.,

and

Averoa SAS

Dated as of December 22, 2022

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Page

LICENSE AGREEMENT

THIS LICENSE AGREEMENT ("**Agreement**") is made effective as of December 22, 2022 (the "**Effective Date**"), by and among Akebia Therapeutics, Inc., a Delaware corporation with its principal place of business at 245 First Street, Cambridge, MA 02142 and its Subsidiary, Keryx Biopharmaceuticals, Inc. ("**Keryx**," and collectively, "**Akebia**"), on the one hand, and Averoa SAS, an French corporation, having a place of business at 11 avenue Paul Verlaine, 38100 Grenoble, France, represented by Luc-André Granier in his capacity as CEO, duly empowered for the purposes hereof ("**Licensee**") on the other hand. Akebia and Licensee may, from time to time, be individually referred to as a "**Party**" and collectively referred to as the "**Parties**."

RECITALS

WHEREAS, Akebia Controls certain Patent Rights and Know-How related to the Licensed Product; and

WHEREAS, Licensee wishes to obtain, and Akebia wishes to grant, certain licenses under such Patent Rights and Know-How to Develop and Commercialize the Licensed Product on the terms and conditions set forth herein.

NOW, THEREFORE, the Parties, intending to be legally bound hereby, agree as follows:

DEFINITIONS

1.1 "**Accounting Standards**" means, as applicable, (a) International Financial Reporting Standards, or (b) GAAP.

1.2 "**Additional Development**" has the meaning set forth in Section 4.3.4 (Additional Development).

1.2 "**Affiliate**" means, with respect to a Party, any Person that controls, is controlled by, or is under common control with that Party. For the purpose of this definition, "control" will refer to: (a) the possession, directly or indirectly, of the power to direct the management or policies of an entity, whether through the ownership of voting securities, by contract or otherwise; or (b) the ownership, directly or indirectly, of more than 50% of the voting securities of such entity.

1.4 "**Agreement**" has the meaning set forth in the Preamble.

1.5 "**Akebia**" has the meaning set forth in the Preamble.

1.6 "**Akebia Cost Defense Action**" has the meaning set forth in 6.5.2 (Control and Cost).

1.7 "**Akebia Defense Action**" has the meaning set forth in Section 6.5.1 (Rights to Defend).

1.8 "**Akebia Housemarks**" means (a) the corporate logos of Akebia and Keryx, (b) the trademarks "AKEBIA" and "KERYX," (c) any other trademark, trade name, or service mark (whether registered or unregistered) containing the word "Akebia" or "Keryx," (d) any trademark, trade name, or service mark (whether registered or unregistered) used as the name of any clinical trial for the Licensed Product, (e) any other corporate logo or trademark of Akebia used by Akebia to identify Akebia or its Affiliates, (f) all registrations, applications for registrations, and other intellectual property rights associated with any of the foregoing, and (g) all goodwill associated with any and all of the foregoing in clauses (a) through (f).

1.9 "**Akebia Improvements**" means any Improvement invented, conceived, discovered, created, or otherwise developed solely by or on behalf of Akebia (or its Affiliates) in the performance of activities under this Agreement during the Term.

1.10 "**Akebia Indemnitees**" has the meaning set forth in Section 9.1 (Indemnification by Licensee).

1.11 "**Akebia Know-How**" means Know-How that is Controlled by Akebia on the Effective Date that is necessary to Develop, package in accordance with the Approved Labeling, or Commercialize the Licensed Product in the Territory in the form that it exists on the Effective Date, including any data that supports Akebia's pediatric study plan, but expressly excluding all Akebia Pediatric Data (unless and until the Parties agree as to the terms of a license to be granted to Licensee with respect to such Akebia Pediatric Data and an appropriate cost sharing arrangement as set forth under Section 2.5.1 (By Akebia)), in each case, as set forth in Section 4.3.2 (Pediatric Investigation Plan). Akebia Know-How will also include all Akebia Improvements.

1.12 "**Akebia Patent Rights**" means (a) the Patent Rights listed on Schedule 1.12 (Akebia Patent Rights); (b) all Patent Rights in the Territory that directly or indirectly claim priority thereto or share common priority therewith whether filed before or after the Effective Date, to the extent Akebia Controls such patents and patent applications; and (c) all Patent Rights Controlled by Akebia or its Affiliates that are necessary to Develop, package in accordance with the Approved Labeling, or Commercialize the Licensed Product in the Territory.

1.13 "**Akebia Pediatric Clinical Trials**" has the meaning set forth in Schedule 1.13.

1.14 "**Akebia Pediatric Data**" means any data, results, or other Akebia Know-How generated in the performance of any ongoing or future clinical trials included in Akebia's pediatric investigation plan, including the Akebia Pediatric Clinical Trials.

1.15 "**Akebia Technology**" means collectively, the Akebia Patent Rights and Akebia Know-How.

1.16 "**Alliance Manager**" has the meaning set forth in Section 3.8 (Alliance Managers).

1.17 "**API**" means active pharmaceutical ingredient, which is also commonly referred to as drug substance.

1.18 "**Applicable Laws**" means any applicable federal, state, local, municipal, foreign or other law, statute, legislation, constitution, principle of common law, resolution, ordinance, code, edict, decree, proclamation, treaty, convention, rule or regulation issued, enacted, adopted, passed, approved, promulgated, made, implemented or otherwise put into effect by or under the authority of any Governmental Authority, including (a) the applicable regulations and guidance of the FDA and E.U. (and national implementations thereof) that constitute good laboratory practices, good manufacturing practices, good clinical practices, and any regulations or guidance of any applicable Regulatory Authority (and national implementations thereof) concerning healthcare, promotional, or regulatory matters, and, if and as appropriate under the circumstances, International Conference on Harmonization (ICH) guidance or other comparable regulation and guidance of any applicable Governmental Authority; and (b) data privacy and protection laws and regulations.

1.19 "**Approved Labeling**" means: (a) the Regulatory Authority-approved full prescribing information for the Licensed Product; and (b) the Regulatory Authority-approved labels and other written, printed, or graphic materials on any container, wrapper, or any package insert that is used with or for the Licensed Product.

1.20 "**Arbitration Request**" has the meaning set forth in Section 11.2.1 (Arbitration Request).

1.21 "**Base Royalties**" has the meaning set forth in Section 5.1.1 (Base Royalties).

1.22 "**Business Day**" means any day other than a Saturday, a Sunday, or a day on which commercial banks located in Boston, Massachusetts, Ireland, or France are authorized or required by law to remain closed.

1.23 "**Breaching Party**" has the meaning set forth in Section 10.2 (Termination for Breach).

1.24 "**Calendar Quarte**r" means the respective periods of three consecutive calendar months ending on March 31, June 30, September 30, and December 31.

1.25 "**Calendar Year**" means any 12-month period commencing on January 1.

1.26 "**Challenge**" means, with respect to any Akebia Patent Right or Joint Patent Right, to contest the ownership, validity, scope, or enforceability of any such Akebia Patent Right or Joint Patent Right, in whole or in part, in any action, suit, claim, notice, arbitration, administrative or other legal proceeding. As used in this definition the term "contest" includes (a) filing an action under 28 U.S.C. §§ 2201-2202 seeking a declaration of invalidity or unenforceability of any such Akebia Patent Right or Joint Patent Right; (b) filing, or joining in, a petition under 35 U.S.C. § 311 to institute *inter partes* review of any such Patent Right or any portion thereof; (c) filing, or joining in, a petition under 35 U.S.C. § 321 to institute post-grant review of any such Akebia Patent Right or Joint Patent Right or any portion thereof; or (d) filing or commencing any opposition, invalidity, nullity, request for revocation or limitation, third party observation or similar proceedings challenging the validity of any such Akebia Patent Right or Joint Patent Right in any forum in any country or before any legal or administrative body, including the European Patent Office.

1.27 "**CKD**" means chronic kidney disease.

1.28 "**Claims**" means collectively, any and all Third Party demands, claims, actions, suits, and proceedings (whether criminal or civil, in contract, tort or otherwise) for damages, debts, obligations, and other liabilities, losses, claims, taxes, interest obligations, deficiencies, judgments, assessments, fines, fees, penalties, or expenses (including amounts paid in settlement, interest, court costs, costs of investigators, reasonable fees and expenses of attorneys, accountants, financial advisors, consultants and other experts, and other expenses of litigation).

1.29 "**Commercialization Plan**" means a rolling [**] plan for the Commercialization of the Licensed Product in the Territory that is prepared, updated, and amended by Licensee in accordance with Section 4.4.3 (Commercialization Plan).

1.30 "**Commercialize**" or "**Commercialization**" means to market, promote, otherwise offer for sale, distribute, and sell. When used as a verb, "**to Commercialize**" and "**Commercializing**" means to engage in Commercialization and "**Commercialized**" has a corresponding meaning.

1.31 "**Commercially Reasonable Efforts**" means, with respect to the Development, Manufacture, or Commercialization of the Licensed Product by a Party, those efforts and resources, including reasonably necessary personnel, equivalent to the efforts that a similarly situated biopharmaceutical company or a pharmaceutical company would typically devote to a product of similar market potential, profit potential, and strategic value and at a comparable stage in development or product life as the Licensed Product, based on conditions then prevailing and taking into account issues of safety and efficacy, anticipated or actual product labeling, the competitiveness of alternative Third Party products in the marketplace, the expected likelihood of regulatory approval, and the potential profitability of such Licensed Product marketed or to be marketed.

1.32 "**Confidential Information**" has the meaning set forth in Section 7.1 (Definition).

1.33 "**Control**" or "**Controlled**" means, with respect to any Intellectual Property Rights, the legal authority or right (whether by ownership, license or otherwise other than pursuant to this Agreement) of a Party or its Affiliates to grant a license or a sublicense under the terms and conditions set forth in this Agreement of or under such Intellectual Property Rights to the other Party without breaching the terms of any agreement with a Third Party or being required to make any payment to any Third Party (other than any amounts due to [**] pursuant to the [**] Agreement). If a Party or its Affiliates only can grant a license or sublicense to Intellectual Property Rights, or provide access to a material or document, of a limited scope due to an encumbrance or other limitation imposed by a Third Party, "**Control**" or "**Controlled**" will be

construed to so limit the license or sublicense to such Intellectual Property Rights or the provision of, or provision of access to, such materials or documents (as applicable). Notwithstanding the foregoing, no Intellectual Property Right will be "Controlled" by either Party hereunder if such Intellectual Property Right is owned or in-licensed by a Third Party that becomes an Affiliate of such Party after the Effective Date as a result of such Party being acquired by such Third Party, whether by merger, stock purchase, or purchase of assets.

1.34 "**Cost of Goods Sold**" or "**COGS**" (a) with respect to any Licensed Product in API form, bulk form, or Finished Form that is Manufactured or supplied by any Third Party(ies), the total actual prices paid by Akebia to all such Third Party(ies) for released batches of such Licensed Product together with all reasonably allocated indirect costs and overhead applicable to managing its supply of Licensed Product and such Third Party suppliers (including internal FTE costs associated therewith); and (b) to the extent any Licensed Product in API form, bulk form, or Finished Form is manufactured and supplied by Akebia or its Affiliates, the fully-burdened cost of all direct materials and labor and fully-allocated manufacturing overhead directly attributable to the manufacture, storage, packaging, and shipping of such Licensed Product, calculated in accordance with the Accounting Standards applicable to Akebia or its Affiliates, including all Licensed Product testing and yield loss costs, quality control, quality assurance, or other testing of such Licensed Product, together with all reasonably allocated indirect costs and overhead applicable to the manufacturing of such Licensed Product (including internal FTE costs associated with supply thereof), or technical operations functions, less costs of goods returned in accordance with Akebia's or its Affiliates' or suppliers' return policy.

1.35 "**CTA**" means: (a) a clinical trial application filed with the European Medicines Agency or another Regulatory Authority in a European Union country, as described in Council Directive 2001/20/EC; (b) any foreign equivalents as filed with the applicable Regulatory Authorities in other countries or regulatory jurisdictions in the Territory, as applicable; and (c) all supplements and amendments that may be filed with respect to the foregoing.

1.36 "**Develop**" or "**Development**" means all internal and external research, development, and regulatory activities regarding the Licensed Product, including conducting non-clinical research or clinical trials prior to or after receiving Regulatory Approval, preparation and submission of all Regulatory Submissions to obtain and maintain Regulatory Approval of the Licensed Product, and any formulation or process development with respect to the Licensed Product. When used as a verb, "**Develop**" means to engage in Development.

1.37 "**Deferred Royalties**" has the meaning set forth in Section 4.9.3(d).

1.38 "**Disclosing Party**" has the meaning set forth in Section 7.1 (Definition).

1.39 "**Distributor**" means a Third Party that purchases the Licensed Product in Finished Form from Licensee or any of its Affiliates or its Sublicensees with the intent or purpose of reselling such Licensed Product, but does not make any royalty or profit share payment to Licensee or its Affiliates or its Sublicensee with respect to its resale of such Licensed Product, even if such Third Party is granted a sublicense under the Akebia Technology in the Field in the Territory in order to facilitate such Third Party's distribution, marketing, or sale of the Licensed Product in the Territory.

1.40 "**Drug Substance**" means Fexeric® (ferric citrate) drug substance.

1.41 "**EAP**" or "**Early Access Program**" means any program to provide patients with a Licensed Product prior to receipt of Regulatory Approval and prior to First Commercial Sale in any country in the Territory. Early Access Programs include treatment INDs / protocols, named patient programs and compassionate use programs in other countries. For clarity, an EAP with respect to any of the Licensed Products may continue to be performed following Regulatory

Approval of such Licensed Product and costs may continue to be incurred in accordance with the performance of such EAP after Regulatory Approval.

1.42 "**Effective Date**" has the meaning set forth in the Preamble.

1.43 "**EMA**" means the European Medicines Agency, or any successor agency thereto.

1.44 "**EMA Approval Date**" means the first date on which the EMA approves the MAA for the Licensed Product.

1.45 "**E.U.**" means the European Union as constituted as of the Effective Date.

1.46 "**[**] Pricing and Reimbursement Date**" means the first date on which the Licensed Product has received Reimbursement Approval in [**] of the Major Market Countries. For clarity, any EAP authorization granted with regards to the Licensed Product will not be deemed a "Reimbursement Approval" for the purposes of this Section 1.46 ([**] Pricing and Reimbursement Date).

1.47 "**Executive Officer**" means the chief executive officer of a Party or any of its Affiliates or his or her designee.

1.48 "**Exploit**" means to Develop, Commercialize, Manufacture, and otherwise exploit. When used as a verb, "**Exploit**" and "**Exploiting**" means to engage in Exploitation and "**Exploited**" has a corresponding meaning.

1.49 "**FDA**" means the United States Food and Drug Administration, or any successor federal agency thereto.

1.50 "**FFDCA**" means the United States Federal Food, Drug and Cosmetic Act, as amended from time to time, together with any rules, regulations, and requirements promulgated thereunder (including all additions, supplements, extensions and modifications thereto).

1.51 "**Field**" means the treatment, prevention, and diagnosis of any human diseases, including hyperphosphatemia and IDA.

1.52 "**Finished Form**" means the Licensed Product in finished form and with all applicable Packaging and Labeling.

1.53 "**First Commercial Sale**" means with respect to the Licensed Product and a country in the Territory, the date on which Licensee or its Affiliate or Sublicensee first sells the Licensed Product to a Third Party (other than to any Sublicensee or to an affiliate of any Sublicensee) for monetary consideration.

1.54 "**FTE**" means the equivalent of the work of one duly qualified employee of Akebia full time for one year (consisting of a total of [**] hours per year) carrying out scientific or technical work under this Agreement. Overtime, and work on weekends, holidays and the like will not be counted with any multiplier (*e.g.*, time-and-a-half or double time) toward the number of hours that are used to calculate the FTE contribution. The portion of an FTE billable by Akebia for one individual during a given accounting period will be determined by dividing the number of hours worked directly by said individual on the work to be conducted under this Agreement during such accounting period and the number of FTE hours applicable for such accounting period based on [**] working hours per Calendar Year.

1.55 "**GAAP**" means the generally accepted accounting principles in the United States, consistently applied.

1.56 "**Generic Product**" means, on a country-by-country basis in a particular country in the Territory, any pharmaceutical product sold by a Third Party (other than an Affiliate or Sublicensee of Licensee) in such country that: (a) contains the same API as the Licensed Product in the same dosage form and formulation (*e.g.*, oral, injectable, or intranasal) as the Licensed Product, (b) relies on the Regulatory Submissions of the Licensed Product to obtain Regulatory Approval in such country; and (c) is categorized by the applicable Regulatory Authority in such country to be therapeutically equivalent to, or interchangeable with, the Licensed Product, such that the pharmaceutical product may be substituted for the Licensed Product at the point of dispensing without any intervention by the prescribing physician in such country.

1.57 "**Governmental Authority**" means any arbitrator, court, judicial, legislative, administrative or Regulatory Authority, commission, department, board, bureau or body, or other government authority or instrumentality or any person or entity exercising executive, legislative, judicial, regulatory or administrative functions of or pertaining to government, whether foreign or domestic, whether federal, state, provincial, municipal, or other. For clarity, Governmental Authorities include all Regulatory Authorities.

1.58 "**ICH**" means the International Conference on Harmonization.

1.59 "**IDA**" means iron deficiency anemia.

1.60 "**Improvement**" means any process, method, composition of matter, article of manufacture, discovery, or finding that is conceived or reduced to practice (whether or not patentable) relating to, arising from the use of, or including the Licensed Product or its Exploitation.

1.61 "**Incremental Royalties**" has the meaning set forth in Section 5.1.2 (Incremental Royalties).

1.62 "**Indemnified Party**" has the meaning set forth in Section 9.3 (Indemnification Procedure).

1.63 "**Indemnifying Party**" has the meaning set forth in Section 9.3 (Indemnification Procedure).

1.64 "**Infringement Claim**" has the meaning set forth in Section 6.7.1 (Infringement Claim).

1.65 "**Intellectual Property Rights**" means all rights in Know-How, Patent Rights, copyrights, Marks, design rights, database rights, domain names, moral rights, and any and all other intellectual property or proprietary rights (whether registered or unregistered and whether patentable or unpatentable) now known or hereafter recognized in any jurisdiction, and all applications and rights to apply for any of them, anywhere in the world.

1.66 "**Invalidation Proceeding**" has the meaning set forth in Section 6.7.4(a) (Initiation).

1.67 "**Joint Improvements**" means any Improvement that is invented, conceived, discovered, created, or otherwise developed during the Term in the performance of any activities under this Agreement jointly by at least one employee of Akebia or its Affiliate or any Third Party contractually required to assign or license such Improvement to Akebia and at least one employee of Licensee or its Affiliate or Third Party contractually required to assign such Improvement to Licensee.

1.68 "**Joint Patent Rights**" means all Patent Rights that cover or claim the Joint Improvements.

1.69 "**JSC**" has the meaning set forth in Section 3.1 (Formation and Purpose of the JSC).

1.70 "**Keryx**" has the meaning set forth in the Preamble.

1.71 "**Know-How**" means any proprietary records, chemical or biological materials, know-how, processes, techniques, show-how, design information, information, formulations, technology,

practices, trade secrets, inventions, methods, data (including animal data, raw data, clinical data, and quality control data) and results in any form whatsoever, whether patentable or unpatentable.

1.72 "**Know-How Transfer**" has the meaning set forth in Section 2.5.1 (Know-How Transfer By Akebia).

1.73 "**Knowledge**" means the actual knowledge, without any inquiry or investigation, of Akebia's officers as defined under Rule 16a-1(f) of the Securities Exchange Act of 1934 (or amendment thereto or replacement or successor law) as of the Effective Date.

1.74 "**Launch Countries**" has the meaning set forth in Section 4.4.1 (Launch Sequence).

1.75 "**Launch Sequence**" has the meaning set forth in Section 4.4.1 (Launch Sequence).

