

**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, 2020

OR

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

Commission File Number 001-36352

**AKEBIA THERAPEUTICS, INC.**

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of  
incorporation or organization)

245 First Street, Cambridge, MA  
(Address of principal executive offices)

20-8756903

(I.R.S. Employer  
Identification No.)

02142  
(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 Global 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	<input checked="" type="checkbox"/>	Accelerated Filer	<input type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/>	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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.

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, 2020, was \$1,913,868,347.

The number of shares of registrant's Common Stock outstanding as of February 19, 2021 was 153,502,435.

**DOCUMENTS INCORPORATED BY REFERENCE**

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2021 Annual Meeting of Stockholders within 120 days after the end of the registrant's fiscal year ended December 31, 2020. Portions of the proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

## TABLE OF CONTENTS

	<u>Page No.</u>
<u>PART I</u>	<u>6</u>
<u>Item 1. Business</u>	<u>6</u>
<u>Item 1A. Risk Factors</u>	<u>42</u>
<u>Item 1B. Unresolved Staff Comments</u>	<u>95</u>
<u>Item 2. Properties</u>	<u>95</u>
<u>Item 3. Legal Proceedings</u>	<u>95</u>
<u>Item 4. Mine Safety Disclosures</u>	<u>100</u>
<u>PART II</u>	<u>101</u>
<u>Item 5. Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	<u>101</u>
<u>Item 6. Selected Financial Data</u>	<u>103</u>
<u>Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations</u>	<u>104</u>
<u>Item 7A. Quantitative and Qualitative Disclosures About Market Risk</u>	<u>128</u>
<u>Item 8. Financial Statements and Supplementary Data</u>	<u>129</u>
<u>Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	<u>188</u>
<u>Item 9A. Controls and Procedures</u>	<u>188</u>
<u>Item 9B. Other Information</u>	<u>191</u>
<u>PART III</u>	<u>191</u>
<u>Item 10. Directors, Executive Officers and Corporate Governance</u>	<u>191</u>
<u>Item 11. Executive Compensation</u>	<u>191</u>
<u>Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	<u>192</u>
<u>Item 13. Certain Relationships and Related Transactions, and Director Independence</u>	<u>192</u>
<u>Item 14. Principal Accountant Fees and Services</u>	<u>192</u>
<u>PART IV</u>	<u>193</u>
<u>Item 15. Exhibits, Financial Statement Schedules</u>	<u>193</u>
<u>Item 16. Form 10-K Summary</u>	<u>199</u>
<u>SIGNATURES</u>	<u>200</u>

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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;
- establishing vadadustat as a new oral standard of care for treatment of adult patients with anemia due to chronic kidney disease;
- the timing, investment and associated activities involved in continued commercialization of Auryxia<sup>®</sup> (ferric citrate), its growth opportunities and Akebia's 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 timing of or likelihood of regulatory filings and approvals, including labeling or other restrictions, such as the anticipated timing of filing a New Drug Application for vadadustat to the U.S. Food and Drug Administration or the E.U. Marketing Authorization Application to the European Medicines Agency, the potential approval of vadadustat and our outlook related thereto, and potential indications for vadadustat;
- the potential therapeutic applications of the hypoxia inducible factor pathway;
- our pipeline and portfolio, including its potential, and our related research and development activities;
- our competitive position, including estimates, developments and projections relating to our competitors and their products and product candidates, and our industry;
- our expectations with respect to (i) the ongoing anticipated financial impact and potential benefits to us related to our merger with Keryx Biopharmaceuticals, Inc. that was completed on December 12, 2018, (ii) integration of the businesses subsequent to the merger, and (iii) other matters related to the merger;
- 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, our internal control over financial reporting and disclosure controls and procedures, and remediation of the material weakness we have identified in our internal control over financial reporting relating to our inventory process or any future deficiencies or material weaknesses in our internal controls and procedures;
- the direct or indirect impacts of the coronavirus 2 (SARS-CoV-2) 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, contingent consideration, 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 targeted timing of enrollment of our clinical trials;
- the timing of initiation of our clinical trials and plans to conduct preclinical and clinical studies 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, as well as Abbreviated New Drug Applications filed by generic drug manufacturers and potential U.S. Food and Drug Administration approval thereof, and associated patent infringement suits that we have filed or may file, or other actions that we may take against such 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 our key 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; 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.

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 following:

- 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 could force us to delay, limit, reduce or terminate our product development or commercialization efforts;
- Our obligations in connection with the Loan Agreement with Pharmakon 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;
- Royalties from commercial sales of vadadustat under our Collaboration Agreement with Mitsubishi Tanabe Pharma Corporation will likely fluctuate and will impact our rights to receive future payments from our Royalty Interest Acquisition Agreement with HealthCare Royalty Partners IV, L.P.;
- 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 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;
- We may fail to realize the anticipated benefits of our merger with Keryx, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties and liabilities, which may have a material adverse effect on our business and financial position;
- Our business has been and may continue to be, directly or indirectly, adversely affected by the COVID-19 pandemic;
- Our ability to successfully commercialize any approved product, including our ability to achieve their widespread market acceptance, is critical to the success of our business;
- If we are unable to maintain sales, marketing and distribution capabilities or to enter into additional agreements with third parties, we may not be successful in commercializing any approved product;
- If we are unable to obtain or maintain contracts with key distribution partners, our business could be materially harmed;
- 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<sup>TM</sup> 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;
- In addition to Auryxia, we will continue to depend heavily on the success of our product candidate, vadadustat, which recently completed Phase 3 clinical development. Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates;
- We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of Auryxia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired;
- Auryxia, vadadustat or any other product and product candidate, including those that may be in-licensed or acquired, may cause undesirable side effects or have other properties that delay or limit their commercial potential, or in the case of vadadustat, prevent its marketing approval;
- We may not be successful in our efforts to identify, acquire, discover, develop and commercialize additional products or product candidates, which could impair our ability to grow;
- We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat, 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 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. Failure to comply with applicable laws could subject us to government scrutiny or government enforcement, potentially resulting in costly investigations and/or fines or sanctions, or impacting our relationships with key regulatory agencies such as the U.S Food and Drug Administration, the U.S. Securities and Exchange Commission or the European Medicines Agency;
- Our relationships with healthcare providers, physicians and third party payors are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings;
- 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 rely on third parties to conduct our clinical studies and certain of our preclinical studies for our product and product candidates. If they do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to optimize the commercialization of Auryxia or obtain marketing approval for or commercialize vadaystat or any other product candidates, and our business could be substantially harmed;
- We rely on third parties to conduct all aspects of our product manufacturing. The loss of these manufacturers, their failure to supply us on a timely basis, or their failure to successfully carry out their contractual duties or comply with regulatory requirements or guidance could cause delays in or disruptions to our supply chain and substantially harm our business;
- We may seek to establish additional collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans;
- 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;
- If we fail to attract, keep and motivate senior management and key personnel, we may be unable to successfully develop and commercialize any product candidates and approved product(s);
- Our employees, independent contractors, principal investigators, contract research organizations, contract manufacturing organizations, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading;
- We may encounter difficulties in managing our growth and expanding our operations successfully;
- Our stock price has been and may continue to be volatile, which could result in substantial losses for purchasers of our common stock and lawsuits against us and our officers and directors;
- We have identified a material weakness in our internal control over financial reporting relating to our inventory process. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting which would harm our business and the trading price of our common stock; and
- 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.

## PART I

### Item 1. Business

#### Overview

We are a biopharmaceutical company with the purpose of bettering the life of each person impacted by kidney disease. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative renal therapeutics that we believe serves as a foundation for future growth. As a leader in the kidney community, we remain committed to helping patients and others where we believe our current and future products have the ability to deliver value. Our portfolio includes a late-stage product candidate and a commercial product:

- **Vadadustat** is an investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which stimulates erythropoietin, or EPO, production and leads to red blood cell, or RBC, production and improved oxygen delivery to tissues. The significance of the HIF pathway was recognized by the 2019 Nobel Prize and the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. We believe that, based on the HIF-PHI mechanism of action and clinical data to date, vadadustat has the potential to set a new oral standard of care for the treatment of anemia due to chronic kidney disease, or CKD.

We recently completed the global Phase 3 clinical development program for vadadustat, which included two separate programs, INNO<sub>2</sub>VATE and PRO<sub>2</sub>TECT. INNO<sub>2</sub>VATE evaluated vadadustat for the treatment of anemia due to CKD in adult patients on dialysis, or DD-CKD, and PRO<sub>2</sub>TECT evaluated vadadustat for the treatment of anemia due to CKD in adult patients not on dialysis, or NDD-CKD.