1.76 "**LCIA**" has the meaning set forth in Section 11.2.3 (Arbitration Procedure).

1.77 "**Licensee**" has the meaning set forth in the Preamble.

1.78 "**Licensee Cost Defense Action**" has the meaning set forth in 6.5.2 (Control and Cost).

1.79 "**Licensee Manufacturing Process**" has the meaning set forth in Section 4.6 (Licensee Manufacturing Process Development).

1.80 "**Licensed Product**" means Fexeric® (ferric citrate) (currently marketed by Akebia in the United States under the brand name Auryxia®), and any other preparation, formulation, or dosage form thereof that has ferric citrate as its sole active ingredient, including ferric citrate coordination complexes, but excluding any product that includes Fexeric® (ferric citrate), Auryxia®, or any other form of ferric citrate, in each case, together with any other active ingredient.

1.81 "**Licensee Defense Action**" has the meaning set forth in Section 6.6.1 (Rights to Defend).

1.82 "**Licensee Development Data**" means and includes all data relating to the Licensed Product and all chemistry, manufacturing, and control data relating to the Development and Manufacture of the Licensed Product, results of pre-clinical and clinical trials (including all Post-Approval Studies) and all other documentation containing or embodying any preclinical, clinical, chemistry, manufacturing, and control data relating to any Regulatory Submissions for the Licensed Product, in each case, that is generated by or on behalf of Licensee, or its agents, Affiliates, or Sublicensees during the Term.

1.83 "**Licensee Development Know-How**" means all information and materials, including discoveries, processes, instructions, formulas, data, inventions, knowhow and trade secrets, patentable or otherwise, in each case, that arise out of the Development, Manufacture, Commercialization, or other Exploitation by or on behalf of Licensee of the Licensed Product, including all biological, chemical, pharmacological, toxicological, pharmaceutical, physical, analytical, clinical, safety, manufacturing and quality control data and information related thereto, and all applications, registrations, licenses authorizations, documents, approvals, and correspondence relating to the Licensed Product, including correspondence submitted to Regulatory Authorities and all information and data contained in Regulatory Submissions. Licensee Development Know-How will also include all Licensee Improvements and Licensee Development Data.

1.84 "**Licensee Housemarks**" means (a) the corporate logos of Licensee, (b) the trademarks "Averoa," (c) any other trademark, trade name, or service mark (whether registered or unregistered) containing the word "Averoa," (d) any other corporate logo or trademark of Licensee used by Licensee to identify Licensee or its Affiliates, (e) all registrations, applications for registrations, and other intellectual property rights associated with any of the foregoing, and (f) all goodwill associated with any and all of the foregoing in clauses (a) through (e).

1.85 "**Licensee Improvements**" means any Improvements invented, conceived, discovered, created, or otherwise developed during the Term by or on behalf of Licensee (or its Affiliates or its Sublicensees) in the performance of activities under this Agreement.

1.86 "**Licensee Indemnitees**" has the meaning set forth in Section 9.2 (Indemnification by Akebia).

1.87 "**Licensee Patent Rights**" means any and all Patent Rights Controlled by Licensee or its Affiliates as of the Effective Date or during the Term that are directed to or otherwise pertain to the Licensed Product or its Manufacture or use, including those Patent Rights that cover or claim Licensee's interest in Improvements or any Licensee Development Know-How.

1.88 "**Licensee Technology**" means collectively, the Licensee Patent Rights and Licensee Development Know-How.

1.89 "**MAA**" has the meaning set forth in Section 1.95 (Marketing Authorization).

1.90 "**MA Holder**" means the entity that holds the marketing authorization for the Licensed Product in a given country.

1.91 "**Major Market Country**" means each of [**].

1.92 "**Manufacture**" or "**Manufacturing**" means to make, produce, manufacture, process, fill, finish, package, label, perform quality assurance testing, release, ship or store the Licensed Product or any component thereof. When used as a noun, "**Manufacture**" or "**Manufacturing**" means any and all activities involved in Manufacturing the Licensed Product or any component thereof.

1.93 "**Manufacturing Technology Transfer**" has the meaning set forth in Section 4.7.2.

1.94 "**Mark**" means any trademark, trade name, service mark, service name, product name, brand, domain name, trade dress, logo, slogan, or other indicia of origin or ownership, and (a) all registrations, applications for registrations, and other intellectual property rights associated with any of the foregoing, and (b) the goodwill associated with each of the foregoing.

1.95 "**Marketing Authorization**" means (a) a marketing authorization application filed with (i) the EMA under the centralized EMA filing procedure to gain approval to market a pharmaceutical or diagnostic product in the E.U. ("**MAA**"), or (ii) a Regulatory Authority in any E.U. country if the centralized EMA filing procedure is not used to gain approval to market a pharmaceutical or diagnostic product in the E.U., or (b) any other equivalent or related Regulatory Submissions filed in support of approval to market a pharmaceutical or diagnostic product in any country outside the E.U., and, in each case ((a) and (b)), including any amendments thereto, and supplemental applications.

1.96 "**Minimum Royalty**" has the meaning set forth in Section 5.1.3 (Minimum Royalties).

1.97 "**Net Sales**" with respect to any Licensed Product means the gross sales (*i.e.*, gross invoice prices) of such Licensed Product billed by Licensee or its Affiliates, as applicable, or their respective Sublicensees to Third Party customers (including Distributors) on all sales of the Licensed Product and exclusive of intercompany transfer or sales, less the following deductions from such gross sales:

(a) actual credited allowances to such Third Party customers for spoiled, damaged, outdated, recalled, or returned Licensed Product and for retroactive price reductions or billing corrections,

(b) the amounts of trade, cash discounts and rebates, to the extent such discounts and rebates were not deducted by Licensee or Akebia, as applicable, or their respective Sublicensees at the time of invoice in order to arrive at the gross invoice prices,

(c) all transportation, handling charges and freight insurance, sales taxes, excise taxes, use taxes, import/export duties paid or distribution fees paid to Third Parties, and

(d) invoiced amounts from a prior period that have not been collected and have been written off by Akebia or Licensee or its Sublicensee (as applicable), including bad debts, to the extent such amounts have not been previously deducted and do not exceed, in the aggregate, [**]% of Net Sale in the applicable period; *provided* that any such amounts that are written off will be added back in a subsequent period to the extent later collected; and

(e) all other reasonable and customary allowances and adjustments whether during the specific royalty period or not.

Subject to the above, Net Sales will be determined in accordance with the applicable Accounting Standards, consistently applied.

If Licensee or a Sublicensee receives [**] for the Licensed Product sold to a Third Party, then the Net Sales amount for such Licensed Product will be [**].

With respect to [**] of the Licensed Product, "Net Sales" will [**]; *provided* that, upon [**] will be [**].

1.98 "**Non-Breaching Party**" has the meaning set forth in Section 10.2 (Termination for Breach).

1.99 "**Non-Disclosure Agreement**" has the meaning set forth in Section 12.2 (Entire Agreement; Amendment).

1.100 "**Packaging and Labeling**" means primary, secondary, or tertiary packaging and labeling of the Licensed Product (in its commercial packaging presentation) for sale or use in the Territory, including the Approved Labeling and insertion of materials such as patient inserts, patient medication guides, and professional inserts and any other written, printed, or graphic materials accompanying the Licensed Product and any brand security or anti-counterfeiting measures included in the packaging elements for the Licensed Product considered to be part of the finished packaged Licensed Product, and all testing and release thereto.

1.101 "**[**]**" means [**].

1.102 "**[**] Agreement**" means that certain [**] Agreement, dated as of [**], by and between Akebia and [**].

1.103 "**[**] Patent Rights**" means any and all Akebia Patent Rights that are Controlled by Akebia pursuant to the [**] Agreement

1.104 "**[**] Royalty Term**" means on a country-by country basis, the period commencing on the date of First Commercial Sale of the first Licensed Product in such country and expiring upon the expiration of the last Valid Claim included in the [**] Patent Rights in such country.

1.105 "**Party**" or "**Parties**" has the meaning set forth in the Preamble.

1.106 "**Patent Rights**" means all rights, title and interests in and to (a) all national, regional, and international patents and patent applications filed in any country of the world including provisional patent applications and all supplementary protection certificates, (b) all patent applications filed either from such patents, patent applications, or provisional applications or from an application claiming priority from any of these, including any continuation, continuation-in part, divisional, provisional, converted provisionals and continued prosecution applications, or any substitute applications, (c) any patent issued with respect to or in the future issued from any such patent applications, including utility models, petty patents, and design patents and

certificates of invention, and (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, reexaminations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications.

1.107 "**Person**" means an individual, corporation, partnership, limited liability company, trust, business trust, association, joint stock company, joint venture, pool, syndicate, sole proprietorship, unincorporated organization, Governmental Authority or any other form of entity not specifically listed herein.

1.108 "**Pharmacovigilance Agreement**" has the meaning set forth in Section 4.11 (Pharmacovigilance).

1.109 "**Post-Approval Studies**" means any post-approval study as required by the EMA, including any post-authorization safety study and any pediatric clinical study, in each case, related to the Licensed Product conducted with the aim of identifying, characterizing, or quantifying a safety hazard, confirming the safety profile of the Licensed Product, or of measuring the effectiveness of risk management measures.

1.110 "**Product Marks**" means the Marks Controlled by Licensee relating to the Licensed Product.

1.111 "**Professional Requirements**" means (a) the codes and standards of the European Accreditation Council for Continuing Medical Education (EACCME) and the European Federation of Pharmaceutical Industries and Associations (EFPIA), (b) the codes of the Prescription Medicines Code of Practice Authority (PMCPA) and the Association of the British Pharmaceutical Industry (ABPI), and (c) all other accepted national and international pharmaceutical industry codes of practice in and for the relevant countries in the Territory, as any of the foregoing may be amended from time-to-time.

1.112 "**Quality Agreement**" has the meaning set forth in Section 4.9.6 (Quality Agreement).

1.113 "**Receiving Party**" has the meaning set forth in Section 7.1 (Definition).

1.114 "**Regulatory Approval**" means, with respect to the Licensed Product in any country or regulatory jurisdiction, any approval (including where required, Reimbursement Approvals), registration, license, or authorization that is required by the applicable Regulatory Authority to Manufacture and Commercialize such Licensed Product in such country or regulatory jurisdiction.

1.115 "**Regulatory Authority**" means, in a particular country or jurisdiction, any applicable Governmental Authority involved in granting Regulatory Approval in such country or jurisdiction, including (a) in the E.U., the EMA and any other applicable Governmental Authority in the countries in the E.U. having jurisdiction over the Licensed Product, and (b) in other countries, other analogous Governmental Authorities having jurisdiction over the Licensed Product.

1.116 "**Regulatory Submissions**" means all applications, filings, dossiers, and other documents submitted to a Regulatory Authority in support of Development, Manufacture, or Commercialization of the Licensed Product inside and outside of the Territory, including for the purpose of obtaining Regulatory Approval from that Regulatory Authority. Regulatory Submissions include all CTAs, Marketing Authorizations, and other Regulatory Approval applications and their equivalents inside and outside of the Territory.

1.117 "**Reimbursement Approval**" means an approval, agreement, determination, or other decision by the applicable Governmental Authority that establishes prices charged to end-users for biopharmaceutical products that the Licensed Product will be reimbursed by the Regulatory Authorities or other Governmental Authorities in the European Economic Area and European Union.

1.118 "**Representatives**" has the meaning set forth in Section 7.2 (Obligations).

1.119 "**Royalties**" has the meaning set forth in Section 5.1.2 (Incremental Royalties).

1.120 "**Royalty Term**" means, on a country-by country basis, the period commencing on the date of First Commercial Sale of the first Licensed Product in such country and expiring upon the latest of: (a) 10 years following the date of First Commercial Sale of the Licensed Product in such country; (b) expiration of the last Valid Claim of the Akebia Patent Rights and Joint Patent Rights in such country; or (c) the date of expiration of the data, regulatory, or marketing exclusivity period conferred by the applicable Regulatory Authority in such country with respect to the Licensed Product.

1.121 "**Subcontractor**" has the meaning set forth in Section 2.3 (Licensee's Right to Subcontract).

1.122 "**Sublicensee**" has the meaning set forth in Section 2.2 (Licensee's Right to Grant Sublicenses).

1.123 "**Supply Agreement**" has the meaning set forth in Section 4.9 (Supply Agreement).

1.124 "**Supply Price**" has the meaning set forth in Section 4.9.1 (Supply Price).

1.125 "**Supply Termination Right**" has the meaning set forth in Section 4.9.2 (Supply Termination Right).

1.126 "**Target Indication**" means the use of the Licensed Product for the treatment of [**] in adult CKD patients [**].

1.127 "**Term**" has the meaning set forth in Section 10.1 (Term).

1.128 "**Territory**" means the European Economic Area, Turkey, Switzerland, and the United Kingdom.

1.129 "**Third Party**" means any Person other than a Party or an Affiliate of a Party.

1.130 "**Trademark License**" has the meaning set forth in Section 4.10.3 (Trademark License).

1.131 "**Valid Claim**" means, with respect to a particular country or region, a claim in any: (a) issued and unexpired patent that has not been permanently revoked or declared unenforceable or invalid by an unreversed and unappealable or unreversed and unappealed decision of a court or other appropriate body of competent jurisdiction in such country or region and that has not been abandoned, disclaimed, denied, or admitted to be invalid or unenforceable through reissue, re-examination, disclaimer, or otherwise; or (b) a claim of a pending patent application that has not been cancelled, withdrawn, abandoned, or finally disallowed without the possibility of appeal or refiling of such application and has not been pending for more than [**] from the first substantive action on the merits in such country or region; *provided* that, if a claim ceases to be a Valid Claim by reason of foregoing subclause (b), then such claim would again be deemed a Valid Claim in the event such claim subsequently issues prior to the end of the then-current Royalty Term in such country or region.

1.132 "**Withholding Party**" has the meaning set forth in Section 5.4 (Taxes).

1.133 "**Year 1**" has the meaning set forth in Section 5.1.3 (Minimum Royalties).

1.134 "**Year 2**" has the meaning set forth in Section 5.1.3 (Minimum Royalties).

1.135 "**Year 3**" has the meaning set forth in Section 5.1.3 (Minimum Royalties).

2. LICENSE GRANTS

2.1. License Grants to Licensee.

2.1.1. **Development and Commercialization License**. Subject to the terms and conditions of this Agreement (including Section 2.6 (Retained Rights)), Akebia hereby grants to Licensee and its Affiliates a sublicensable (subject to Section 2.2 (Licensee's Right to Grant Sublicenses)), royalty-bearing right and license under the Akebia Technology to Develop (in accordance with the Development Plan) and Commercialize (in accordance with the Commercialization Plan) the Licensed Product in the Field in the Territory during the Term. The foregoing license will be co-exclusive with Akebia in the Field in the Territory during the Term with respect to Development of the Licensed Product, and exclusive in the Field in the Territory during the Term with respect to Commercialization of the Licensed Product.

2.1.2. **Packaging License**. Subject to the terms and conditions of this Agreement (including Section 2.6 (Retained Rights)), Akebia hereby grants to Licensee a sublicensable (subject to Section 2.2 (Licensee's Right to Grant Sublicenses)), royalty-bearing non-exclusive right and license under the Akebia Technology to package the Licensed Product in the Field in the Territory during the Term in accordance with the Approved Labeling.

2.2. Licensee's Right to Grant Sublicenses. Licensee and its Affiliates may sublicense the rights granted to it by Akebia under the license granted in Section 2.1 (License Grants to Licensee), upon Akebia's prior written approval (such approval not to be unreasonably withheld) (a) to any Subcontractor that requires a sublicense of the rights granted to Licensee under Section 2.1 (License Grants to Licensee) or (b) to any other Third Party (each, a "**Sublicensee**"). Any and all sublicenses will be in writing and will be subject to the following requirements, and any sublicense granted hereunder that is inconsistent with this Section 2.2 (Licensee's Right to Grant Sublicenses) will be null and void. If Licensee requests in writing Akebia's written approval to any proposed Sublicensee pursuant to this Section 2.2 (Licensee's Right to Grant Sublicenses), then Akebia will use good faith efforts to provide a written response to Licensee within [**] of Akebia's receipt of such written request.

2.2.1 **Sublicensing Terms**. All sublicenses will be subject to and consistent with the terms and conditions of this Agreement and will: (a) require each Sublicensee and Affiliate to comply with the applicable terms and conditions of this Agreement (including the Royalty reporting obligations set forth under Section 4.4.2 (Progress Reports), Section 5.1.5 (Flash Reports), and Section 5.1.6 (Royalty Reports and Records)) and the record keeping and audit requirements set forth under Section 5.5 (Accounting; Audit), (b) include Akebia as an intended third party beneficiary under the sublicense with the right to enforce the applicable terms of such sublicense, (c) preclude the granting of further sublicenses, and (d) include a sublicensable license back to Licensee of all Intellectual Property Rights made or generated by the Sublicensee in the performance of activities under the applicable sublicense agreement (such that Licensee Controls such Intellectual Property Rights for the purposes of this Agreement).

2.2.2 **Responsibility of Licensee**. Licensee will remain responsible and liable for the performance of all Sublicensees and Affiliates under their sublicensed rights to the same extent as if such activities were conducted by Licensee and any breach of this Agreement by a Sublicensee or Affiliate of Licensee will be deemed a breach by Licensee hereunder. In no event will any sublicense relieve Licensee of any of its obligations under this Agreement.

2.2.3 **Copies of Sublicenses**. Licensee will furnish to Akebia a true and complete copy of each agreement with a Sublicensee or an Affiliate and each amendment thereto no later than [**] after the execution of such sublicense or amendment.

2.3. Licensee's Right to Subcontract. In performing its Development activities under this Agreement, Licensee may engage any consultant, subcontractor, Distributor, co-promotion partner, or other vendor to conduct Licensee's obligations thereunder or hereunder (each, a "**Subcontractor**"), subject to the terms of Section 2.2 (Licensee's Right to Grant Sublicenses), which will apply to any Subcontractor that requires a sublicense of the rights granted to Licensee under Section 2.1 (License Grants to Licensee); *provided* that (a) Licensee remains responsible for (i) the management of its Subcontractors, (ii) fulfillment by its Subcontractors of all obligations set forth under this Agreement as if the Subcontractor were a party hereto, and (iii) any uncured breach by Subcontractor of any obligation of Licensee under this Agreement, and (b) Licensee will terminate promptly any Subcontractor, and will give Akebia notice of such termination, in the case of any breach of this Agreement by a Subcontractor. Without limitation, such contracts entered into with Subcontractors will contain provisions, including those relating to Intellectual Property Rights, confidentiality, and non-use, in each case, that are consistent with, and no less restrictive than, those set forth in this Agreement. The engagement of any Subcontractor in compliance with this Section 2.3 (Licensee's Right to Subcontract) will not relieve Licensee of its obligations under this Agreement.

2.4. License Grant to Akebia. Subject to the terms and conditions of this Agreement, Licensee hereby grants to Akebia a non-exclusive, worldwide, royalty-free, fully paid-up, perpetual, irrevocable, sublicensable (through multiple tiers) right and license under all Licensee Technology to Develop, Manufacture, Commercialize, and otherwise Exploit the Licensed Product.

2.5. Know-How Transfer.

2.5.1. **By Akebia**. Within a [**] period from the Effective Date, to the extent not previously provided to Licensee, Akebia will provide and transfer to Licensee copies of Akebia Know-How that exists on the Effective Date and that is necessary, in Akebia's reasonable discretion, for Licensee to perform its obligations under this Agreement (the "**Know-How Transfer**"). Akebia may make such Akebia Know-How available in such reasonable form as Akebia determines. Notwithstanding any provision to the contrary set forth in this Agreement, the Know-How Transfer will not include any Akebia Pediatric Data, unless and until the Parties agree as to the terms of a license to be granted to Licensee with respect to such Akebia Pediatric Data and an appropriate cost sharing arrangement, in each case, as set forth in Section 4.3.2 (Pediatric Investigation Plan).