In May of 2020, we announced positive top-line results from our Phase 3 INNO<sub>2</sub>VATE program that showed vadadustat was non-inferior to darbepoetin alfa, an injectable erythropoiesis-stimulating agent, or ESA, with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (assessed in a time to the first occurrence of a major adverse cardiovascular event (MACE) analysis, which is the composite of all-cause mortality, nonfatal myocardial infarction, or a nonfatal stroke) in treating anemia due to CKD in DD-CKD adult patients. In addition to meeting the primary endpoints of the INNO<sub>2</sub>VATE program, vadadustat met the key secondary hematological efficacy endpoint in each of the two studies in the program and also met the program's key secondary safety endpoints. The results of the INNO<sub>2</sub>VATE program were presented at American Society of Nephrology, or ASN, in October of 2020.

In September of 2020, we announced top-line results from our Phase 3 PRO<sub>2</sub>TECT program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients. While the PRO<sub>2</sub>TECT data showed that vadadustat achieved both the primary and key secondary hematological efficacy endpoints, it did not meet the program's primary cardiovascular safety (MACE) endpoint. These cardiovascular outcomes contrast with those reported within the INNO<sub>2</sub>VATE program, which evaluated vadadustat for the treatment of anemia due to CKD in DD-CKD adult patients. The results of the PRO<sub>2</sub>TECT program were presented at ASN in October of 2020. Simultaneous with the PRO<sub>2</sub>TECT ASN presentation, we presented additional analyses, conducted by Akebia, of data from the PRO<sub>2</sub>TECT program that 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.

We plan to proceed with the submission of a New Drug Application, or NDA, for vadadustat by the middle of the second quarter of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. We are also working in close collaboration with our collaboration partner, Otsuka Pharmaceutical Co. Ltd., to prepare a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients for submission to the European Medicines Agency, or EMA, expected in 2021. However, as vadadustat did not meet the PRO<sub>2</sub>TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in NDD-CKD adult patients in the United States and Europe.

In June of 2020, we announced the first regulatory approval of vadadustat for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients in Japan. Our collaboration partner in Japan, Mitsubishi

Tanabe Pharma Corporation, or MTPC, commenced commercial sales of vadadustat in Japan under the trade name, Vafseo™, in August 2020.

In addition to anemia due to CKD, we believe that vadadustat has the potential to treat other serious or life-threatening conditions, including preventing and lessening the severity of acute respiratory distress syndrome, or ARDS, a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, infection. More specifically, in July of 2020, we announced an investigator-sponsored clinical study 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 lessen the severity of ARDS in up to 400 adult patients who have been hospitalized due to COVID-19. Within this randomized, double-blind, placebo-controlled study, patients will be dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. This study is being conducted under a U.S. Food and Drug Administration, or FDA, Investigational New Drug application, or IND, with UTHealth as the study sponsor and is currently enrolling patients. In January of 2021, UTHealth announced that it had been awarded \$5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at its facilities.

- **Auryxia® (ferric citrate)** is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, under the trade name Riona (ferric citrate hydrate).

We plan to commercialize vadadustat, subject to FDA approval, in the United States with our existing nephrology-focused commercial organization, while also leveraging our collaboration with Otsuka Pharmaceutical Co. Ltd., or Otsuka, and its U.S. commercial organization. We granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. We granted MTPC exclusive rights to commercialize vadadustat in Japan, where MTPC is currently commercializing vadadustat under the trade name, Vafseo™, and in certain other countries in Asia, subject to marketing approvals. We also granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, which manages approximately 40% of the dialysis patients in the United States, at its U.S. dialysis clinics, and to certain third party dialysis organizations in the United States, approved by us, or Third Party Dialysis Organizations, which account for up to an additional 20% of the dialysis market in the United States. The license granted to Vifor Pharma would be effective upon FDA approval of vadadustat in the DD-CKD indication, the earlier of a determination by the Centers for Medicare & Medicaid Services, or CMS, that vadadustat will be included in Medicare's bundled reimbursement model or that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment, or TDAPA, and a milestone payment by Vifor Pharma.

We market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona in Japan.

On December 12, 2018, we completed a merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx, combining a nephrology-focused commercial organization with our robust development organization. Following the Merger, Keryx is our wholly owned subsidiary.