2.5.2. **By Licensee**. In addition, prior to each meeting of the JSC, Licensee will disclose to Akebia all Licensee Development Data and Licensee Development Know-How, in each case, not previously disclosed to Akebia.

2.6 Retained Rights. Any rights of Akebia not expressly granted to Licensee under the provisions of this Agreement will be retained by Akebia (and may be exercised by Akebia itself or through its Affiliates or Third Parties in its sole discretion), including, in each case, (a) the right to Develop, Manufacture, Commercialize, or otherwise Exploit the Licensed Product in any country outside of the Territory, including under the brand name Auryxia® in the United States, (b) the right to Develop and Manufacture the Licensed Product in the Territory, (c) the right to Develop, Manufacture, Commercialize, or otherwise Exploit in any Field and in any country products and technologies practicing the Akebia Technology, other than the Licensed Product, (d) the right to exploit or license the Akebia Technology other than for the purposes of Exploiting any Licensed Product, and (e) the right to perform its obligations and exercise its rights under this Agreement. Licensee will not practice or sublicense the Akebia Technology or Exploit the Licensed Product, in each case, except as expressly permitted under this Agreement. In addition, Akebia expressly

retains the right to perform or exercise, or have performed or exercised by an Affiliate, Akebia's obligations and rights under this Agreement.

2.7 No Additional Rights; Compliance with [**] License. Nothing in this Agreement will be construed to confer any rights upon Licensee by implication, estoppel, or otherwise as to any active pharmaceutical ingredients, molecules, compounds, products, technology, or Intellectual Property Rights of Akebia other than the rights under the Akebia Technology expressly granted herein. Notwithstanding any provision to the contrary set forth in this Agreement, the Parties acknowledge that the rights and license granted to Licensee hereunder are subject to Akebia's rights and license under the [**] Agreement, and nothing in this Agreement will be construed to grant to Licensee any rights beyond those that Akebia has the right to grant to Licensee pursuant to the [**] Agreement. All rights, title, and interests not specifically and expressly granted by Akebia hereunder are hereby reserved.

3. GOVERNANCE

3.1. Formation and Purpose of the JSC. The Joint Steering Committee ("**JSC**") will coordinate and monitor the Development, Manufacturing, and Commercialization of the Licensed Product in the Field in the Territory in accordance with this Section 3.1 (Formation and purpose of the JSC) and will have the responsibilities set forth herein. The JSC may establish a charter that will not be binding on the Parties and that will include details regarding the operation of the JSC consistent with this Article 3 (Governance). The JSC will dissolve upon the expiration of the Term.

3.2. Membership. Each Party will designate up to [**] representatives from appropriate functional areas with appropriate knowledge, expertise, and decision-making authority to serve as members of the JSC. Each Party may replace its JSC representatives at any time upon written notice to the other Party. Licensee will designate one of its JSC members to serve as chairperson. The chairperson or his or her designee, in collaboration with the Alliance Managers, will be responsible for calling meetings, preparing, and circulating an agenda in advance of each meeting, and preparing and issuing minutes of each meeting within [**] thereafter. Such minutes will not be finalized until all JSC members have had an adequate opportunity to review and confirm the accuracy of such minutes.

3.3. Meetings. The JSC will hold meetings at such times as it elects to do so, but in no event will such meetings be held less frequently than [**], unless otherwise agreed by the Parties. The JSC will meet alternatively at Licensee's facilities in Europe and Akebia's facilities in Massachusetts, or at such locations as the Parties may otherwise agree. Meetings of the JSC may be held by audio or video teleconference at the request of either Party. The Alliance Manager of each Party will attend each meeting of the JSC as a non-voting participant. Each Party will be responsible for all of its own expenses of participating in any JSC meeting.

3.4. Specific Responsibilities of the JSC. The responsibilities of the JSC will be to:

3.4.1. manage the overall strategic alignment between the Parties under this Agreement and maintain the relationship between the Parties;

3.4.2. [**] whether to establish, and so establish, subcommittees and delegate specifically-defined duties to such subcommittees on an "as needed" basis to oversee particular projects or activities hereunder;

3.4.3. meet regularly to conduct the responsibilities set forth in this Agreement, as described in Section 3.3 (Meetings);

3.4.4. [**] regulatory activities and strategy for obtaining and maintaining all Regulatory Approvals and Reimbursement Approvals, as described in Section 4.2 (Regulatory);

3.4.5. [**] whether to approve the Development Plan, and all amendments or updates thereto, as described in Section 4.3.1 (Development Responsibilities; Development Plan) and [**]

any Additional Development of the Licensed Product proposed by either Party as described in Section 4.3.4 (Additional Development);

3.4.6. [**] any updates or modifications to the Target Indication as described in Section 4.3.5 (Target Indication);

3.4.7. [**] any amendments to the Launch Sequence to be prepared by Licensee, subject to and as described in Section 4.4.1 (Launch Sequence);

3.4.8. [**] the Commercialization Plan or any amendments thereto, as described in Section 4.4.3 (Commercialization Plan);

3.4.9. [**] the Manufacture and supply of the Licensed Product for the Territory, pursuant, if applicable, to the Supply Agreement;

3.4.10. [**] whether to approve any Marks other than the Licensee Housemarks and the Product Marks to be used by Licensee in the Commercialization of the Licensed Product in the Territory in accordance with Section 4.10.2 (Ownership; Branding);

3.4.11. [**] any required modifications to the Licensed Products to avoid infringement of any Patent Rights owned or controlled by a Third Party, as described in Section 6.7.3 (Responsibility for Third Party Licenses); and

3.4.12. perform such other functions as appropriate to further the purposes of this Agreement as determined by the Parties.

3.5 Additional Participants. At the request of either Party, other employees of such Party or any of its Affiliates involved in the Development, Manufacturing, or Commercialization of the Licensed Product may attend meetings of the JSC as non-voting participants. In addition, with the consent of each Party, consultants, representatives, or advisors involved in the same activities may attend meetings of the JSC as non-voting observers; *provided* that such Third Party participants and observers are under written obligations of confidentiality and non-use applicable to the Confidential Information of each Party that are at least as stringent as those set forth in Article 7 (Confidentiality).

3.6 Decision-Making and Committee Dispute Resolution.

3.6.1 **Voting; Consensus**. With respect to decisions of the JSC, the representatives of each Party will have collectively one vote on behalf of such Party. For each meeting of the JSC, at least [**] representatives of each Party will constitute a quorum. Action on any matter may be taken at a meeting by teleconference, videoconference, or by written agreement. The JSC will attempt to resolve any and all disputes before it for decision by consensus.

3.6.2 **Escalation to Executive Officers**. If the JSC is unable to reach consensus with respect to a dispute for a period in excess of [**], then the dispute will be submitted to the Executive Officers of the Parties, or their designees (any such designee to be a senior member of the designating Executive Officer's management team), for resolution in accordance with Section 11.1 (Executive Officers; Disputes).

3.6.3 **Final Decision-Making Authority**. If the Executive Officers of the Parties are not able to agree on the resolution of any issue referred to them pursuant to Section 3.6.2 (Escalation to Executive Officers) within [**] after such issue has been referred to them, then the matter will be decided as follows: (a) any dispute relating to (i) [**], (ii) [**], and (iii) [**], in each case ((i) – (iii)), will be determined by the Executive Officer of

[**]; (b) any dispute relating to (i) [**], (ii) [**], or (iii) [**], in each case ((i) – (iii)), will be determined by the Executive Officer of [**]; and (c) neither Party will have final decision-making authority with respect to any other dispute and the *status quo* will persist (or, if applicable, no decision will be implemented) with respect to such matter unless and until the Parties reach agreement thereon.

3.7 Limitations on Decision Making. Notwithstanding any provision to the contrary set forth in this Agreement, without the other Party's prior written consent, no decision of the JSC or a Party's Executive Officer (in the exercise of a Party's final decision making authority on any such matters), in each case, may (a) result in a material increase in the other Party's obligations, costs or expenses under this Agreement, (b) require the other Party to take any action that such other Party reasonably believes would (i) require such other Party to violate any Applicable Law, the requirements of any Regulatory Authority, or any agreement with any Third Party entered into by such other Party or (ii) require such other Party to infringe or misappropriate any intellectual property rights of any Third Party, (c) impose any obligation on either Party that would be in violation of such Party's written standard operating procedures, written business policies, or written compliance policies or procedures, (d) conflict with this Agreement, the Quality Agreement to be entered into by the Parties or the Pharmacovigilance Agreement or any other agreement between the Parties related to the subject matter set forth herein, (e) have a material adverse effect on the Development or Commercialization of Licensed Products outside the Territory, or (f) modify the terms of this Agreement.

3.8 Alliance Managers. Each of the Parties will appoint a single individual to manage Development and Commercialization obligations between the Parties (each, an "**Alliance Manager**"). The role of the Alliance Manager is to act as a single point of contact between the Parties to ensure a successful relationship under this Agreement. The Alliance Managers will attend all JSC meetings. Alliance Managers will be non-voting participants in all JSC meetings. Each Party will designate its initial Alliance Manager promptly after the Effective Date and each Party may change its designated Alliance Manager at any time upon written notice to the other Party.

4. DEVELOPMENT, MANUFACTURING, REGULATORY, AND COMMERCIALIZATION

4.1. General Responsibilities. Except as expressly provided herein or expressly set forth in this Agreement, the Supply Agreement, or as otherwise agreed by the Parties in writing, as between the Parties with respect to the Licensed Product in Field in the Territory, Licensee will be solely responsible for managing and conducting all Development and Commercialization activities, and the Parties will be responsible for managing and conducting all Manufacturing activities as described in Section 4.6 (Licensee Manufacturing Process Development), Section 4.7 (Licensee Manufacturing Process Completion and Transfer), Section 4.8 (Licensee Manufacturing Process Completion – No Minimum Royalties) and Section 4.9 (Supply Agreement). Licensee will be responsible for all costs and expenses related to the Development and Commercialization of the Licensed Product in the Territory after the Effective Date.

4.2. Regulatory. Licensee or one of its Affiliates will be responsible for all regulatory activities and interactions with Regulatory Authorities in the Territory leading up to and including obtaining (to the extent not already obtained) and thereafter maintaining, all Regulatory Approvals and any Reimbursement Approvals, as applicable, for the Licensed Product in the Territory in Licensee's or its Affiliate's own name.

4.2.1 **Letter of Authorization**. Promptly following the Effective Date, Akebia will provide Licensee with a letter of authorization that grants to Licensee those rights and permissions required to: (a) prepare and submit a request for scientific advice from the EMA and (b) under confidentiality agreements that contain restrictions no less stringent than those set forth in this Agreement, contact CMOs to evaluate the costs and expenses

associated with performing the final steps in the Manufacture of the Licensed Product in Finished Form.

4.2.2 **Regulatory Submissions.** From and after the Effective Date, Licensee will be responsible, at its sole cost and expense, for preparing, filing, and submitting, directly or through its Affiliates and permitted Sublicensees, (a) all Regulatory Submissions in all countries and jurisdictions in the Territory, and each material amendment or update thereto, in its name; and (b) briefing packages for meetings with Regulatory Authorities relating to Regulatory Submissions in each such country and jurisdiction in the Territory for such Licensed Product. Akebia will reasonably cooperate in a timely manner (*i.e.*, in accordance with the timelines imposed by the Regulatory Authorities) with Licensee in obtaining any Regulatory Approvals and Reimbursement Approvals, as applicable, for the Licensed Product in the Territory by providing access to Regulatory Approvals, Regulatory Submissions, clinical data, and other data, information, and documentation for the Licensed Product that is relevant to obtaining or maintaining Regulatory Approval for the Licensed Product in the Field in the Territory, to the extent Controlled by Akebia. In the event Akebia determines in its sole discretion that Licensee's request for cooperation by Akebia is not reasonable, then Licensee and Akebia will meet and discuss regarding such requested cooperation. The Parties acknowledge and agree that Akebia may determine in its sole discretion whether any requested cooperation by Licensee is reasonable, and that Akebia has no obligation to provide any assistance to Licensee under this Section 4.2.2 (Regulatory Submissions). If Akebia provides any such requested cooperation to Licensee pursuant to this Section 4.2.2 (Regulatory Submissions), then Akebia will provide to Averoa a good faith calculation of the costs and expenses incurred by Akebia in connection with such cooperation, and the Parties will discuss in good faith whether Averoa will reimburse Akebia for such costs and expenses. For clarity, Akebia will not be required to expend any resources, whether internal or external, in connection with the Development of, including obtaining or maintaining Regulatory Approval for, the Licensed Product unless expressly agreed by Akebia in writing. Licensee will provide to Akebia for review and comment drafts of all Regulatory Submissions in the Territory for the Licensed Product. Licensee will consider in good faith and, where appropriate, incorporate any such comments received from Akebia on such Regulatory Submissions. In addition, Licensee will notify Akebia of any Regulatory Submissions for the Licensed Product and any comments or other correspondences related thereto submitted to or received from any Regulatory Authority in the Territory and will provide Akebia with copies thereof as soon as reasonably practicable, but in all events within [**] after submission or receipt thereof (or such longer time period as may be necessary to obtain translations thereof). If any such Regulatory Submission, comment, or correspondence is not in English, then Licensee will provide Akebia with a certified English translation as soon as practicable after receipt of such Regulatory Submission, comment, or correspondence, at Licensee's sole cost and expense. Akebia will have the right, but not the obligation, to review and comment on all such Regulatory Submissions, and Licensee will consider in good faith and incorporate such comments where appropriate.

4.2.3 **Meetings with Regulatory Authorities**. Licensee will provide Akebia with notice of any meeting or discussion with any Regulatory Authority in the Territory related to the Licensed Product no later than [**] after receiving notice thereof or in any event with as much advanced notice as is possible prior to such meeting or discussion if Licensee receives notice thereof less than [**] in advance of the applicable meeting or discussion. Akebia or its designee will have the right, but not the obligation, to have up to [**] representatives attend and participate in any such meeting or discussion unless prohibited or restricted by Applicable Law or Regulatory Authority. Akebia will also have the right to attend any meetings of Licensee to prepare for such meeting or discussion with Regulatory Authorities in the Territory (and Licensee will notify Akebia of all such preparatory meetings sufficiently in advance thereof). If Akebia elects not to attend such meeting or discussion, then Licensee will provide to Akebia a written summary thereof in English promptly following such meeting or discussion. Akebia's attendance of and

participation in any meetings or discussions with Regulatory Authorities pursuant to this Section 4.2.3 (Meetings with Regulatory Authorities) will be at its sole cost and expense.

4.2.4 **Right of Reference**. Each Party will grant, and hereby does grant, to the other Party and its Affiliates, licensees, and Sublicensees a right of reference to all Regulatory Submissions pertaining to the Licensed Product in the Field submitted by or on behalf of such Party or its Affiliates. Licensee will grant, and hereby does grant, to Akebia and its Affiliates, licensees (including [**]), and Sublicensees a right of reference to all Licensee Development Data developed in Licensee's activities under this Agreement. Licensee and its Affiliates and Sublicensees may use such right of reference to Akebia's Regulatory Submissions solely for the purpose of seeking, obtaining, supporting, and maintaining Regulatory Approvals and any Reimbursement Approvals, as applicable, for the Licensed Product in the Field in the Territory. Akebia and its Affiliates, licensees, and Sublicensees may use such right of reference to Licensee's Regulatory Submissions solely for the purpose of seeking, obtaining, supporting, and maintaining Regulatory Approval and any Reimbursement Approvals of the Licensed Product outside of the Territory. Each Party will bear its own costs and expenses associated with providing the other Party with the right of reference pursuant to this Section 4.2.4 (Right of Reference). Each Party will take such actions as may be reasonably requested by the other Party to give effect to the intent of this Section 4.2.4 (Right of Reference) and to give the other Party the benefit of the granting Party's Regulatory Submissions in the other Party's territory as provided herein. Such actions may include providing to the other Party copies of correspondence and communications received from the applicable Regulatory Authorities related to such Party's application for Regulatory Approval of the Licensed Products in the Territory or outside of the Territory, as applicable.

4.3 Development in the Territory.

4.3.1. **Development Responsibilities; Development Plan**. Licensee will be responsible for, and will conduct, any Development of the Licensed Product that is necessary to obtain and maintain Regulatory Approval of the Licensed Product in the Target Indication in the Territory, including the conduct of all Post-Approval Studies. All such Development to be conducted by or on behalf of Licensee, including any non-clinical, pre-clinical, and clinical Development of the Licensed Product, whether for the Target Indication or any other indication, will be in accordance with and governed by a development plan submitted by Licensee to the JSC (the "**Development Plan**"). Licensee will submit a draft of the initial Development Plan to the JSC following the validation of the Target Indication by a Regulatory Authority. Licensee will not conduct any Development activities for the Licensed Product other than as set forth in the Development Plan. If Licensee wishes to make a change to the Development Plan, including to include Additional Development activities, then Licensee will submit the proposed updated to the Development Plan to the JSC. The JSC will review, discuss, and determine whether to approve any such proposed update. Each such update to the Development Plan will become effective and will supersede the previous iteration of the Development Plan upon approval thereof by the JSC.

4.3.2. **Pediatric Investigation Plan**. The Parties will discuss in good faith whether, based on the pediatric investigation plan approved by the EMA for the Licensed Product in the Target Indication, Licensee will be able to use, in the Territory, the Akebia Pediatric Data. If the Parties agree that Licensee will be able to use such Akebia Pediatric Data, then the Parties will use good faith efforts to negotiate and agree upon (a) a collaborative arrangement pursuant to which Akebia would grant to Licensee a license to use and rely on such Akebia Pediatric Data, as well as any considerations or amendments to such clinical trials that are part of Akebia's pediatric investigation plan that might be made such that Licensee would be able to use in its Regulatory Submissions for the Licensed Product in the Territory the data generated from the performance thereof; *provided* that Akebia will not be required to modify the protocol of any previously initiated clinical trials that may be part of Akebia's pediatric investigation plan, and (b) a cost sharing

arrangement between the Parties with respect to the costs and expenses associated with the performance of those clinical trials described in clause (a) of this Section 4.3.2 (Pediatric Investigation Plan). For clarity, Licensee's costs incurred in connection with any such pediatric investigation plan will not exceed [**] percent ([**]%) of the total costs of the pediatric clinical trials, up to a maximum amount of [**] United States Dollars, VAT excluded.

4.3.3. **Development Diligence Obligations**. Licensee will be responsible for and will use Commercially Reasonable Efforts (a) to conduct all Development of the Licensed Product that is necessary to obtain or maintain Regulatory Approval and Reimbursement Approval, where applicable, for the Licensed Product in the Territory in the Target Indication and (b) to file for Regulatory Approval and Reimbursement Approval for the Licensed Product in the Territory in the Target Indication.

4.3.4. **Additional Development**. If Licensee desires to conduct any Development of the Licensed Product in the Territory for any indication other than the Target Indication ("**Additional Development**"), then Licensee will present a proposal to the JSC to review, discuss, and determine whether to approve pursuant to Section 3.4 (Specific Responsibilities of the JSC), including a synopsis of the Development activities related to such Additional Development, the potential role of Akebia with respect to such Additional Development (*provided* that Akebia has no obligation to participate in any Additional Development), the timeline for the performance of such Additional Development, the estimated costs and expenses associated with such Additional Development, and a proposed amendment to the then-current Development Plan to include Additional Development activities. Licensee will not conduct any Additional Development without Akebia's prior written consent. In the event Akebia conducts any Additional Development in the Territory, it will provide notice thereof to the JSC and the JSC may review and discuss such Additional Development and related activities.