## Strategy

Our mission and our culture are centered around the goal of improving the lives of people impacted by kidney disease through the discovery, development and commercialization of innovative therapeutics. Our strategy is to execute on the following initiatives, which we believe will create significant market opportunities for us:

- **Prepare for the potential commercialization of vadadustat for the treatment of anemia due to CKD in the United States and Europe.** We believe vadadustat has the potential to address limitations of injectable ESAs, and set a new oral standard of care for the treatment of anemia due to CKD, subject to regulatory approval. We plan to submit an NDA for vadadustat to the FDA by the middle of the second quarter of 2021. In addition, we and Otsuka are working in close collaboration to prepare an MAA for vadadustat for submission to the EMA in 2021. We believe we are well positioned to commercialize vadadustat in the United States with our nephrology-focused commercial team, our partnership with Otsuka, and our agreement with Vifor Pharma, subject to FDA approval. We plan to support Otsuka's commercialization of vadadustat in Europe



and certain other markets, subject to regulatory approvals. We retain full commercial rights to vadadustat in Latin America, allowing us maximum flexibility in the region.

- **Support vadadustat (Vafseo) adoption and growth in Japan.** We plan to continue to support MTPC's commercialization of Vafseo in Japan. We also plan to support MTPC's commercialization efforts for vadadustat in certain other markets in Asia for which MTPC has commercialization rights, subject to regulatory approvals.
- **Maximize the value of Auryxia, and leverage the product as a commercial foundation for vadadustat, in CKD.** We aim to 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, patients and their families. In addition to bringing meaningful clinical benefits to patients, Auryxia provides strategic value to Akebia by allowing us to leverage our existing nephrology-focused commercial footprint and deepen key customer and prescriber relationships that we believe will be important for the future commercialization of vadadustat, if approved, and other potential future renal products.
- **Advance vadadustat clinical development for additional therapeutic indications.** In addition to our CKD program and the ARDS study, we plan to identify and initiate development planning for other programs where vadadustat may have therapeutic benefits.
- **Expand our pipeline and portfolio of novel therapeutics.** We aim to add to our pipeline and portfolio of novel therapeutics through internal discovery and development, and through strategic transactions, such as in-licenses, collaborations and acquisitions. In addition, given our expertise in research and development, we believe there may be opportunities to leverage these assets and establish mutually beneficial relationships with other companies that are looking to enter the renal market or attempting to develop renal therapeutics.

Our management team has extensive experience in developing and commercializing drugs for the treatment of renal and metabolic disorders, 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 kidney 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, affecting about 37 million patients and costing Medicare over \$120 billion annually in 2017 for treating Medicare beneficiaries with CKD of end-stage renal disease or end-stage kidney disease, or ESRD or ESKD. 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 dependence on dialysis or kidney transplant for survival, causing renal failure, directly or indirectly, by accelerating the onset of CKD. 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. It is our vision, in time, 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. As illustrated in the table below, CKD patients are categorized in one of five stages based on the degree of their loss of kidney function as measured by the glomerular filtration rate, or GFR, and the level of protein in the urine, referred to as albuminuria.

Stages and Prevalence of CKD in the United States

Stage	Description	GFR (mL/min/1.73m <sup>2</sup> ) <sup>a</sup>	U.S. Prevalence Rates <sup>b, c</sup>	Estimated Number of U.S. Patients (millions) <sup>d, e</sup>
1	Kidney damage with normal or increased GFR	≥90	4.6%	11.2
2	Kidney damage with mildly decreased GFR	60-89	3.0%	7.3
3	Moderately decreased GFR	30-59	6.7%	16.4
4	Severely decreased GFR	15-29	0.4%	1.0
5	Kidney failure (includes non dialysis, dialysis and transplant)	<15 (or dialysis)	0.3% (calculated)	0.7

Sources:

- a. GFR categories defined in the August 2012 Kidney Disease Improving Global Outcomes Clinical Practice Guideline for Anemia in Chronic Kidney Disease, p. vii.
- b. U.S. Prevalence Rates for Stages 1-4 based on averages of data from 2011-2012, 2013-2014, and 2015-2016, CDC CKD Surveillance System, National Health and Nutrition Examination Survey, or NHANES.
- c. U.S. Prevalence Rate for Stage 5 is based on a calculation using estimated number of U.S. patients with ESRD from 2018 U.S. Renal Data System Annual Report, as set forth in this table, and U.S. population data for people 20 years and older from www.census.gov.
- d. Estimated Number of U.S. Patients for Stages 1-4 based on the 2018 U.S. Prevalence rates, as set forth in this table, as applied by Akebia to U.S. population data for people 20 years and older from www.census.gov.
- e. Estimated Number of U.S. End-Stage Renal Disease Patients from 2018 U.S. Renal Data System Annual Report.