4.3.5. **Target Indication**. Licensee may propose to modify the Target Indication from time to time and will submit all such proposals to the JSC to review and discuss. Following review of and discussion at the JSC of any such proposals, the Target Indication will be deemed updated or modified upon written notice from Licensee to the JSC of such update or modification.

4.3.6. **Development Costs**. Except as otherwise set forth in this Agreement, Licensee will be responsible for all costs and expenses related to the Development of the Licensed Product in the Territory after the Effective Date.

4.3.7. **Licensee Development Data**. Licensee will grant, and hereby does grant, to Akebia and its Affiliates, licensees (including [**]), and Sublicensees a right to use all Licensee Development Data developed in Licensee's activities under this Agreement. Licensee acknowledges and agrees that Akebia may provide the Licensee Development Data to [**] on a continuing basis. Each Party will take such actions as may be reasonably requested by the other Party to give effect to the intent of this Section 4.3.7 (Licensee Development Data).

4.4 Commercialization.

4.4.1. **Launch Sequence**. No later than [**] following Licensee's submission of the MAA for the Licensed Product to the EMA, Licensee will prepare and submit to the JSC for its review and discussion a list of those countries in the Territory in which Licensee intends to Commercialize the Licensed Product and timelines reflecting the target date of the First Commercial Sale (the "**Launch Sequence**", and the countries included in the Launch Sequence, the "**Launch Countries**"). Licensee will amend or update the Launch Sequence at least [**] thereafter, including updating such sequence so as to provide reasonable prior notice of the target date of the First Commercial Sale in any additional countries in the Territory not included in the initial Launch Sequence. Each amendment

and update to the Launch Sequence will be reviewed and discussed by the JSC pursuant to Section 3.4 (Specific Responsibilities of the JSC).

4.4.2. **Progress Reports**. No later than [**] after the end of each [**] during the Term, Licensee will provide to Akebia a written high-level summary of Licensee's or its Affiliates' or Sublicensees' progress and activities performed since the prior report, and planned for the upcoming [**], in each case, with respect to the Commercialization of the Licensed Product throughout the Territory.

4.4.3. **Commercialization Plan**. No later than [**] following Licensee's submission of the MAA dossier for the Licensed Product to the EMA, Licensee will prepare and submit to the JSC for its review and discussion a Commercialization Plan. Such Commercialization Plan will be a high-level strategic plan for Commercialization of the Licensed Product throughout the Territory, and will include overall pricing strategy, sales, and supply forecasts for the Licensed Product throughout the Territory and method for launch.

4.4.4. **Commercial Diligence Obligations**. During the Term, Licensee will use Commercially Reasonable Efforts to Commercialize the Licensed Product in the Field in each Country in the Territory for which Regulatory Approval has been obtained.

4.5 Breach of Diligence Obligations. Without limiting Akebia's rights under Section 10.2 (Termination for Breach), if at any time during the Term Akebia has a reasonable basis to believe that Licensee is in material breach of its obligations under Section 4.3.3 (Development Diligence Obligations) or Section 4.4.4 (Commercialization Diligence Obligations), then Akebia may so notify Licensee, specifying the basis for its belief, and, at Akebia's request, the appropriate representatives of each Party will meet within [**] after such notice to discuss in good faith Akebia's concerns, and Licensee's plans, with respect to Licensee's compliance with its obligations under Section 4.3.3 (Development Diligence Obligations) or Section 4.4.4 (Commercialization Diligence Obligations), as applicable to the notice so provided by Akebia.

4.6 Licensee Manufacturing Process Development. Licensee may develop a drug product manufacturing process for the Licensed Product (the "**Licensee Manufacturing Process**"), at its own cost and expense. If Licensee requires any technical assistance from Akebia in the development of the Licensee Manufacturing Process during the first [**] of the Term, then Akebia, upon written request of Licensee and agreement by the Parties, will provide reasonable cooperation and technical assistance to Averoa in such development. Such reasonable cooperation and assistance may include, at Akebia's discretion and agreement, (a) providing Drug Substance for use solely in connection with the development of the Licensee Manufacturing process (and not, for clarity, for commercialization purposes), in amounts to be determined by Akebia in its sole discretion, or (b) allocating Akebia employees to support the development of the Licensee Manufacturing Process. Upon Akebia's request, Licensee will reimburse Akebia for all costs incurred in connection with Akebia's assistance in developing the Licensee Manufacturing Process upon terms to be agreed by the Parties, such terms to be agreed upon prior to Akebia providing assistance.

4.7 Licensee Manufacturing Process Completion and Transfer. If Licensee successfully develops the Licensee Manufacturing Process pursuant to Section 4.6 (Licensee Manufacturing Process Development), then:

4.7.1 Upon Akebia's written request, Licensee will transfer to Akebia or its designees all analytical and manufacturing Know-How, including all data and documentation related thereto, related to the Licensee Manufacturing Process that is Controlled by Licensee or any of its Affiliates and is necessary or useful to enable Akebia to Manufacture Licensed Product using the Licensee Manufacturing Process;

4.7.2 Akebia will bear the costs and expenses related to the activities carried out in accordance with Section 4.7.1 (such activities, the "**Manufacturing Technology Transfer**"); and

4.7.3 Akebia will reimburse Licensee for all costs incurred in connection with Licensee's assistance in the Manufacturing Technology Transfer upon terms to be agreed by the Parties, which terms will be agreed by the Parties in writing prior to Licensee providing assistance.

4.8. Licensee Manufacturing Process Completion – No Minimum Royalties. Effective upon the date that Licensee completes development of the Licensee Manufacturing Process pursuant to Section 4.6 (Licensee Manufacturing Process Development), Licensee will no longer be obligated to pay the Minimum Royalties to Akebia set forth in Section 5.1.3 (Minimum Royalties). For clarity, nothing in this Section 4.8 (Licensee Manufacturing Process Completion – No Minimum Royalties) will affect the Licensee's obligation to pay to Akebia the Incremental Royalties, as described in Section 5.1.2 (Incremental Royalties).

4.9. Supply Agreement. Promptly following the Effective Date, the Parties will negotiate in good faith and execute a supply agreement consistent with the terms and conditions of this Agreement (the "**Supply Agreement**"), pursuant to which Akebia will supply Licensee or its designee with Licensed Product in brite stock for commercial use in the Territory in connection with this Agreement. The terms and conditions of the Supply Agreement will be reasonable and customary for agreements of this type, and will include the terms and conditions set forth in this Section 4.9 (Supply Agreement).

4.9.1 **Supply Price**. The Supply Agreement will provide that the supply price for the Licensed Product will be equal to its applicable [**] (the "**Supply Price**").

4.9.2 **Supply Termination Right**. The Supply Agreement will provide that Akebia may terminate the Supply Agreement for any reason upon 24 months' prior written notice to Averoa, which notice Akebia may provide to Licensee on or after January 1, 2024 (such right to terminate, "**Supply Termination Right**"); *provided* that if Akebia delivers such notice of termination of the Supply Agreement to Licensee prior to Licensee's submission of the MAA for the Licensed Product to the EMA or during the period in which the EMA is reviewing of such MAA submission, then the termination of the Supply Agreement will be effective on the date that is [**] following the earlier of (a) the EMA's decision regarding Licensee's MAA submission for the Licensed Product or (b) [**] after the date of the Licensee's MAA submission to the EMA.

4.9.3 **Supply Agreement Termination Consequences**. The Supply Agreement will provide that if Akebia exercises its Supply Termination Right, then:

(a) Effective upon the date of termination of the Supply Agreement, Licensee will no longer be obligated to pay any Minimum Royalties to Akebia pursuant to Section 5.1.3 (Minimum Royalties);

(b) Licensee will have the option to request in writing that Akebia assign to Licensee its then-existing supply agreements with Third Party manufacturers relating solely to the Licensed Product, and Akebia will use reasonable efforts to assign such agreements to Licensee;

(c) If Akebia assigns to Licensee its then-existing supply agreements with Third Party manufacturers relating solely to Licensed Product to Licensee in accordance with Section 4.9.3(b), then Licensee will not be obligated to pay to Akebia any Incremental Royalties owed pursuant to Section 5.1.2(a) or Section 5.1.2(b) for [**]; and

(d) Licensee may defer payment of the Incremental Royalties due during the [**] in which the assignment of Akebia's supply agreements occurs pursuant to Section 4.9.3(b) (the "**Deferred Royalties**") until [**], on which date such Deferred Royalties will become due and payable. For clarity, nothing in Section 4.9.3(c) or this Section 4.9.3(d) will affect the Licensee's obligation to pay to Akebia the Base Royalties.

4.9.4 **Exclusive Supplier**. Licensee will purchase exclusively from Akebia all of Licensee's and its Affiliates' and Sublicensees' requirements for the Licensed Product, to the extent Akebia is able to manufacture and supply to Licensee and its Affiliates and Sublicensees the quantities of Licensed Product as set forth under the Supply Agreement.

4.9.5 **Additional Formulations**. If additional formulations of the Licensed Product are required for use in the Field in the Territory (such as for pediatric use), then the Parties will discuss such requirements through the JSC. If Akebia agrees to participate in the Development and Manufacture of such additional formulations, then the Parties will discuss in good faith and agree upon the applicable process and respective responsibilities of each Party in connection with such activities and an appropriate cost sharing arrangement between the Parties for the costs and expenses to be incurred in the performance of such activities.

4.9.6 **Quality Agreement**. As soon as reasonably practicable after the Effective Date, the Parties will negotiate in good faith and execute a related quality agreement consistent with the terms and conditions of this Agreement and the Supply Agreement, governing the supply of Licensed Product under this Agreement (the "**Quality Agreement**").

4.9.7 **Licensee Responsibilities**. Licensee will be responsible, at its cost and expense, for converting brite stock of Licensed Product supplied by Akebia into Finished Form, including supplying all Packaging and Labeling for use of the Licensed Product in the Territory, and serialization and release of the Licensed Product in Finished Form.

4.10 Trademarks.

4.10.1 **Housemarks**. Licensee will be responsible for the registration and maintenance of the Product Marks and the Licensee Housemarks throughout the Territory, as well as all expenses associated therewith. Akebia will be responsible for the registration and maintenance of the Akebia Housemarks throughout the Territory, as well as all expenses associated therewith.

4.10.2 **Ownership; Branding**. Licensee will develop and prosecute, when appropriate following the Effective Date, at least [**] in the Territory. Licensee will be the sole and exclusive owner of all Product Marks, including all trademark registrations and applications therefor and all goodwill associated therewith. To the extent Akebia acquires any rights, title, or interests in and to any Product Mark (including any trademark registration or application therefor or goodwill associated with any Product Mark), Akebia will, and hereby does, assign the same to Licensee. Licensee will use the Product Marks as the primary and most prominent trademark and logo associated with the Licensed Product throughout the Territory. Licensee may use the Licensee Housemarks and, subject to Section 4.10.3 (Trademark License), the Akebia Housemarks on the packaging of the Licensed Product. The Parties, acting through the JSC, will agree upon any other Marks to be used in the Commercialization of the Licensed Product in the Territory. Upon the termination or expiration of this Agreement, Licensee agrees to, and hereby does, (a) assign all rights, title, and interest in and to all Product Marks (including any trademark registration or application therefor), and all goodwill associated with all Product Marks and (b) grant to Akebia, during the transition period following the effective date of termination or expiration of this Agreement and ending on that date that Akebia is designated as the MA Holder of the Licensed Product in the Territory, a non-exclusive, royalty-free, perpetual, irrevocable, fully-paid up license under the Licensee Housemarks to Exploit the Licensed Product in the Territory. To the extent following

such termination or expiration Licensee acquires any rights, title, or interests in and to any Product Mark (including any trademark registration or application therefor or goodwill associated with any Product Mark) during such transition period, Licensee will, and hereby does, assign the same to Akebia.

4.10.3 **Trademark License**. Subject to the terms and conditions of this Agreement (including Section 2.6 (Retained Rights)), Akebia hereby grants and agrees to grant to Licensee a non-exclusive, sublicensable (subject to Section 2.2 (Licensee's Right to Grant Sublicenses)), royalty-free license to use the Akebia Housemarks to the extent required for the Approved Labeling for the Licensed Product or requested by Akebia and subject to Applicable Law, solely in connection with the Commercialization of the Licensed Product in the Territory in accordance with to this Agreement (the "**Trademark License**"). All goodwill arising from Licensee's use of the Akebia Housemarks in the Territory will inure to the benefit of Akebia.

4.10.4 **Quality Control**. As a condition of the Trademark License, Licensee agrees that it and its Affiliates and Sublicensees will: (a) ensure that all Licensed Products that are sold bearing the Akebia Housemarks are of a high quality consistent with industry standards for global pharmaceutical and biologic therapeutic products; (b) ensure that each use of the Akebia Housemarks by Licensee and its Affiliates and Sublicensees is accompanied by an acknowledgement that such Akebia Housemarks are owned by Akebia; (c) not use such Akebia Housemarks in a way that might materially prejudice their distinctiveness or validity or the goodwill of Akebia therein and includes the trademark registration symbol ® or ™ as appropriate; (d) not use any trademarks or trade names so resembling any of such Akebia Housemarks as to be likely to cause confusion or deception; and (e) place and display the Product Marks on and in connection with the Licensed Products in a way that acknowledges Akebia's role in discovering the Licensed Products and that such Licensed Product is under license from Akebia. In addition, Licensee will abide by any commercially reasonable brand guidelines provided by Akebia to Licensee reasonably in advance of Licensee's first use of any of the Akebia Housemarks.

4.11 **Pharmacovigilance**. No later than [**] after the Effective Date, the Parties will develop and agree in writing upon a pharmacovigilance agreement ("**Pharmacovigilance Agreement**") that will include safety data exchange procedures governing the coordination of collection, investigation, reporting, and exchange of information concerning any adverse experiences and any product quality and product complaints involving adverse experiences, related to the Licensed Product, sufficient to enable each Party to comply with its legal and regulatory obligations. Licensee will bear all costs and expenses associated with pharmacovigilance activities related to the Licensed Product in the Territory. The Pharmacovigilance Agreement will contain terms no less stringent than those required by ICH or other applicable guidelines in order to allow the Parties to meet the applicable regulatory and legal requirements regarding the management of safety data within and outside the Territory.

5. PAYMENTS

5.1. Royalty Payments.

5.1.1 **Base Royalties**. In addition to the amounts payable to Akebia under Section 5.1.2 (Incremental Royalties), during each Calendar Quarter, Licensee will pay to Akebia an amount equal to [**]% of Net Sales of the Licensed Product in the Territory (the "**Base Royalties**") during the Royalty Term. Upon the expiration of the [**], the Base Royalties will be reduced to [**]% of Net Sales of the Licensed Product in the Territory if [**].

5.1.2 **Incremental Royalties**. In addition to the Base Royalties, Licensee will pay to Akebia, with respect to sales of the Licensed Product in the Territory during the Royalty Term for the applicable country, an amount equal to (such payments collectively, "**Incremental Royalties**", and together with the Base Royalties, "**Royalties**"):

(a) [**]% of Net Sales for the portion of aggregate Net Sales of the Licensed Product in the Territory in any Calendar Year less than or equal to €[**]; *provided* that for the first [**] following the First Commercial Sale in the Territory the Royalty due on Net Sales for the portion of aggregate Net Sales of the Licensed Product in the Territory in any Calendar Year less than or equal to €[**] will be [**]%; *plus*

(b) [**]% of Net Sales for the portion of aggregate Net Sales of the Licensed Product in the Territory in any Calendar Year greater than €[**] and less than or equal to €[**]; *plus*

(c) [**]% of Net Sales for the portion of aggregate Net Sales of the Licensed Product in the Territory in any Calendar Year greater than €[**] and less than or equal to €[**]; *plus*

(d) [**]% of Net Sales for the portion of aggregate Net Sales of the Licensed Product in the Territory in any Calendar Year greater than €[**] and less than or equal to €[**]; *plus*

(e) [**]% of Net Sales for the portion of aggregate Net Sales of the Licensed Product in the Territory in any Calendar Year greater than €[**].

5.1.3 **Minimum Royalties**. If the Incremental Royalties in a Calendar Year set forth in the table below in this Section 5.1.3 (Minimum Royalties) during Term equal an amount less than the Minimum Royalty set forth opposite the applicable Calendar Year, then Licensee will pay to Akebia an amount equal to the difference of the applicable Minimum Royalty and the Incremental Royalties paid to Akebia in such Calendar Year (each such amount, the "**Minimum Royalty**").

Calendar Year	Minimum Royalty
Year 1	[**]
Year 2	[**]
Year 3	[**]
Each Calendar Year following Year 3	[**]

As used in this Section 5.1.3 (Minimum Royalties), the following capitalized terms will have the meanings set forth opposite them:

"**Year 1**" will mean the date that is the earlier of (i) [**] and (ii) [**];

"**Year 2**" will mean the date that is the earlier of (i) [**] and (ii) [**]; and

"**Year 3**" will mean the date that is the earlier of (i) [**] and (ii) [**].

5.1.4 **Timing of Payments**. Royalty and Minimum Royalty payments (as applicable) will be due at the same time as a written report for a given Calendar Quarter is due as set forth in Section 5.1.6 (Royalty Reports and Records).

5.1.5 **Flash Reports**. No later than [**] after the end of each Calendar Quarter during the Term, Licensee will provide to Akebia a "flash" report that will set forth (a) for the first and second month of such Calendar Quarter: (i) the actual gross sales of the Licensed Product sold by Licensee and its Affiliates and Sublicensees in the Territory in such months; and (ii) the actual total aggregate Net Sales of the Licensed Product sold by Licensee and its Affiliates and Sublicensees in the Territory in such months, and (b) for the third month of such Calendar Quarter, Licensee's good faith estimate of the amounts set forth in the foregoing clauses (a)(i) and (a)(ii).

5.1.6 **Royalty Reports and Records**. In addition to the "flash" reports to be provided in accordance with Section 5.1.5 (Flash Reports), beginning with the First Commercial Sale by Licensee or any Sublicensee, as the case may be, of the Licensed Product in any country in the Territory, and continuing thereafter during the Term, Licensee will furnish, and will cause any Sublicensee to furnish, to Akebia a written report covering each such Calendar Quarter showing (a) the Net Sales of the Licensed Product in each country of the Territory during such Calendar Quarter; (b) the Royalties, payable in Euros, that will have accrued hereunder in respect of such sales with a computation of such royalties during such Calendar Quarter; (c) withholding taxes, if any, required by Applicable Law to be deducted in respect of such sales in such Calendar Quarter; and (d) the exchange rates used in determining the amount of United States Dollars payable in respect of sales made other than in Euros. Licensee will deliver such written report to Akebia no later than [**] after the end of each such Calendar Quarter and pay any Royalties or Minimum Royalties (as applicable) due for such Calendar Quarter no later than [**] after the end of each such Calendar Quarter. For each written report delivered to Akebia pursuant to this Section 5.1.6 (Royalty Reports and Records) that covers the end of a Calendar Year in which a Minimum Royalty is due, as set forth in the table in Section 5.1.3 (Minimum Royalties), such written report will also indicate whether a Minimum Royalty, if any, is due to Akebia for such Calendar Year, and, if so, the amount of such Minimum Royalty. With respect to sales of Licensed Product invoiced in a currency other than Euros, the Net Sales and royalty payable will be expressed in the domestic currency of the party making the sale together with the Euro equivalent of the royalty payable, calculated using the simple average of the exchange rate published in the *Wall Street Journal* on the last day of each month of the Calendar Quarter. If any sales are invoiced in a currency other than its domestic currency, then the Net Sales will be converted to its domestic currency in accordance with its normal accounting principles. Licensee will furnish to Akebia, upon request, appropriate evidence of payment of, and itemize any tax, credits, or specific amount deducted from any royalty payment.

5.2 Late Payments; Disputed Payments. Any amount owed by a Party to the other Party under this Agreement that is not paid within the applicable time period set forth herein will accrue interest at the lesser of (a) the prime rate as quoted by Citibank NA *plus* [**]%, or (b) the highest rate permitted under Applicable Law. If a Party disputes an invoice or other payment obligation under this Agreement, then such Party will timely pay the undisputed amount of the invoice or other payment obligation, and the Parties will resolve such dispute in accordance with Article 11 (Dispute Resolution; Governing Law).

5.3 Payment Method. Except as provided in Section 5.1.6 (Royalty Reports and Records), all payments from Licensee to Akebia will be made within [**] following Licensee's receipt of an invoice from Akebia, by wire transfer in Euros to the credit of such bank account as may be designated by Akebia in writing to Licensee from time to time. Any payment that falls due on a date which is not a Business Day may be made on the next succeeding Business Day.

5.4 Taxes. If under any law or regulation of any country of the Territory withholding of taxes of any type, levies or other charges is required with respect to any amounts payable hereunder to a Party, the other Party ("**Withholding Party**") will apply the withholding or deduction as so required and will promptly pay such tax, levy, or charge to the proper Governmental Authority, and will promptly furnish the Party with proof of such payment. The Withholding Party will have the right to withhold or deduct any such tax, levy, or charge actually paid from payment due the Party

or be promptly reimbursed by the Party if no further payments are due the Party. Any amounts so withheld or deducted from the payment due the Party pursuant to the relevant law or regulation will be deemed paid to such Party for all purposes of this Agreement. Each Withholding Party agrees to assist the other Party in claiming exemption from (or reduction in) such deductions or withholdings under double taxation or similar agreement or treaty from time-to-time in force and in minimizing the amount required to be so withheld or deducted. Notwithstanding the foregoing, all sums payable by either Party hereunder are stated exclusive of any sales tax, value added tax, or other similar taxes, assessments, and charges imposed by the jurisdiction of the Withholding Party or the payee and any such taxes will be paid by the Withholding Party.

5.5 Accounting; Audit. Licensee agrees to keep full, clear, and accurate records in accordance with the Accounting Standards applicable to Licensee, consistently applied, for a period of at least [**] after the relevant payment is owed pursuant to this Agreement, setting forth gross sales and Net Sales of the Licensed Product in sufficient detail to enable amounts owed or payable to Akebia hereunder, to be determined. Licensee further agrees to permit its books and records to be examined by an independent accounting firm selected by Akebia and reasonably acceptable to the Licensee to verify the royalty payments based on Net Sales (subject to such independent accounting firm's written obligations of confidentiality and non-use applicable to each Party's Confidential Information that are at least as stringent as those set forth described in Article 7 (Confidentiality)). Such auditor will be bound by a legal agreement obligating it to maintain the confidentiality of such information. Such audit will not be (a) performed more frequently than [**], (b) conducted for any Calendar Year more than [**] after the end of such year, or (c) repeated for any Calendar Year. If such audit shows any underpayment of royalties, Licensee will pay to Akebia the amount of such underpayment no later than [**] after Akebia's receipt of such audit report. Such examination is to be made at the expense of Akebia, except in the event that the results of the audit reveal an underpayment, excess credit, or overcharge by Licensee of [**]% or more during the period being audited, in which case reasonable audit fees for such examination will be paid by Licensee.

6. INTELLECTUAL PROPERTY RIGHTS

6.1. Ownership.

6.1.1 **Akebia Intellectual Property**. Ownership of the Akebia Technology will be and remain vested at all times in Akebia.

6.1.2 **Licensee Improvements**. Ownership of the Licensee Technology will be and remain vested at all times in Licensee. Without limiting the generality of Licensee's obligations under Section 2.5.2 (By Licensee), Licensee will promptly disclose to Akebia any Licensee Improvements, but no later than [**], after Licensee's intellectual property department receives notice of such conception or reduction to practice.

6.1.3 **Joint Improvements**.

(a) The Parties will promptly disclose to each other any Joint Improvements, but no later than [**] after the applicable Party's intellectual property department receives notice of such conception or reduction to practice.

(b) All Joint Improvements will be jointly owned by the Parties, with each Party entitled to the free use and enjoyment of such Joint Improvements, but subject to the terms and conditions of this Agreement, including the license grants under Article 2 (License Grants). Subject to the terms and conditions of this Agreement, neither Party will have a duty to account to the other or seek any consent with respect to the licensing or practice of any Joint Improvements. To the extent any further consent is required to enable a Party to so license or practice its interest in the Joint Improvements, the other Party will grant such consent promptly upon request.

6.2. Prosecution and Maintenance of Akebia Patent Rights and Joint Patent Rights.

6.2.1 **Akebia's First Right to Prosecute**. As between the Parties, Akebia will have the first right, but not the obligation, to file, prosecute, and maintain the Akebia Patent Rights and Joint Patent Rights using patent counsel of its own choosing.

6.2.2 **Status Updates and Information Sharing**. Akebia will consult with Licensee as to the prosecution and maintenance of the Akebia Patent Rights and the Joint Patent Rights, including providing to Licensee for review all relevant material drafts and documents reasonably prior to any deadline or submission to or action with any patent office. Akebia shall consider in good faith any reasonable comments thereto provided by Licensee within a reasonable time following Licensee's receipt of such drafts and documents. If reasonably requested by Licensee, no more than [**], Akebia shall provide Licensee with an update on progress with regard to the prosecution and maintenance of such Akebia Patent Rights and Joint Patent Rights, and Akebia shall provide to Licensee copies of all patent office submissions and material correspondence directly related to the Akebia Patent Rights and the Joint Patent Rights within a reasonable amount of time following submission or receipt thereof by Akebia. Akebia will provide notice to Licensee of, and the Parties will discuss, any significant actions to be taken with respect to the Akebia Patent Rights or Joint Patent Rights reasonably prior to any associated deadline.

6.2.3 **Assistance; Costs**. Licensee undertakes to reasonably assist Akebia with respect to the filing, prosecution, issuance, and maintenance of the Akebia Patent Rights and Joint Patent Rights, without cost to Licensee, to provide to Akebia the necessary documents available to Licensee and render all signatures that will be necessary for Akebia Patent Right and Joint Patent Right filings, and to assist Akebia in all other reasonable ways that are necessary for the issuance of the Akebia Patent Rights and Joint Patent Rights, as well as for the prosecution and maintenance of such Patent Rights. Akebia will provide to Licensee on at least an [**], and the Parties will review and discuss with each Party's intellectual property counsel, a budget of the estimated costs and expenses expected to be incurred by or on behalf of Akebia in connection with the filing, prosecution, and maintenance of the Akebia Patent Rights and Joint Patent Rights in the Territory (the "**IP Budget**"). For clarity, the IP Budget may include a range of estimated costs and expenses expected to be incurred by or on behalf of Akebia in connection with such activities. Licensee agrees to reimburses the actual reasonable costs and expenses incurred by or on behalf of Akebia in connection with the filing, prosecution, and maintenance of the Akebia Patent Rights in the Territory and the Joint Patent Rights in the Territory based on documentation provided by Akebia to Licensee, to the extent consistent with the aggregate amounts set forth in the IP Budget. Akebia may provide Licensee an updated version of the IP Budget from time to time as may be required. If the actual costs and expenses incurred by Akebia in connection with the filing, prosecution, and maintenance of the Akebia Patent Rights and Joint Patent Rights in the Territory exceed the last update of the IP Budget communicated to Licensee, Licensee and Akebia shall discuss in good faith the additional costs and expenses that Licensee will reimburse Akebia. Licensee will reimburse Akebia for all such costs and expenses as set forth under this Section 6.2.3 (Assistance; Costs) no later than [**] of receipt of an invoice therefor from Akebia. If Licensee disagrees with any costs or expenses for which Akebia seeks reimbursement for from Licensee in excess of the IP Budget, then the Parties will discuss in good faith. If despite such good faith discussions the Parties cannot agree on whether Licensee should reimburse such costs and expenses actually incurred by Akebia in excess of the IP Budget, then such dispute shall be resolved in accordance with Article 11 (Dispute Resolution; Governing Law).

6.2.4 **Abandonment**. If Akebia decides that it is no longer interested in prosecuting or maintaining a particular Akebia Patent Right or Joint Patent Right in any country in the Territory during the Term, then it will promptly provide written notice to Licensee of this decision, and in any case in a timing that reasonably allows Licensee to meet the next

deadline related to the applicable Akebia Patent Right or Joint Patent Right. Licensee may, upon written notice to Akebia, assume the prosecution and maintenance of such Akebia Patent Right or Joint Patent Right, as applicable, in such countries in the Territory at its sole cost and expense. If Licensee assumes the prosecution and maintenance of an Akebia Patent Right or a Joint Patent Right, then Akebia undertakes to reasonably assist Licensee with respect to the issuance, prosecution and maintenance of such Akebia Patent Rights and Joint Patent Rights, without cost to Akebia, and to provide to Licensee the necessary documents available to Akebia for Akebia Patent Right and Joint Patent Right filings by Licensee or on behalf of Licensee.

6.3 Prosecution of Licensee Patent Rights.

6.3.1 **Filing of Licensee Patent Rights**. Licensee will have the first right to file patent applications claiming Licensee Improvements. If Licensee declines to file such applications, then Akebia may do so, but regardless of which Party files patent applications claiming such Licensee Improvements, Licensee will have the first right, but not the obligation, to prosecute and maintain Licensee Patent Rights.

6.3.2 **Status Updates**. Licensee will provide notice to Akebia of, and the Parties will discuss, any significant actions to be taken with respect to the Licensee Patent Rights.

6.3.3 **Abandonment**. If Licensee decides that it is no longer interested in maintaining or prosecuting a particular Licensee Patent Right during the Term, then it will promptly provide written notice to Akebia of this decision. Akebia may, upon written notice to Licensee, assume the prosecution and maintenance of such Licensee Patent Right at its sole cost and expense. If Akebia assumes the prosecution and maintenance of a Licensee Patent Right, then Licensee undertakes to reasonably assist Akebia with respect to the issuance, prosecution and maintenance of such Licensee Patent Right, without cost to Licensee, and to provide to Akebia the necessary documents available to Licensee for Licensee Patent Right filings by Akebia or on behalf of Akebia.

6.4 Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory.

6.4.1 **Notice of Infringement**. If either Party becomes aware of any Third Party activity in the Territory, including any Development activity in the Territory (whether or not an exemption from infringement liability for such Development activity is available under Applicable Law), that infringes (or that is directed to the Development of a product that would infringe) an Akebia Patent Right, a Joint Patent Right, or a Licensee Patent Right, then the Party becoming aware of such activity will give prompt written notice to the other Party, and in any event no later than within [**] of becoming aware of such infringement, regarding such alleged infringement.

6.4.2 **Rights to Enforce Akebia Patent Rights and Joint Patent Rights outside the Territory**. As between the Parties, Akebia will have the first right, but not the obligation, to attempt to resolve a Third Party activity that infringes (or that is directed to the Development of a product that would infringe) (a) an Akebia Patent Right and (b) a Joint Patent Right outside the Territory, in either case ((a)-(b)), in its sole discretion, including the filing of an infringement suit to enforce the such Akebia Patent Rights or Joint Patent Rights (as applicable) using counsel of its own choice. Akebia will keep Licensee reasonably informed regarding the status of any substantive meetings, hearings, or other proceedings related to such infringement suit (to the extent relevant, together with its own counsel, at Licensee's sole cost and expense). Akebia will provide to Licensee, and the Parties will review and discuss, a budget of the costs and expenses to be incurred by or on behalf of Akebia in connection with any such action to abate such infringement, and Licensee will be responsible for [**] costs and expenses incurred by or on behalf or Akebia in connection with any such action and abate such infringement. Licensee will reimburse Akebia for [**] such costs and expenses related to any such action to abate

such infringement of the Akebia Patent Rights or the Joint Patent Rights outside the Territory no later than [**] of receipt of an invoice therefor from Akebia. If Akebia fails to initiate a suit or take other action to terminate such alleged infringement within [**] after the notice provided under Section 6.4.1 (Notice of Infringement) and does not provide Licensee commercially reasonable reasons why such suit has not been initiated or other action has not been taken within such [**] period, then Licensee will have the second right, but not the obligation, to attempt to resolve such Third Party activity in the Territory by commercially appropriate steps at its own expense, including the filing of an infringement suit to enforce the Akebia Patent Rights using counsel of its own choice.

6.4.3 **Rights to Enforce Licensee Patent Rights and Joint Patent Rights in the Territory**. As between the Parties, Licensee will have the first right, but not the obligation, to attempt to resolve a Third Party activity in the Territory that infringes (or that is directed to the Development of a product that would infringe) one or more Licensee Patent Rights or Joint Patent Rights in the Territory by commercially appropriate steps at its own expense, including the filing of an infringement suit to enforce one or more Licensee Patent Rights or Joint Patent Rights (as applicable) using counsel of its own choice. Licensee will keep Akebia reasonably informed with respect to any substantive meetings, hearings, or other proceedings related to such infringement suit (to the extent relevant, together with its own counsel, at Akebia's own cost and expense). Licensee will be responsible for [**]% of the costs incurred with respect to such actions. If Licensee fails to initiate a suit or take other action to terminate any such alleged infringement by a product that competes with the Licensed Product in the Territory within [**] after the notice provided under Section 6.4.1 (Notice of Infringement), then Akebia will have the second right, but not the obligation, to attempt to resolve such Third Party activity in the Territory at its own expense, including the filing of an infringement suit to enforce the applicable Licensee Patent Rights or the Joint Patent Rights using counsel of its own choice.

6.4.4 **Allocation of Recoveries in the Territory**. Any amounts recovered by a Party as a result of an action pursuant to this Section 6.4 (Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory), whether by settlement or judgment, will be allocated as follows: (a) first each Party will be reimbursed its internal costs and external expenses, including internal costs of FTEs, incurred in conducting, or cooperating with, such action, and if amounts recovered are insufficient to reimburse all such internal costs and external expenses incurred by both Parties, then such recovered amounts will be shared *pro-rata* in proportion to the relative amount of such internal costs and external expenses incurred by each Party; and (b) second, the balance of such recovered amounts will be retained by the Party bringing such action.

6.4.5 **Cooperation; Procedures**. In any event, at the request of the Party bringing an infringement action under this Section 6.4 (Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory) and at its own cost and expense, the other Party will provide reasonable assistance and cooperation in any such action (including entering into a common interest agreement if reasonably deemed necessary by any Party) and agrees to be joined as a party to the suit if necessary for the initiating Party to bring or continue an infringement action hereunder. In addition, the Party bringing an infringement action under this Section 6.4 (Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory) will provide the other Party with copies of all pleadings and other documents filed with the court and will consider reasonable input from the other Party during the course of the action. Neither Party may settle any action or proceeding brought under this Section 6.4 (Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory) or knowingly take any other action in the course thereof, in a manner that materially adversely affects the other Party's interest in the Akebia Patent Rights or Joint Patent Rights in the Territory, in each case, without the written consent of such other Party. Each Party will have the right to be represented by counsel of its own selection at its own expense in any suit or other action instituted by the other Party pursuant to this

Section 6.4 (Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory). In addition, the Parties will reasonably assist each other and cooperate in any such investigation, pre-litigation preparation, or litigation to ensure that there is an aligned global litigation and enforcement strategy.

6.5 Defense Against a Third Party Challenge to Akebia Patent Rights and Joint Patent Rights outside the Territory.

6.5.1 **Rights to Defend**. If a Third Party initiates a challenge to the validity, scope, or enforceability of, or any opposition proceeding against, any (a) Akebia Patent Right (inside the Territory), or (b) Joint Patent Right (outside the Territory) ("**Akebia Defense Action**"), then in either case ((a) – (b)) Akebia will have the first right, but not the obligation, to defend against any such claim using the counsel of its own choosing; *provided* that Akebia will keep Licensee reasonably informed regarding any such claim. Licensee will provide to Akebia all assistance reasonably requested by Akebia in connection with any such Akebia Defense Action, including, when mandatory under Applicable Laws, required to establish standing or for recovering damages, or requested by the applicable jurisdiction, the participation of Licensee in the defense action as a party. When participation of Licensee in the defense action is not mandatory under Applicable Laws, required to establish standing or for recovering damages, or requested by the applicable jurisdiction, Licensee may decide, at its own discretion, to participate to the defense action as a party. Akebia will have sole control of any negotiations for settlement or compromise of all Akebia Defense Actions. If Akebia notifies Licensee that it does not wish to exercise its right to defend an Akebia Defense Action solely with regards to a challenge or opposition proceeding against a Joint Patent Right outside the Territory, then Akebia shall notify Licensee in writing of such intent and within [**] of Licensee's receipt of such notice, Licensee shall have the second right, at its own cost and expense, to defend against any such Akebia Defense Action by counsel of its own choice. In this event, Akebia shall provide to Licensee all reasonable cooperation, solely to the extent required to allow Licensee to defend such Akebia Defense Action, and Licensee will, subject to Section 9.3 (Indemnification Procedure), have sole control of any negotiations for settlement or compromise of such Akebia Defense Action.

6.5.2 **Control and Cost**. With regard to any Akebia Defense Action, Akebia will be responsible for controlling such Akebia Defense Action using the counsel of its own choosing, including the right to control the strategy, any appeals, and other material factors related to such Akebia Defense Action. In addition, the Parties will reasonably assist each other and cooperate and share information with respect to such Akebia Defense Actions, including any appeals thereof. For Akebia Defense Actions initiated (a) prior to the Effective Date or (b) on or after the Effective Date related to a Joint Patent Right outside the Territory (an "**Akebia Cost Defense Action**"), Akebia will be responsible for [**]% of out-of-pocket costs and fees, including attorneys' fees, expert fees, court fees, and translation costs, incurred by Akebia in connection with any Akebia Cost Defense Action, including any appeals related to such Akebia Cost Defense Action. Akebia will provide to Licensee, and the Parties will review and discuss, a budget of the costs and expenses to be incurred by or on behalf of Akebia in connection with any Akebia Defense Action in the Territory initiated on or after the Effective Date, and Licensee will be responsible for [**] costs and expenses, including attorneys' fees, expert fees, court fees, and translation costs, incurred by either Party in connection with any Akebia Defense Action related to an Akebia Patent Right initiated on or after the

Effective Date (a "**Licensee Cost Defense Action**"), including any appeals related to such Licensee Cost Defense Action. Licensee will reimburse Akebia for [**] costs and expenses related to any such Licensee Cost Defense Action initiated on or after the Effective Date no later than [**] of receipt of an invoice therefor from Akebia.

6.6 Defense Against a Third Party Challenge to Joint Patent Rights in the Territory and Licensee Patent Rights.

6.6.1 **Rights to Defend**. If a Third Party initiates a challenge to the validity, scope, or enforceability of any Joint Patent Right in the Territory or any Licensee Patent Right, or an opposition proceeding against any Joint Patent Rights in the Territory or any Licensee Patent Rights ("**Licensee Defense Action**"), then Licensee will have the first right, but not the obligation, to defend against any such claim using the counsel of its own choosing; *provided* that Licensee will keep Akebia reasonably informed regarding any such claim. Akebia will provide to Licensee all assistance reasonably requested by Licensee in connection with any such Licensee Defense Action. Licensee will have sole control of any negotiations for settlement or compromise of all Licensee Defense Actions. If Licensee notifies Akebia that it does not wish to exercise its right to defend an Licensee Defense Action solely with regards to a challenge or opposition proceeding against a Joint Patent Right inside the Territory, then Licensee shall notify Akebia in writing of such intent and within [**] of Akebia's receipt of such notice, Akebia shall have the second right, at its own cost and expense, to defend against any such Licensee Defense Action by counsel of its own choice. In this event, Licensee shall provide to Akebia all reasonable cooperation, solely to the extent required to allow Akebia to defend such Licensee Defense Action, and Akebia will, subject to Section 9.3 (Indemnification Procedure), have sole control of any negotiations for settlement or compromise of such Licensee Defense Action.