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. According to an article in *The Lancet* published in May 2013, projected worldwide population changes suggest that the potential number of cases of CKD, specifically end-stage, will increase disproportionately in countries such as Japan, China and India where the number of elderly people is increasing. This effect will be accelerated further if the growth in the prevalence of hypertension and diabetes persists, along with the associated increased risk of stroke and cardiovascular disease, and access to treatment does not improve.

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, anemia is characterized by low hemoglobin levels and is typically associated with a worsening quality of life, increased hospitalizations and increased mortality. The prevalence of anemia increases with the severity of CKD from an estimated 20% in patients with Stage 3 NDD-CKD to an estimated 95% in patients with Stage 5 DD-CKD.

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 production of red blood cells 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.

The global Phase 3 clinical development program for vadadustat evaluated the efficacy and safety of vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients.

IDA in adult patients with NDD-CKD is an FDA-approved indication for Auryxia. Hyperphosphatemia in DD-CKD patients is also an FDA-approved indication for Auryxia. Hyperphosphatemia is another condition associated with CKD that is characterized by elevated serum phosphorus levels and is also typically associated with a worsening of health including increased cardiovascular risk and increased mortality.

## Market Opportunity for Vadadustat

### *Anemia due to Chronic Kidney Disease*

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 37 million people in the United States have CKD and approximately 5.7 million of these individuals suffer from anemia. The current standard of care for anemia due to CKD is treatment by injectable recombinant human ESAs, such as EPOGEN® (epoetin alfa) and Aranesp® (darbepoetin alfa), 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 \$6.1 billion in 2018. The vast majority of these sales are believed to have been for the treatment of anemia due to CKD.

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 ( $\geq 13.0$  to  $14.0$  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, injectable ESAs remain the current standard of care for both DD-CKD and NDD-CKD patients with anemia.

### *DD-CKD Market*

We believe there is a significant opportunity for vadadustat to address limitations of injectable ESAs and set a new oral standard of care for the treatment of anemia due to CKD in DD-CKD adult patients, subject to approval. In addition to clinical data from our Phase 3 INNO<sub>2</sub>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 U.S. dialysis market dynamics.

According to the U.S. Renal Data System, or USRDS, 2020 Annual Data Report, there were approximately 556,000 patients in the United States on dialysis in 2018, of which 88% were on in-center hemodialysis and the remainder on home dialysis, which includes both peritoneal dialysis and home hemodialysis. 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 FKC accounting for a vast majority of the dialysis population in the United States, treatment is usually driven by medical protocols that are rolled out 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 End Stage Renal Disease, or 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 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, including the process and timing associated with applying for and receiving codes to allow for reimbursement under TDAPA, which codes are assigned on a quarterly basis, the rule provides support for our assumption that new anemia treatments, including those in the HIF-PHI class, will be included in the ESRD Bundle and will be eligible for separate payment initially under TDAPA.

We believe these and other factors will help position vadadustat as a potential new oral standard of care for the treatment of anemia due to CKD in adult DD-CKD patients, upon approval.

## *NDD-CKD Market*

Data from the USRDS 2015 Annual Data Report indicate that the collective injectable ESA treatment rate in NDD-CKD patients in the United States decreased by approximately half from 2009 to 2013. As a result of the safety concerns associated with ESAs, today, a high proportion of NDD-CKD patients with anemia are either not treated or inadequately treated despite having low hemoglobin levels. In contrast to treatment with ESAs, we believe vadadustat, subject to regulatory approval, has the potential to expand the number of NDD-CKD patients receiving treatment by offering an alternative oral treatment for anemia due to CKD.

Results from our Phase 3 PRO<sub>2</sub>TECT program showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients, meeting both the primary and key secondary hematological efficacy endpoints. However, it did not meet the program's primary cardiovascular safety (MACE) endpoint. We plan to pursue regulatory approval for vadadustat for the treatment of anemia due to CKD in NDD-CKD adult patients; however, as PRO<sub>2</sub>TECT did not meet the program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat as a treatment for anemia due to CKD in NDD-CKD adult patients.