6.6.2 **Control and Cost**. With regard to any Licensee Defense Action, Licensee will be responsible for controlling such Licensee Defense Action using the counsel of its own choosing, including the right to control the strategy, any appeals, and other material factors related to such Licensee Defense Action. In addition, the Parties will reasonably assist each other and cooperate and share information with respect to such Licensee Defense Actions, including any appeals thereof. Licensee will be responsible for [**]% of out-of-pocket costs and fees, including attorneys' fees, expert fees, court fees, and translation costs, incurred by License in connection with any Licensee Defense Action, including any appeals related to such Licensee Defense Action.

6.7 Defense of Third Party Infringement Claims; Third Party IP.

6.7.1 **Infringement Claim**. If a Third Party asserts that a Patent Right Controlled by it is or will be infringed by a Party's activities in the Territory under this Agreement ("**Infringement Claim**") or a Party becomes aware of a Patent Right that might form the basis for an Infringement Claim, then the Party first obtaining knowledge of such Infringement Claim or such potential Infringement Claim will immediately provide the other Party with written notice thereof and the related facts in reasonable detail. The Parties will discuss whether to use commercially appropriate steps to avoid infringement of such Third Party Patent Rights or other right controlled by such Third Party in the Territory. Akebia will make the final decision in its sole discretion as to how to address such Infringement Claim or potential Infringement Claim, including whether it will seek a license from such Third Party pursuant to Section 6.7.3 (Responsibility for Third Party Licenses) or take an action to challenge such Third Party Patent Rights or other right controlled by such Third Party in the Territory; *provided*, *however*, that Akebia will consult with and reasonably consider Licensee's views regarding any such action. Akebia will provide updates to Licensee on a regular basis and reasonably discuss and consult with Licensee, upon Licensee's request, regarding strategies in the Territory regarding any Third Party Patent Rights.

6.7.2 **Responsibility to Defend**. If, during the Term of this Agreement, a Third Party asserts that a Patent Right or other right controlled by such Third Party is infringed or will be infringed in the Territory by the exercise of the licenses granted under Article 2 (License Grants), then, subject to Section 6.7.4 (Challenge to Certain Third Party Patents), Akebia will have the sole right to defend against any such claim using the counsel of its own choosing; *provided* that Akebia will keep Licensee reasonably informed regarding any such claim. For such proceedings initiated prior to the Effective Date, Akebia will be responsible for [**]% of out-of-pocket costs and fees, including attorneys' fees, expert fees, court fees, and translation costs, incurred by Akebia in connection with any such proceeding, including any appeals related to such proceeding. Akebia will provide to Licensee, and the Parties will review and discuss, a budget of the costs and expenses to be incurred by or on behalf of Akebia in connection with any such proceeding initiated on or after the Effective Date, and Licensee will be responsible for [**] such costs and expenses, including attorneys' fees, expert fees, court fees, and translation costs, incurred by either Party in connection with any such proceeding initiated on or after the Effective Date, including any appeals related to such Akebia Defense Action. Licensee will reimburse Akebia for [**] costs and expenses related to any such proceeding initiated on or after the Effective Date no later than [**] of receipt of an invoice therefor from Akebia. Akebia will not settle such claim in a manner that materially adversely affects Licensee's interests and in a manner that is disproportionate to Akebia's interests, without the written consent of Licensee. In addition, the Parties will reasonably assist each other and cooperate and share information with respect to such claim.

6.7.3 **Responsibility for Third Party Licenses**. At any time during the Term, if either Party believes that it is necessary or advisable to seek to acquire or obtain a license under any Patent Rights owned or controlled by a Third Party in order to avoid infringement thereof by the exercise of the licenses granted under Article 2 (License Grants), whether or not there has been the institution of any infringement claim, then the Parties will discuss whether to acquire or obtain a license under such Patent Rights in the Territory. Akebia will have the sole right, but not the obligation, to negotiate and acquire or obtain a license under such Patent Rights from such Third Party; *provided*, *however*, that Akebia will consult with and reasonably consider Licensee's views regarding any such decision to acquire or obtain a license under such Patent Rights and regarding the terms of such license to the extent pertaining to the Territory. If Akebia is not able to so acquire or obtain a license under any such Patent Rights owned or controlled by such a Third Party, then the Parties will in good faith discuss at the JSC modifications to the Licensed Product to avoid infringement of such Patent Rights. If Akebia does so acquire or obtain a license under any such Patent rights and the applicable acquisition or license agreement relates solely to the Development, Manufacture, Commercialization, or other Exploitation of the Licensed Product in the Territory, then Akebia will be responsible for [**]% and Licensee will be responsible for [**]%, in each case, of all amounts payable to such Third Party assignor, licensor, or grantor of rights pursuant to such agreement. If such acquisition or license agreement relates to the Development, Manufacture, Commercialization, or other Exploitation of the Licensed Product in countries both inside and outside of the Territory, then (a) Akebia will be responsible for [**]% and Licensee will be responsible for [**]%, in each case, of any such payments thereunder that arise out of the Development, Manufacture, Commercialization, or other Exploitation of the Licensed Product in the Territory (*e.g.*, any milestone payments for achievement of milestone events in the Territory or royalties on net sales of the Licensed Product in the Territory), (b) Licensee will be responsible for [**]% of any such payments thereunder that are not directly attributable to the Development, Manufacture, Commercialization, or other Exploitation of the Licensed Product in the Territory or outside of the Territory (*e.g.*, an upfront payment), and (c) Akebia will be responsible for [**]% of any such payments thereunder that arise out of the Development, Manufacture, Commercialization, or other Exploitation of the Licensed Product in countries outside of the Territory (*e.g.*, any milestone payments for achievement of any milestone events in a country outside of the Territory or royalties on net sales of the Licensed Product outside of the Territory). Licensee will reimburse Akebia for Licensee's share of such payments no later than [**]

of receipt of an invoice therefor from Akebia. This Section 6.7 (Defense of Third Party Infringement Claims; Third Party IP) will not be interpreted as placing on either Party a duty of inquiry regarding Third Party intellectual property rights. Each Party will keep the other Party informed of the status of any Third Party claim of infringement.

6.7.4 **Challenge to Certain Third Party Patent Rights**.

(a) **Initiation**. The Parties, together with each Party's patent counsel (in each Party's discretion), will discuss whether or not to initiate an invalidity action (including oppositions), either in the applicable patent office or court, challenging any Third Party Patent Rights that claim the Licensed Product (each, on a Third Party Patent-by-Third Party Patent basis, an "**Invalidation Proceeding**"), and the strategy and timeline for any Invalidation Proceeding that Akebia pursues in accordance with this Section 6.7.4 (Challenge to Certain Third Party Patent Rights). Immediately following such discussion, Akebia, in consultation and discussion with Licensee, will begin preparing the documents for filing any such Invalidation Proceedings that the Parties have agreed to initiate pursuant to the previous sentence, and the Parties will attempt to agree (including, if necessary, following escalation to the Parties' Executive Officers) on the timeline for filing and pursuing any such Invalidation Proceedings. Subject to the remainder of this Section 6.7.4(a) (Initiation), Akebia will make the final decision in its sole discretion as to whether to initiate any Invalidation Proceeding. If the Parties are unable to agree on whether to initiate any Invalidation Proceeding, or on the timeline for pursuing any such Invalidation Proceeding, then, to the extent required or advisable to prevent a Third Party from interfering with or obstructing Commercialization of the Licensed Product, Licensee will have the right to require Akebia to initiate and pursue Invalidation Proceedings; *provided* that prior to exercising the foregoing right to cause Akebia to initiate any such Invalidation Proceeding in such country, Licensee will consider in good faith any comments by Akebia regarding the merits of initiating such proceeding in such country and, if initiated, the best type of proceeding to pursue in each such country. Akebia will control the strategy, venue, type of proceeding, selection of counsel, and, subject to the previous sentence, the timeline, in each case, for filing and pursuing all such Invalidation Proceedings in accordance with Section 6.7.4(b) (Control and Costs); *provided* that Akebia will consult with and reasonably consider in good faith Licensee's (and Licensee's outside patent counsel's) views regarding any such Invalidation Proceeding, including the strategy and timeline for initiating and pursuing any Invalidation Proceeding and the best type of proceeding to pursue in each such country.

(b) **Control and Costs**. With regard to any Invalidation Proceeding, Akebia will be responsible for preparing, filing, pursuing, and controlling such Invalidation Proceeding and the counsel of its own choosing, including the right to control the strategy, choice of venue, type of proceeding, timing (subject to Section 6.7.4(a) (Initiation)), any appeals, and other material factors related to such Invalidation Proceeding. In addition, the Parties will reasonably assist each other and cooperate and share information with respect to such Invalidation Proceedings, including any appeals thereof. For Invalidation Proceedings initiated prior to the Effective Date, Akebia will be responsible for [**]% of out-of-pocket costs and fees, including attorneys' fees, expert fees, court fees, and translation costs, incurred by Akebia in connection with any Invalidation Proceeding, including any appeals related to such Invalidation Proceeding. Akebia will provide to Licensee, and the Parties will review and discuss, a budget of the costs and expenses to be incurred by or on behalf of Akebia in connection with any Invalidation Proceeding initiated on or after the Effective Date, and Licensee will be responsible for [**] costs and expenses incurred by or on behalf of Akebia in connection with any Invalidation Proceeding initiated on or after the Effective Date, including attorneys' fees, expert fees, court fees, and translation costs,

incurred by either Party in connection with any Invalidation Proceeding initiated on or after the Effective Date, including any appeals related to such Invalidation Proceeding. Licensee will reimburse Akebia for [**] costs and expenses related to any such Invalidation Proceeding initiated on or after the Effective Date no later than [**] of receipt of an invoice therefor from Akebia.

(c) **Cooperation**. Akebia will keep Licensee reasonably informed regarding substantive meetings, hearings, or other proceedings related to such Invalidation Proceeding (to the extent relevant, together with its own counsel, at its own expense).

6.8 Patent Term Extensions. Akebia will be solely responsible for making all decisions regarding patent term extensions, including supplementary protection certificates and any other extensions that are now or become available in the future, with respect to the Licensed Product; *provided* that Akebia will consult with Licensee with respect to such decisions and will consider the comments and concerns of Licensee in good faith. Licensee will reimburse Akebia for all costs and expenses incurred by Akebia pursuant to this Section 6.8 (Patent Term Extensions) no later than [**] of receipt of an invoice therefor from Akebia.

6.9 Unified Patent Court. In the event that the Unified Patent Court Agreement enters into force during the Term of this Agreement, Akebia will be solely responsible for making all decisions regarding Patent Rights, including decisions regarding the opting-out or opting-in of existing European Patent Rights into the jurisdiction of the Unified Patent Court or the registration of European Patents with Unitary Effect; *provided* that Akebia will consult with Licensee with respect to such decisions and will consider the comments and concerns of Licensee in good faith.

7. CONFIDENTIALITY

7.1. Definition. "**Confidential Information**" means the terms and provisions of this Agreement and other Know-How, inventions, materials, and other non-public or proprietary information and data of a financial, commercial, or technical nature that a Party (the "**Disclosing Party**") or any of its Affiliates has supplied or otherwise made available to the other Party (the "**Receiving Party**") or its Affiliates, whether in writing or orally and whether or not specifically marked or designated by the Disclosing Party as confidential. All Akebia Know-How will be considered Akebia's Confidential Information and Akebia will be the Disclosing Party with respect thereto. The terms of this Agreement and all Licensee Development Data will each be considered the Confidential Information of both Parties and both Parties will be the Receiving Party with respect thereto.

7.2. Obligations. During the Term of this Agreement and for [**] thereafter, the Receiving Party will (a) protect all Confidential Information of the Disclosing Party against unauthorized disclosure to Third Parties and (b) not use or disclose the Confidential Information of the Disclosing Party, except as permitted by or in furtherance of exercising rights or carrying out obligations hereunder. The Receiving Party will treat all Confidential Information provided by the Disclosing Party with the same degree of care as the Receiving Party uses for its own similar information, but in no event less than a reasonable degree of care. The Receiving Party may disclose the Confidential Information to its Affiliates, and their respective directors, officers, employees, Subcontractors, prospective Sublicensees, Sublicensees, consultants, attorneys, accountants, banks, financial or legal advisors, lenders, prospective lenders, financing sources, prospective financing sources, prospective acquirers, investors and prospective investors (collectively, "**Representatives**") who have a need-to-know such information to carry out the activities and transactions or to exercise its rights contemplated by this Agreement, *provided* that such Representatives are bound by obligations of confidentiality at least as restrictive as those set forth in this Agreement. Each Party will promptly notify the other Party of any misuse or unauthorized disclosure of the other Party's Confidential Information.

7.3. Exceptions to Confidentiality. The obligations under this Article 7 (Confidentiality) will not apply to any information to the extent the Receiving Party can demonstrate by competent evidence that such information:

7.3.1. is (at the time of disclosure) or becomes (after the time of disclosure) known to the public or part of the public domain through no breach of this Agreement by the Receiving Party or any Representatives to whom it disclosed such information;

7.3.2. was rightfully known to, or was otherwise lawfully in the possession of, the Receiving Party prior to the time of disclosure by the Disclosing Party;

7.3.3. is disclosed to the Receiving Party on a non-confidential basis by a Third Party who is entitled to disclose it without breaching any confidentiality obligation to the Disclosing Party; or

7.3.4. is independently developed by or on behalf of the Receiving Party or any of its Affiliates, as evidenced by its written records, without use or access to the Confidential Information.

7.4. Permitted Disclosures.

7.4.1. **Compliance with Law**. The restrictions set forth in this Article 7 (Confidentiality) will not apply to any Confidential Information that the Receiving Party is required to disclose under Applicable Laws a valid court order or other governmental order or to enforce any Akebia Patent Rights under Article 6 (Intellectual Property Rights), *provided* that the Receiving Party: (a) provides the Disclosing Party with prompt notice of such disclosure requirement if legally permitted; (b) affords the Disclosing Party, to the extent permitted, an opportunity to oppose or limit, or secure confidential treatment for, such required disclosure; and (c) if the Disclosing Party is unsuccessful in its efforts pursuant to clause (b), discloses only that portion of the Confidential Information that the Receiving Party is legally required to disclose as advised by the Receiving Party's legal counsel.

7.4.2. **SEC Filings and Other Disclosures**. Either Party may disclose the terms of this Agreement only to the extent required, in the reasonable opinion of such Party or such Party's outside legal counsel, to comply with Applicable Law, regulation, or legal process or by applicable stock exchange rule. If a Party must disclose this Agreement or any of the terms hereof in accordance with the preceding sentence, then such Party agrees, at its own cost and expense, to seek confidential treatment of portions of this Agreement or such terms as may be reasonably requested by the other Party, and to cause all Persons to whom any terms of this Agreement are disclosed to be bound by written obligations of confidentiality and non-use no less stringent than the confidentiality terms of this Agreement.

7.4.3. **Disclosure of Agreement Terms**. Notwithstanding the restrictions set forth in this Article 7 (Confidentiality), a Party may, without the prior consent of the other Party, disclose the terms and provisions of this Agreement to any actual or *bona fide* potential investors, acquirors, (sub)licensees, lenders, and other financial or commercial partners (including in connection with any royalty factoring transaction), and their respective attorneys, accountants, banks, investors, and advisors, solely for the purpose of evaluating or carrying out an actual or potential investment, acquisition, (sub)license, debt transaction, or collaboration; *provided* that such Third Party is bound by written obligations of confidentiality at least as stringent as those set forth in this Agreement or otherwise customary for such type and scope of disclosure and that any such disclosure is limited to the maximum extent practicable for the particular context in which it is being disclosed.

7.4.4. **Other Permitted Disclosures**. In addition, and notwithstanding the restrictions set forth in this Article 7 (Confidentiality), a Party may, without the prior consent of the other Party, disclose the other Party's Confidential Information (including this Agreement and the terms hereof) to the extent such disclosure is reasonably necessary in the following circumstances: (a) the prosecution, enforcement, and defense of Akebia Patent Rights, Joint Patent Rights, or Licensee Patent Rights, in each case, as contemplated by this Agreement, (b) to prosecute or defend litigation, so long as there is [**] prior written

notice given by the Receiving Party before filing, (c) to present, disclose, and discuss general information about the existence of the Agreement and the general progress of the Licensed Products at investor press conferences or similar events; and (d) disclosure pursuant to Section 7.6 (Public Announcements); *provided* that any Confidential Information disclosed pursuant to this Section 7.4.4 (Other Permitted Disclosures) is be limited to that information that is legally required or necessary for the particular in which it is being disclosed.

7.5. Right to Injunctive Relief. Notwithstanding any provision to the contrary set forth in this Agreement, the Parties each stipulate and agree that (a) the Confidential Information includes highly sensitive trade secret information, (b) a breach of this Article 7 (Confidentiality) by a Party with respect to such information may cause irrevocable harm for which monetary damages would not provide a sufficient remedy, and (c) in such case of a breach of this Article 7 (Confidentiality), the non-breaching Party will be entitled to equitable relief, including a temporary restraining order, preliminary injunction, or permanent injunction from any court of competent jurisdiction.

7.6. Public Announcements. Except as required to comply with Applicable Law, for appropriate market disclosure, or for disclosures that are consistent with information disclosed in prior releases properly made hereunder, neither Party will originate any publicity, news release, or public announcements, written or oral, whether to the public or press, stockholders, or otherwise, relating to the terms of this Agreement without the prior written consent of the other Party, not to be unreasonably withheld. Any such release, publicity, or announcement made previously in accordance with this Section 7.6 (Public Announcements) may be re-issued; *provided* that the information contained therein remains current, correct, and accurate at the time of re-issue.

7.7. Use of Marks. Subject to the rights granted to Licensee pursuant to Section 4.10.3 (Trademark License), neither Party (nor any of its Affiliates or agents) will use the Marks of the other Party or its Affiliates in any press release, publication, or other form of public promotional disclosure without the prior written consent of the other Party in each instance.

8. REPRESENTATIONS, WARRANTIES, AND COVENANTS

8.1. Representations and Warranties by Each Party. Each Party represents and warrants to the other Party as of the Effective Date as follows:

8.1.1. It is a corporation duly organized, validly existing, and in good standing under the laws of its jurisdiction of formation.

8.1.2. It has full corporate power and authority to execute, deliver, and perform under this Agreement, and has taken all corporate action required by Applicable Laws and its organizational documents to authorize the execution and delivery of this Agreement and the consummation of the transactions contemplated by this Agreement.

8.1.3. This Agreement constitutes a valid and binding agreement enforceable against it in accordance with its terms.

8.1.4. All consents, approvals and authorizations from all Governmental Authorities or other Third Parties required to be obtained by such Party in connection with this Agreement have been obtained.

8.1.5. The execution and delivery of this Agreement and all other instruments and documents required to be executed pursuant to this Agreement, and the consummation of the transactions contemplated hereby do not and will not: (a) conflict with or result in a breach of or a default under any provision of its organizational documents; (b) result in a

breach of or default under any agreement to which it is a party that would impair the performance of its obligations hereunder; or (c) violate any Applicable Laws.

8.2. Representations and Warranties by Akebia. Except as set forth in the Disclosure Schedule attached hereto as Schedule 8.2 (Disclosure Schedule), Akebia represents and warrants to Licensee as of the Effective Date as follows:

8.2.1. Akebia Controls the Akebia Patent Rights and the Akebia Know-How, and has the rights to grant the license granted in Section 2.1 (License Grants to Licensee).

8.2.2. Schedule 1.12 (Akebia Patent Rights) includes all Patent Rights Controlled by Akebia that are necessary to Exploit the Licensed Product in the Field in the Territory.

8.2.3. To Akebia's Knowledge, all Akebia Patents Rights existing as of the Effective Date are (i) being diligently prosecuted in the respective patent offices in the Territory in accordance with Applicable Law, and (ii) have been filed and maintained and all applicable fees have been paid on or before the due date for such payments;

8.2.4. Akebia has not previously assigned, transferred, conveyed or otherwise encumbered its right, title and interest in and to the Licensed Product in a manner that could or would prevent Akebia from granting the rights to Licensee pursuant to this Agreement;

8.2.5. Akebia has not received any written notice from a Third Party and, to Akebia's Knowledge, there is no claim pending or threatened by a Third Party alleging that the Exploitation of the Licensed Product by or on behalf of Akebia in the Field within the Territory has infringed, misappropriated, or otherwise violated the Intellectual Property Rights of a Third Party, and to Akebia's Knowledge, such Exploitation has not infringed, misappropriated, or otherwise violated the Intellectual Property Rights of a Third Party.

8.2.6. To the extent permitted under the [**] Agreement, Akebia has provided to Licensee a true and complete copy of the [**] Agreement.

8.2.7. In performing under this Agreement, Akebia and its Affiliates will comply with the US anti-bribery laws applicable to Akebia. Akebia has not and will not directly or indirectly offer or pay, or authorize such offer or payment of, any money, or transfer anything of value, to improperly seek to influence any: (a) any elected or appointed government official (*e.g.*, a member of a ministry of health); (b) any employee or person acting for or on behalf of a Governmental Authority; (c) any political party officer or employee acting for or on behalf of a political party or candidate for public office; (d) an employee or person acting for or on behalf of a public international organization; or (e) any person otherwise categorized as a government official under local law.

8.2.8. As of the Effective Date, neither it nor any of its Affiliates has been debarred or is subject to debarment, and neither it nor any of its Affiliates will use in any capacity, in connection with its activities under this Agreement, any person who has been debarred pursuant to Section 306 of the FFDCA, or who is the subject of a conviction described in such Section 306, or who is subject to any similar sanction of any Governmental Authority in the Territory. Akebia will inform Licensee in writing promptly if it or any such Person who is performing services hereunder is debarred or is the subject of a conviction described in such Section 306 or if any action, suit, claim, investigation, or legal or administrative proceeding is pending, or is threatened, relating to the debarment or conviction of it or any such Person performing services hereunder.

8.3. Covenants of Licensee. Licensee covenants to Akebia as follows:

8.3.1. Licensee will perform, or will ensure that each of its Affiliates, permitted Sublicensees (as applicable), and Subcontractors perform, all activities under this Agreement in a professional and ethical business manner and in compliance with Applicable Law,

applicable Professional Requirements, the Approved Labeling, and the Commercialization Plan, including, as applicable, the European Data Protection Directive 95/46/EC, the European General Data Protection Regulation (Regulation (EU) 2016/679), and any other applicable national data protection legislation.

8.3.2. In performing under this Agreement, it and its Affiliates will comply with all applicable anti-corruption laws, including the Foreign Corrupt Practices Act of 1977 and the Bribery Act 2010, as amended from time-to-time; the anti-corruption laws of the Territory, and all laws enacted to implement the Organization for Economic Co-operation and Development Convention on Combating Bribery of Foreign Officials in International Business Transactions.

8.3.3. It has not and will not directly or indirectly offer or pay, or authorize such offer or payment of, any money, or transfer anything of value, to improperly seek to influence any: (a) any elected or appointed government official (*e.g.*, a member of a ministry of health); (b) any employee or person acting for or on behalf of a Governmental Authority; (c) any political party officer, employee, or person acting for or on behalf of a political party or candidate for public office; (d) an employee or person acting for or on behalf of a public international organization; or (e) any person otherwise categorized as a government official under local law.

8.3.4. As of the Effective Date, neither it nor any of its Affiliates has been debarred or is subject to debarment, and neither it nor any of its Affiliates will use in any capacity, in connection with its activities under this Agreement, any person who has been debarred pursuant to Section 306 of the FFDCA, or who is the subject of a conviction described in such Section 306, or who is subject to any similar sanction of any Governmental Authority in the Territory. Licensee will inform Akebia in writing promptly if it or any such Person who is performing services hereunder is debarred or is the subject of a conviction described in such Section 306 or if any action, suit, claim, investigation, or legal or administrative proceeding is pending, or is threatened, relating to the debarment or conviction of it or any such Person performing services hereunder.

8.3.5. Licensee will have responsibility for tracking and reporting payments or other transfers of value made directly or indirectly to health care professionals or other persons and entities under the so-called federal "sunshine law" or Open Payments (42 U.S.C. §1320a-7a) and analogous state laws and foreign laws in the Territory in connection with the performance of this Agreement in accordance with their respective compliance policies.

8.4. **Covenant of Akebia**. Akebia will not amend the [**] Agreement in a way that adversely affects the rights granted to Licensee under this Agreement or increases the amount of the Base Royalties without Licensee's prior written consent.

8.5. **No Other Warranties**. EXCEPT AS EXPRESSLY STATED IN THIS ARTICLE 8 (REPRESENTATIONS, WARRANTIES, AND COVENANTS), NEITHER PARTY MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES OR CONDITIONS OF ANY KIND, EITHER EXPRESS OR IMPLIED, STATUTORY OR OTHERWISE, INCLUDING WARRANTIES OF TITLE, NON-INFRINGEMENT, VALIDITY, ENFORCEABILITY, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO THE LICENSED PRODUCT OR THE SUBJECT MATTER OF THIS AGREEMENT. ANY INFORMATION PROVIDED BY AKEBIA OR ITS AFFILIATES IS MADE AVAILABLE ON AN "AS IS" BASIS WITHOUT WARRANTY WITH RESPECT TO COMPLETENESS, OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER KIND OF WARRANTY WHETHER EXPRESS OR IMPLIED.

9. INDEMNIFICATION

9.1. **Indemnification by Licensee**. Licensee agrees to indemnify, hold harmless, and defend Akebia and its Affiliates, and their respective officers, directors, employees, successors, and assigns, and

representatives (collectively, "**Akebia Indemnitees**"), from and against any Claims arising from or relating to: (a) the Development of the Licensed Product in the Territory by or on behalf of Licensee, or its Affiliates, Subcontractors, or Sublicensees; (b) the Manufacturing, Commercialization, or other Exploitation of the Licensed Product in the Territory by or on behalf of Licensee, or its Affiliates, Subcontractors, or Sublicensees, including the content of any promotional materials or medical materials; (c) the negligence or wrongful intentional acts or omissions of Licensee, or its Affiliates, Subcontractors, or Sublicensees; (d) the breach by Licensee or its Affiliates, Subcontractors, or Sublicensees of any obligation, representation, warranty, or covenant set forth in this Agreement; (e) the failure to comply with Applicable Law by or on behalf of Licensee, or its Affiliates, Subcontractors, or Sublicensees; and (f) any claim of death or bodily injury resulting from the use of the Licensed Product sold in the Territory; except, in each case ((a) – (f)), to the extent such Claims arise from or occur as a result of the breach by Akebia of this Agreement or the negligence or willful misconduct on the part of any Akebia Indemnitee.

9.2. **Indemnification by Akebia**. Akebia agrees to indemnify, hold harmless, and defend Licensee and its Affiliates and their respective officers, directors, employees, successors and assigns, and representatives (collectively, "**Licensee Indemnitees**"), from and against any Claims arising from or relating to: (a) the Manufacturing, Commercialization, or other Exploitation of the Licensed Product outside the Territory by or on behalf of Akebia, or its Affiliates, Subcontractors, or Sublicensees (excluding Licensee), including the content of any promotional materials or medical materials, (b) the negligence or wrongful intentional acts or omissions of Akebia or its Affiliates, contractors, or licensees (other than Licensee); (c) the breach by Akebia or its Affiliates, contractors, or licensees (other than Licensee) of any obligation, representation, warranty, obligation, or covenant set forth in this Agreement; or (d) the failure to comply with Applicable Law by or on behalf of Akebia, or its Affiliates, contractors, or licensees (other than Licensee); except, in each case ((a) – (d)), to the extent such Claims arise from or occur as a result of the breach by Licensee of this Agreement or the negligence or willful misconduct on the part of any Licensee Indemnitee.

9.3. **Indemnification Procedure**. In connection with any Claim for which a Party (the "**Indemnified Party**") seeks indemnification from the other Party (the "**Indemnifying Party**") pursuant to this Agreement, the Indemnified Party will: (a) give the Indemnifying Party prompt written notice of the Claim; *provided*, *however*, that failure to provide such notice will not relieve the Indemnifying Party from its liability or obligation hereunder, except to the extent of any material prejudice as a direct result of such failure; (b) cooperate with the Indemnifying Party, at the Indemnifying Party's expense, in connection with the defense and settlement of the Claim; and (c) permit the Indemnifying Party to control the defense and settlement of the Claim. Akebia, in its capacity as the Indemnifying Party, shall not settle any such Claim without Licensee's prior written consent (not to be unreasonably withheld), if such settlement materially adversely impacts Licensee's rights or obligations. Licensee, in its capacity as the Indemnifying Party, shall not settle any such Claim without Akebia's prior written consent (not to be unreasonably withheld). Further, the Indemnified Party will have the right to participate (but not control) and be represented in any suit or action by advisory counsel of its selection and at its own expense. Each notice provided pursuant to this Section 9.3 (Indemnification Procedure) will contain a description of the Claim and the nature and amount of such Claim (to the extent that the nature and amount of such Claim is known at such time).

9.4. **CONSEQUENTIAL DAMAGES WAIVER**. NEITHER OF THE PARTIES WILL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, INDIRECT, CONSEQUENTIAL, OR PUNITIVE DAMAGES OR DAMAGES FOR LOSS OF PROFIT OR LOST OPPORTUNITY IN CONNECTION WITH THIS AGREEMENT, ITS PERFORMANCE OR LACK OF PERFORMANCE HEREUNDER, OR ANY LICENSE GRANTED HEREUNDER, EXCEPT TO THE EXTENT THE DAMAGES RESULT FROM A PARTY'S WILLFUL MISCONDUCT OR INTENTIONAL BREACH OF ITS OBLIGATIONS UNDER THIS AGREEMENT, A BREACH OF THE OBLIGATIONS OF A PARTY UNDER ARTICLE 7 (CONFIDENTIALITY), INFRINGEMENT OF INTELLECTUAL PROPERTY RIGHTS OWNED OR CONTROLLED BY THE OTHER PARTY, AND AMOUNTS

REQUIRED TO BE PAID TO A THIRD PARTY AS PART OF A CLAIM FOR WHICH A PARTY PROVIDES INDEMNIFICATION UNDER ARTICLE 9 (INDEMNIFICATION).

9.5. **Insurance**. Licensee will, at its own expense, obtain and maintain insurance with respect to the Development and Commercialization of the Licensed Product under this Agreement and for [**] thereafter in such amount and subject to such deductibles and other limitations as biopharmaceutical companies customarily maintain with respect to the research, development, and commercialization of similar products in their respective territories. Such insurance policy will name Akebia as an additional insured and will be reasonably acceptable to Akebia. Licensee will provide a copy of such insurance policy to Akebia upon request.

10. TERM; TERMINATION

10.1. **Term**. This Agreement will continue in full force and effect, unless otherwise terminated in accordance with this Article 10 (Term; Termination), until the expiration of all applicable Royalty Terms with respect to the Licensed Product on a country-by-country-basis in the Territory (the "**Term**"). On a country-by-country basis, upon the natural expiration of this Agreement as contemplated in this Section 10.1 (Term), so long as at such time Licensee has paid to Akebia all amounts due under this Agreement and accrued prior to such natural expiration of the Term in accordance with the terms hereof and is not at such time in material breach of any term of this Agreement, (a) the licenses granted to Licensee under Section 2.1 (License Grants to Licensee) will become non-exclusive, perpetual, and irrevocable with respect to such country in the Territory and (b) if Licensee uses any Product Mark or Akebia Housemark in connection with the Commercialization of the Licensed Product in any country in the Territory following the expiration of the Term, then the licenses granted to Licensee under Section 4.10.3 (Trademark License) to use the Product Marks and Akebia Housemarks will become non-exclusive and will bear a royalty of [**]% of Net Sales in each country in the Territory in which Licensee uses the Product Marks or Akebia Housemarks in connection with such Commercialization of the Licensed Product.

10.2. **Termination for Breach**. Subject to the terms and conditions of this Section 10.2 (Termination for Breach), a Party (the "**Non-Breaching Party**") will have the right, in addition to any other rights and remedies, to terminate this Agreement in its entirety in the event the other Party (the "**Breaching Party**") is in material breach of any of its obligations under this Agreement; *provided* that the Parties stipulate and agree that any breach by Licensee of its obligations under Section 4.3.3 (Development Diligence Obligations), Section 4.4.4 (Commercialization Diligence Obligations), or Section 5.1.3 (Minimum Royalties) will each be a material breach of its obligations under this Agreement with respect to which the terms of this Section 10.2 (Termination for Breach) will apply. The Non-Breaching Party will first provide written notice to the Breaching Party, which notice will identify with particularity the alleged breach and state the Non-Breaching Party's intent to terminate this Agreement if such breach is not cured. With respect to material breaches of any payment obligation hereunder, the Breaching Party will have a period of [**] after such written notice is provided to cure such breach. With respect to all other breaches, the Breaching Party will have a period of [**] after the Non-Breaching Party provides written notice to cure such breach.

10.3. **Termination for Bankruptcy**. Subject to the terms and conditions of this Agreement, either Party may terminate this Agreement upon notice to the other Party should the other Party: (a) consent to the appointment of a receiver or a general assignment for the benefit of creditors of the other Party that is not discharged within [**], or (b) file a petition under any bankruptcy or insolvency law or have any such petition filed against it that has not been stayed within [**] of such filing.

10.4. **Termination by Akebia for Patent Challenges**. If Licensee or any of its Affiliates or Sublicensees Challenges an Akebia Patent Right or Joint Patent Right in any country throughout the world, then Akebia may, in its sole discretion either (a) terminate this Agreement in its entirety, or (b) leave the Agreement in effect, but increase the Incremental Royalties payable to Akebia pursuant to Section 5.1 (Royalty Payments) by [**]% and, in any case, if Akebia so

chooses, sue Licensee for infringement in any forum of competent jurisdiction of Akebia's choosing.

10.5. **Termination by Licensee for Convenience**. Commencing on the date that is 12 months following the Effective Date, Licensee may terminate this agreement for convenience, without damage to Akebia, upon not less than 12 months' prior written notice to Akebia (*i.e.*, any such termination would not be effective until at least 24 months following the Effective Date).

10.6. **Termination by Licensee for Marketing Authorization or Exclusivity Failure**. If (a) Licensee has actually submitted for approval an MAA for the Licensed Product to the EMA, the EMA rejects such MAA, and the Parties in good faith agree that, based on communications from the EMA, submitting a modified MAA for the Licensed Product to the EMA will not result in approval of such modified MAA, or (b) Licensee has used Commercially Reasonable Efforts to seek Regulatory Approval of the Licensed Product for the Target Indication in the EMA, and [**], then in either case ((a) – (b)) Licensee may terminate this Agreement upon 30 days' prior written notice to Akebia.

10.7. **Effects of Termination**. In the event of any termination of this Agreement (but not expiration), the following will apply:

10.7.1. **Right of Reference**. The right of reference granted to Licensee pursuant to Section 4.2.4 (Right of Reference) will terminate. The right of reference granted to Akebia pursuant to Section 4.2.4 (Right of Reference) will survive.

10.7.2. **Return of Confidential Information**. Licensee will cease using the Akebia Technology and will return to Akebia or destroy all copies of any documents containing any Akebia Know-How. Each Party will return or destroy all Confidential Information of the other Party in its possession upon expiration or termination of this Agreement at the disclosing Party's election and written request. The Receiving Party will provide a written confirmation of such destruction within [**] of such request; *provided*, *however*, that the foregoing will not apply to any Confidential Information that is necessary to allow such Party to perform its obligations or exercise any of its rights that expressly survive the termination or expiration of this Agreement.

10.7.3. **License Grants to Akebia**. Licensee hereby grants and agrees to grant to Akebia with effect from the effective date of termination, an exclusive, fully paid-up, worldwide, perpetual, irrevocable right and license, with the right to grant sublicenses through multiple tiers, under Licensee's interest in all Licensee Technology to Develop, Manufacture, Commercialize, and otherwise Exploit the Licensed Product inside and outside of the Territory. If Licensee is unable to sublicense any Patent Rights or Know-How owned by Third Parties to Akebia as set forth under this Section 10.7.3 (License Grants to Akebia) without the consent of the Third Party, then Licensee undertakes, on request from Akebia, to use reasonable efforts to procure such licenses on behalf of Akebia in as far as it is able to do so, and Akebia will pay such fees and agree to be bound by the terms agreed between Akebia and the Third Party licensor.

10.7.4. **Appointment as Exclusive Distributor**. If the Licensed Product is being Commercialized by Licensee in any country in the Territory as of the effective date of termination, then, at Akebia's election (in its sole discretion) on a country-by-country basis in the Territory, until such time as all Regulatory Approvals with respect to such Licensed Product in such country have been assigned and transferred to Akebia, either (a) Licensee will appoint Akebia or its designee as its exclusive distributor of the Licensed Product in such country and grant Akebia or its designee the right to appoint sub-distributors, to the extent not prohibited by any written agreement between Licensee or any of its Affiliates and a Third Party; *provided* that Akebia will purchase any and all inventory of Licensed Product held by Licensee or its Affiliates as of the effective date of termination at a price equal to [**] for such inventory, or (b) Licensee will have the continued right to sell the Licensed Product in such country from its inventory; *provided*,

however, that Licensee's obligations under this Agreement with respect to all such Licensed Product that Licensee sells, including the obligation to remit royalties to Akebia hereunder, will continue in full force and effect during such period.

10.7.5. **Assignment and Disclosure**. Licensee will promptly (and in any event within [**] after the effective date of termination): (a) assign and transfer to Akebia or its designee all of Licensee's rights, title, and interests in and to all Regulatory Submissions, Regulatory Approvals, clinical trial agreements, and distribution agreements (to the extent assignable and not cancelled), confidentiality and other agreements, and Licensee Development Data (to the extent in Licensee's Control), in each case, relating to the Licensed Product and that are necessary or useful for the Exploitation of the Licensed Product, and (b) disclose to Akebia all documents that are controlled by Licensee or that Licensee is able to obtain using reasonable efforts, and that embody the foregoing. In addition, Licensee will promptly assign and transfer to Akebia or its designee, as of the effective date of termination, all of Licensee's rights, title, and interests in and to all domain names associated with the Product Marks (to the extent that they are owned by Licensee or its Affiliates), and will promptly (in any event, within [**] after the effective date of termination) provide to Akebia all login and password information necessary to maintain such domain names. Subject to Section 10.7.6 (Termination by Licensee for Breach), the costs associated with the assignments set forth in this Section 10.7.5 (Assignment and Disclosure) will be borne by Licensee.

10.7.6. **Termination by Licensee for Breach**. Notwithstanding any provision to the contrary set forth under this Section 10.7 (Effects of Termination), in the event of any termination of this Agreement by Licensee for Akebia's material breach pursuant to Section 10.2 (Termination for Breach), Akebia will be responsible for reimbursing Licensee for the costs associated with the assignments set forth in Section 10.7.5 (Assignment and Disclosure).

10.8. **Accrued Rights**. Expiration or termination of this Agreement will not relieve the Parties of any liability that accrued hereunder prior to the effective date of such expiration or termination, nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement, and any such termination will be without prejudice to the rights of either Party against the other. The remedies provided in this Article 10 (Term; Termination) are not exclusive of any other remedies a Party may have in law or equity. Without limiting the generality of the foregoing, upon expiration or termination of this Agreement Licensee will pay to Akebia all amounts due under this Agreement to Akebia as of the effective date of termination or expiration within [**] following such effective date of termination or expiration. All payments made pursuant to this Section 10.8 (Accrued Rights) will be non-creditable and non-refundable.

10.9. **No Waiver**. The right of a Party to terminate this Agreement, as provided in this Article 10 (Term; Termination), will not be affected in any way by its waiver or failure to take action with respect to any prior default.

10.10. **Survival**. Expiration or termination of this Agreement will not relieve the Parties of any obligation accruing hereunder prior to such expiration or termination. Without limiting the foregoing, the following provisions will survive expiration or termination of this Agreement: Article 1 (Definitions); Section 2.4 (License Grant to Akebia); Section 2.6 (Retained Rights); Section 2.7 (No Additional Rights; Compliance with [**] License); Section 4.2.4 (Right of Reference); Section 4.3.7 (Licensee Development Data) Section 4.10.2 (Ownership; Branding) (solely with respect to the penultimate and ultimate sentences therein); Section 4.10.3 (Trademark License) (solely with respect to the ultimate sentence therein); Section 5.2 (Late Payments; Disputed Payments) through Section 5.5 (Accounting; Audit); Section 6.1 (Ownership); Section 6.2 (Prosecution and Maintenance of Akebia Patent Rights and Joint Patent Rights) (solely with respect to Joint Patent Rights); Section 6.3 (Prosecution of Licensee Patent Rights); Section 6.4 (Enforcement of Akebia Patent Rights, Joint Patent Rights, and Licensee Patent Rights in the Territory) (solely with respect to Joint Patent Rights and Licensee Patent Rights); Section 6.5

(Defense Against a Third Party Challenge to Akebia Patent Rights and Joint Patent Rights outside the Territory) (solely with respect to Joint Patent Rights); Section 6.6 (Defense Against a Third Party Challenge to Joint Patent Rights in the Territory and Licensee Patent Rights); Article 7 (Confidentiality); Article 9 (Indemnification); Section 10.7 (Effects of Termination) through this Section 10.10 (Survival); Article 11 (Dispute Resolution; Governing Law); and Article 12 (Miscellaneous).

11. DISPUTE RESOLUTION; GOVERNING LAW

11.1. **Executive Officers; Disputes**. Each Party will ensure that an Executive Officer is designated for such Party at all times during the Term for dispute resolution purposes, and will promptly notify the other Party of any change in its designated Executive Officer. Except as expressly set forth in this Agreement, including matters subject to resolution under Section 3.6 (Decision-Making and Committee Dispute Resolution), in the event of a dispute arising under this Agreement between the Parties, the Parties will refer such dispute to their respective Executive Officer, and such Executive Officers or designees will attempt in good faith to resolve such dispute.

11.2. **Arbitration**. If the Parties are unable to resolve a given dispute within [**] of referring such dispute to the designated Executive Officers pursuant to Section 11.1 (Executive Officers; Disputes), then, other than a dispute with respect to the validity, scope, enforceability, or ownership of any Patent Rights or other intellectual property rights under this Agreement (unless otherwise agreed by the Parties), either Party may have such dispute settled by binding arbitration in the manner described below:

11.2.1. **Arbitration Request**. If a Party intends to begin an arbitration proceeding to resolve a dispute arising under this Agreement, then such Party will provide written notice (the "**Arbitration Request**") to the other Party of such intention and the issues for resolution. From the date of the Arbitration Request and until such time as the dispute has become finally settled, the running of the time periods within which a Party must cure a breach of this Agreement will be suspended with respect to the subject matter of the dispute.

11.2.2. **Additional Issues**. Within [**] after the receipt of the Arbitration Request, the other Party may, by written notice, add additional issues for resolution.

11.2.3. **Arbitration Procedure**. Except as expressly provided in this Agreement, any dispute, controversy, or claim arising out of or in connection with this Agreement, including any question regarding its existence, validity, or termination, will be referred to and finally resolved by binding arbitration administered by the London Court of International Arbitration ("**LCIA**") in accordance with its rules as then in effect, which rules are deemed to be incorporated by reference into this Section 11.2.3 (Arbitration Procedure). There will be one arbitrator, and such arbitrator will be chosen pursuant to the LCIA Rules. The seat, or legal place, of arbitration will be London, United Kingdom, or such other venue as the Parties agree. The language to be used in the arbitral proceedings will be English. THE PARTIES UNDERSTAND AND ACKNOWLEDGE THAT UNDER THIS SECTION 11.2.3 (ARBITRATION PROCEDURE) EACH PARTY WAIVES THE RIGHT TO A TRIAL BY JURY IN CONNECTION WITH ANY ARBITRABLE CONTROVERSY OR CLAIM. The Parties hereby agree that the arbitrator has authority to issue rulings and orders regarding all procedural and evidentiary matters that the arbitrator deems reasonable and necessary with or without petition therefor by the Parties as well as the final ruling and judgment. All rulings by the arbitrator will be final. Judgment on the award granted in any arbitration hereunder may be entered in any court having jurisdiction over the award or any of the Parties or any of their respective assets. Nothing in this Agreement will prevent either Party from seeking injunctive relief (or any other provisional remedy) from any court having jurisdiction over the Parties and the subject matter of the dispute as necessary to protect either Party's name, proprietary information, trade secrets, Know-How, or any other proprietary right or otherwise to avoid irreparable harm. If the issues in dispute involve scientific or technical matters, then any arbitrator chosen hereunder will have educational training or experience

sufficient to demonstrate a reasonable level of knowledge in the field of biotechnology and pharmaceuticals. The Parties agree that arbitration of any dispute will be confidential, and all claims, proceedings, and evidence provided in the arbitration and all decisions of the arbitrators will be considered the Confidential Information of both Parties under this Agreement.

11.3. **Intellectual Property Disputes**. Notwithstanding Section 11.2 (Arbitration), if a dispute arises with respect to the validity, scope, enforceability, or ownership of any Patent Right or other intellectual property rights, and such dispute is not resolved in accordance with Section 11.1 (Executive Officers; Disputes), then such dispute will not be submitted to an arbitration proceeding in accordance with Section 11.2 (Arbitration), unless otherwise agreed by the Parties in writing, and instead, either Party may initiate litigation in a court of competent jurisdiction in any country in which such rights apply.

11.4. **Choice of Law; English Language**. This Agreement and all amendments, modifications, alterations, or supplements hereto, and the rights of the Parties hereunder, will be construed under and governed by the substantive laws of the State of New York, exclusive of its conflicts of laws principles. This Agreement has been prepared in the English language and the English language will control its interpretation. All consents, notices, reports, and other written documents to be delivered or provided by a Party under this Agreement will be in the English language, and in the event of any conflict between the provisions of any document and the English language translation thereof, the terms of the English language translation will control.

12. MISCELLANEOUS

12.1. **Assignment**. Licensee may not assign its rights and obligations under this Agreement without Akebia's prior written consent, except that Licensee may assign this Agreement (in whole or in part) without such consent (a) in connection with the transfer or sale of all or substantially all of its assets to a Third Party, (b) in the event of its merger or consolidation with another company, or (c) to an Affiliate. Licensee will provide Akebia with prompt written notice of any such assignment. Any permitted assignee pursuant to clause (a) or (b) above will assume all obligations of its assignor under this Agreement, and no permitted assignment will relieve the assignor of liability for its obligations hereunder. Any attempted assignment in contravention of the foregoing will be void. Akebia may assign its rights and obligations under this Agreement in whole or in part without Licensee's prior written consent, but will inform Licensee of assignment as soon as possible following the effective date of such assignment, which obligation may be satisfied through public disclosure.

12.2. **Entire Agreement; Amendment**. This Agreement, together with all exhibits and schedules attached hereto, constitutes the entire agreement between the Parties with respect to the subject matter hereof including that certain Mutual Confidentiality Agreement dated [**] by and between Licensee and Akebia (the "**Non-Disclosure Agreement**") and all information shared by the Parties pursuant to the Non-Disclosure Agreement will be Confidential Information under this Agreement, and the use and disclosure thereof will be governed by Article 7 (Confidentiality). This Agreement will not be modified, or amended, except by another agreement in writing executed by the Parties.

12.3. **Severability**. If any provision of this Agreement is declared invalid by a court of last resort or by any court or other governmental body from the decision of which an appeal is not taken within the time provided by law, then and in such event, this Agreement will be deemed to have been terminated only as to the portion thereof that relates to the provision invalidated by that decision and only in the relevant jurisdiction, but this Agreement will remain in force, in all other respects and all other jurisdictions; *provided*, *however*, that if the provision so invalidated is essential to the Agreement as a whole, then the Parties will negotiate in good faith to amend the terms hereof as nearly as practical to carry out the original intent of the Parties, and, failing such amendment, either Party may submit the matter for resolution pursuant to Article 11 (Dispute Resolution; Governing Law).

12.4. **Notices**. All notices that are required or permitted hereunder will be in writing and sufficient if delivered by internationally-recognized overnight courier or sent by registered or certified mail, postage prepaid, return receipt requested, and in each case, addressed as follows (with a courtesy copy sent by email, which will not constitute notice):

If to Akebia:

Akebia Therapeutics, Inc.
245 First Street
Cambridge, MA 02142
Attention: Chief Executive Officer
Email: [**]

with a copy to (which will not constitute notice):

Ropes & Gray LLP
800 Boylston Street; Prudential Tower
Boston, MA 02199
Attention: Hannah H. England
Email: [**]

If to Licensee:
Averoa
11 avenue Paul Verlaine
38 100 Grenoble – France
Attention – Chief Executive Officer
Email: [**]
with a copy to:

MCE Carrel
67 rue de Miromesnil
75008 Paris
Attention – Alexandra Carrel
Email: [**]

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith. Any such notice will be deemed to have been given: (a) on the Business Day after dispatch if sent by internationally-recognized overnight courier; or (b) on the fifth Business Day after dispatch if sent by registered or certified mail, postage prepaid, return receipt requested.

12.5. **Force Majeure**. Both Parties will be excused from the performance of their obligations under this Agreement to the extent that such performance is prevented by force majeure and the nonperforming Party promptly provides notice of the prevention to the other Party. Such excuse will continue only so long as the condition constituting force majeure continues and the nonperforming Party takes reasonable efforts to remove the condition. When the force majeure no longer exists, the affected Party must promptly resume performance. For purposes of this Agreement, "force majeure" will include conditions beyond the reasonable control of the non-performing Party, including an act of God, war, civil commotion, terrorist act, labor strike or lock-out, epidemic, pandemic, failure or default of public utilities or common carriers, destruction of production facilities or materials by fire, earthquake, storm or like catastrophe, failure of plant or machinery and act (or failure to act) of a government of any country or of any Governmental Authority (other than as a result of the non-performing Party's failure to comply with Applicable Law). The Parties agree the effects of the COVID-19 pandemic that is ongoing as of the Effective Date may be invoked as a force majeure for the purposes of this Agreement even though the pandemic is ongoing to the extent those effects are not reasonably foreseeable by the Parties as of the Effective Date. Notwithstanding the foregoing, a Party will not be excused from making undisputed payments that have accrued and are owed hereunder because of a force

majeure affecting such Party. The affected Party will notify the other Party in writing of any force majeure circumstances that may affect its performance under this Agreement as soon as reasonably practical, will provide a good faith estimate of the period for which its failure or delay in performance under the Agreement is expected to continue based on currently available information, and will undertake reasonable efforts necessary to mitigate and overcome such force majeure circumstances and resume normal performance of its obligations hereunder as soon as reasonably practicable under the circumstances. If the force majeure circumstance continues, then the affected Party will update such notice to the other Party on a bi-weekly basis, or more frequently if requested by the other Party, to provide updated summaries of its mitigation efforts and its estimates of when normal performance under the Agreement will be able to resume. If Licensee's failure to perform its obligations under this Agreement as a result of a force majeure continues for longer than [**], then Akebia may terminate this Agreement immediately upon written notice to Licensee.

12.6. **Further Assurances**. The Parties agree to reasonably cooperate with each other in connection with any actions required to be taken as part of their respective obligations under this Agreement, and will (a) furnish to each other such further information; (b) execute and deliver to each other such other documents; and (c) do such other acts and things (including working collaboratively to correct any clerical, typographical, or other similar errors in this Agreement), all as the other Party may reasonably request for the purpose of carrying out the intent of this Agreement.

12.7. **Performance by Affiliates**. Notwithstanding anything to the contrary set forth herein, either Party will have the right to perform any or all of its obligations and exercise any or all of its rights under this Agreement through any Affiliate. Each Party hereby guarantees the performance by its Affiliates of such Party's obligations under this Agreement, and will cause its Affiliates to comply with the provisions of this Agreement in connection with such performance.

12.8. **Independent Contractors**. It is expressly agreed that Akebia and Licensee will be independent contractors and that the relationship between the two Parties will not constitute a partnership, joint venture or agency. Neither Akebia nor Licensee will have the authority to make any statements, representations, or commitments of any kind, or to take any action that is binding on the other Party without the prior written consent of the other Party.

12.9. **Exit of the United Kingdom from E.U.** At either Party's request, the Parties will discuss and agree upon such amendments to this Agreement as may be necessary to fairly and reasonably adjust the terms of this Agreement in light of the United Kingdom's exit from the E.U. Any such amendment should preserve the basic economic and legal terms of this Agreement insofar as possible in light of the change in circumstances caused by the United Kingdom's exit from the E.U.

12.10. **Agency**. Except as expressly set forth herein, neither Party is, nor will be deemed to be an employee, agent, or representative of the other Party for any purpose. Each Party is an independent contractor, not an employee or partner of the other Party. Except as expressly set forth herein, neither Party will have the authority to speak for, represent, or obligate the other Party in any way without prior written authority from the other Party.

12.11. **No Waiver**. Any waiver of any provision of this Agreement will be effective only if in writing and signed by Akebia and Licensee. Any omission or delay by either Party at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants, or provisions hereof, by the other Party, will not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement. Any waiver by a Party of a particular breach or default by the other Party will not operate or be construed as a waiver of any subsequent breach or default by the other Party.

12.12. **No Strict Construction**. This Agreement has been prepared jointly by the Parties and will not be strictly construed against either Party.

12.13. Interpretation. (a) Whenever any provision of this Agreement uses the term "including" (or "includes"), such term will be deemed to mean "including without limitation" and "including but not limited to" (or "includes without limitations" and "includes but is not limited to") regardless of whether the words "without limitation" or "but not limited to" actually follow the term "including" (or "includes"); (b) "herein," "hereby," "hereunder," "hereof," and other equivalent words will refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word is used; (c) all definitions set forth herein will be deemed applicable whether the words defined are used herein in the singular or the plural; (d) wherever used herein, any pronoun or pronouns will be deemed to include both the singular and plural and to cover all genders; (e) the recitals set forth at the start of this Agreement, along with the schedules and exhibits to this Agreement, and the terms and conditions incorporated in such recitals and schedules and exhibits will be deemed integral parts of this Agreement and all references in this Agreement to this Agreement will encompass such recitals and schedules and exhibits and the terms and conditions incorporated in such recitals and schedules and exhibits; *provided* that in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the recitals, schedules, or exhibits, the terms of this Agreement will control; (f) in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement, or otherwise, the terms and conditions of this Agreement will govern; (g) this Agreement will be construed as if both Parties drafted it jointly, and will not be construed against either Party as principal drafter; (h) unless otherwise provided, all references to Sections, Articles, and Schedules in this Agreement are to Sections, Articles, and Schedules of and to this Agreement; (i) any reference to any federal, national, state, local, or foreign statute or law will be deemed to also refer to all rules and regulations promulgated thereunder, unless the context requires otherwise; (j) wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another; (k) the word "or" will not be exclusive; (l) references to a particular person include such person's successors and assigns to the extent not prohibited by this Agreement; and (m) the section headings and captions used herein are inserted for convenience of reference only and will not be construed to create obligations, benefits, or limitations.

12.14. Cumulative Remedies. No remedy referred to in this Agreement is intended to be exclusive, but each will be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law.

12.15. Further Actions. Each Party agrees to execute, acknowledge, and deliver such further instruments, and to do all such other acts, as necessary or appropriate in order to carry out the purposes and intent of this Agreement.

12.16. Counterparts. This Agreement may be executed in counterparts, all of which taken together will be regarded as one and the same instrument. Counterparts may be delivered via electronic mail, including Adobe™ Portable Document Format (PDF) or any electronic signature complying with the U.S. Federal ESIGN Act of 2000, and any counterpart so delivered will be deemed to be original signatures, will be valid and binding upon the Parties, and, upon delivery, will constitute due execution of this Agreement.

[*Signatures Page Follows*]

IN WITNESS WHEREOF, the Parties intending to be bound have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

AVEROA SAS

By: /s/ Luc-André Granier

Name: Luc-André GRANIER

Title: CEO

AKEBIA THERAPEUTICS, INC.

By: /s/ David Spellman

Name: David Spellman

Title: Senior Vice President, Chief Financial Officer, and Treasurer

KERYX BIOPHARMACEUTICALS, INC.

By: /s/ David Spellman

Name: David Spellman

Title: Senior Vice President, Chief Financial Officer, and Treasurer

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-196748) pertaining to the Amended and Restated 2008 Equity Incentive Plan, the 2014 Incentive Plan, and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(2) Registration Statement (Form S-8 No. 333-209469) pertaining to the 2014 Incentive Plan and the 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(3) Registration Statement (Form S-8 No. 333-216475) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,

(4) Registration Statement (Form S-8 No. 333-222728) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,

(5) Registration Statement (Form S-8 No. 333-228772) pertaining to the 2014 Incentive Plan of Akebia Therapeutics, Inc. and the 1999 Share Option Plan, 2004 Long-Term Incentive Plan, 2007 Incentive Plan, Amended and Restated 2013 Incentive Plan, and 2018 Equity Incentive Plan of Keryx Biopharmaceuticals, Inc.,

(6) Registration Statement (Form S-8 No. 333-229366) pertaining to the 2014 Incentive Plan, the 2014 Employee Stock Purchase Plan, and the Inducement Grant Awards (January 2018 – December 2018) of Akebia Therapeutics, Inc.,

(7) Registration Statement (Form S-8 No. 333-233140) pertaining to the Amended and Restated 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,

(8) Registration Statement (Form S-8 No. 333-236060) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2019 – December 2019) of Akebia Therapeutics, Inc.,

(9) Registration Statement (Form S-8 No. 333-252336) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2020 – December 2020) of Akebia Therapeutics, Inc.,

(10) Registration Statement (Form S-3 No. 333-253539) of Akebia Therapeutics, Inc.,

(11) Registration Statement (Form S-8 No. 333-262392) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2021 – December 2021) of Akebia Therapeutics, Inc., and

(12) Registration Statement (Form S-8 No. 333-269457) pertaining to the 2014 Incentive Plan and the Inducement Grant Awards (January 2022 – December 2022) of Akebia Therapeutics, Inc.;

of our reports dated March 10, 2023, with respect to the consolidated financial statements of Akebia Therapeutics, Inc. and the effectiveness of internal control over financial reporting of Akebia Therapeutics, Inc. included in this Annual Report (Form 10-K) of Akebia Therapeutics, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 10, 2023

Exhibit 31.1

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John P. Butler, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2023

By: /s/ John P. Butler
John P. Butler
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David A. Spellman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Akebia Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the Audit Committee of the registrant's Board of Directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 10, 2023

By: /s/ David A. Spellman
David A. Spellman
Senior Vice President, Chief Financial Officer
and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002 (18 U.S.C. Section 1350)

In connection with the accompanying Annual Report of Akebia Therapeutics, Inc. (the Company) on Form 10-K for the fiscal year ended December 31, 2022 (the Report), I, John P. Butler, as Chief Executive Officer and President of the Company, and I, David A. Spellman, as Senior Vice President, Chief Financial Officer and Treasurer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date:	March 10, 2023	By:	/s/ John P. Butler John P. Butler President, Chief Executive Officer and Director (Principal Executive Officer)
Date:	March 10, 2023	By:	/s/ David A. Spellman David A. Spellman Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)