### *Vadadustat Has the Potential to Set a New Oral Standard of Care*

Below is a summary of the key clinical findings; further details are included below.

- *Vadadustat stimulated endogenous EPO production.* In two Phase 1 studies in normal healthy volunteers and one Phase 2 study in CKD patients, vadadustat increased serum EPO levels in a dose-dependent manner. Pre-dose EPO levels returned to baseline levels prior to subsequent daily dose. In these studies, vadadustat stimulated endogenous EPO production while avoiding supraphysiologic EPO levels.
- *Vadadustat significantly increased and maintained hemoglobin levels.* Our global Phase 3 program and Phase 2 studies in CKD patients with anemia demonstrated that vadadustat significantly increased and/or maintained hemoglobin levels. In addition, our partner, MTPC's, Phase 3 studies in Japanese NDD-CKD and DD-CKD patients with anemia due to CKD further demonstrated the durability of vadadustat with data that showed that vadadustat's effect on hemoglobin was sustained through to 52 weeks comparable to the control arm, darbepoetin alfa.
- *Vadadustat was dosed orally once daily and three times weekly.* Our Phase 2 studies showed that vadadustat can be orally dosed once daily in NDD-CKD patients with up to 20 weeks of dosing. In addition, our Phase 2 clinical study in DD-CKD patients demonstrated that in patients who remained on therapy, once daily oral dosing of vadadustat maintained stable hemoglobin levels in patients converting from injectable ESA therapy over 16 weeks. This study also showed the potential for three-times weekly dosing of vadadustat in DD-CKD. We are conducting and plan to conduct additional larger studies of vadadustat evaluating a modified approach to once-daily and three-times weekly dosing.
- *Vadadustat resulted in favorable changes in iron parameters.* In three Phase 2 clinical studies, treatment with vadadustat was associated with decreases in ferritin and hepcidin and increases in total iron binding capacity. These changes are consistent with improved iron mobilization and utilization for erythropoiesis in NDD-CKD and DD-CKD patients.

Based on this and other data, we believe vadadustat has the potential to be a treatment for anemia due to CKD by:

- stimulating erythropoiesis and avoiding supraphysiologic EPO levels;
- increasing hemoglobin in a predictable and controlled manner;
- minimizing hemoglobin excursions; and,
- providing convenient oral dosing.

### *Vadadustat Clinical Development Program*

We believe vadadustat has the potential to set a new oral standard of care for the treatment of anemia due to CKD, subject to regulatory approval. Below is a summary of the clinical development work undertaken for vadadustat.

#### *Recently Completed 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<sub>2</sub>VATE and PRO<sub>2</sub>TECT. INNO<sub>2</sub>VATE evaluated vadadustat in adult DD-CKD patients with anemia due to CKD in two studies, and PRO<sub>2</sub>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 once daily oral dosing of vadadustat against an injectable ESA active comparator, darbepoetin alfa.

Both the INNO<sub>2</sub>VATE and PRO<sub>2</sub>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<sub>2</sub>VATE and PRO<sub>2</sub>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<sub>2</sub>VATE and PRO<sub>2</sub>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<sub>2</sub>VATE and PRO<sub>2</sub>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<sub>2</sub>VATE Program within DD-CKD Adult Patients*

The two INNO<sub>2</sub>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<sub>2</sub>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<sub>2</sub>VATE program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE across both INNO<sub>2</sub>VATE studies.

#### Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the INNO<sub>2</sub>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<sub>2</sub>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<sub>2</sub>VATE's *Conversion* study of 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<sub>2</sub>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 prospectively agreed to by FDA and a non-inferiority margin of 1.3 prospectively agreed to by EMA.

The INNO<sub>2</sub>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.

INNO<sub>2</sub>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<sub>2</sub>TECT Program within NDD-CKD Adult Patients*

The two PRO<sub>2</sub>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<sub>2</sub>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<sub>2</sub>TECT program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE, across both PRO<sub>2</sub>TECT studies.

#### Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the PRO<sub>2</sub>TECT 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<sub>2</sub>TECT'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<sub>2</sub>TECT'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<sub>2</sub>TECT program (*Correction* and *Conversion* studies) (n=3,471):

- **Primary Safety MACE Endpoint Result:** Vadadustat did not meet the PRO<sub>2</sub>TECT 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<sub>2</sub>TECT 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<sub>2</sub>TECT analysis plan was prospectively designed to analyze the effect of regional differences, most notably, well-known differences in Hb treatment targets. Within PRO<sub>2</sub>TECT, 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 using age as a dichotomous variable, 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).

In October 2020, we announced that based on these analyses and the totality of the data from our Phase 3 program, we plan to pursue regulatory approval in the United States for vadadustat for the treatment of anemia in adult NDD-CKD patients. However, as vadadustat did not meet the PRO<sub>2</sub>TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in adult NDD-CKD patients and we look forward to working with the FDA in their review of these data.

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 and plan to conduct 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 (600 mg and 900 mg). We believe data from these and other studies could support registration of the modified approach to once daily dosing and supplemental registration of three times weekly dosing, and further strengthen our potential commercial position if vadadustat is approved for marketing.

#### *Hepatic Safety Profile of Vadadustat in Clinical Studies*

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 includes 8 completed Phase 2 and 3 studies in NDD-CKD patients, 10 completed Phase 1, 2, and 3 studies, and 1 ongoing Phase 3b study in subjects with DD-CKD patients, and 18 completed studies in healthy subjects (17 Phase 1 and one Phase 3). The review of hepatic safety included a blinded assessment of all hepatic events in the studies by a panel of hepatic experts and analysis by an independent hepatic expert and our team. Based on this review, we concluded that the data across the clinical program showed that the overall hepatic safety profiles of vadadustat and darbepoetin alfa appear to be similar. In addition, we concluded that there were no events across the clinical program that met the biochemical criteria for Hy's Law. More specifically, we concluded that the case of drug induced liver injury from our Phase 2b study of vadadustat in non-dialysis patients with anemia due to CKD that we previously reported as Hy's Law did not, in fact, meet the biochemical criteria of Hy's Law. Our conclusion on this case will be reflected in our NDA for vadadustat.

#### *Other Studies of Vadadustat*

We completed a series of clinical drug-drug interaction studies largely focusing on transporter pathways evaluating vadadustat as a victim (using probe inhibitors) or perpetrator (using probe substrates) of drug interactions. No meaningful drug interactions were observed with atorvastatin (P-gp/OATP1B1 substrate), pravastatin (OATP1B1/1B3 substrate), digoxin (P-gp substrate), furosemide (OAT1/OAT3 substrate), adefovir (OAT1 substrate), cyclosporine (P-gp/BCRP/OATP inhibitor), probenecid

(OAT3 and UGT inhibitor), or rabeprazole (gastric acid-reducing agent). With concomitant administration of vadadustat, a mild-to-moderate interaction was observed with simvastatin (OATP1B1/B3 substrate), and moderate drug interactions were observed with rosuvastatin (BCRP/OATP1B1/1B3 substrate), ferrous sulfate, and sulfasalazine (BCRP substrate). In addition, in vitro drug-drug interaction studies demonstrated a very low risk of vadadustat for drug interactions due to alteration of metabolic enzyme activities, i.e. cytochrome P450 or UDP-glucuronosyltransferase isoforms. No clinical drug-interaction was observed with celecoxib (CYP2C9).

### **Commercialization**

We are in the process of supporting MTPC's commercial launch of vadadustat in Japan, preparing for a potential commercial launch of vadadustat in the United States and supporting potential commercial launches of vadadustat in certain other markets. Our ability to launch vadadustat in the United States is dependent on the successful filing and defense of an NDA, and approval by the FDA.

We plan to commercialize vadadustat, subject to FDA approval, in the United States with our well-established, nephrology-focused commercial organization, while leveraging our collaboration with Otsuka and its U.S. nephrology commercial organization. We granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. We granted MTPC exclusive rights to commercialize vadadustat in Japan, where MTPC commenced commercial sales of vadadustat under the trade name, Vafseo<sup>TM</sup>, in August 2020, and in certain other countries in Asia, subject to marketing approvals. In addition, we granted Vifor Pharma an exclusive license to sell vadadustat to FKC and Third Party Dialysis Organizations, which combined manage up to approximately 60% of the dialysis patients in the United States, which would be effective upon FDA approval of vadadustat, the earlier of vadadustat's reimbursement under a bundled reimbursement model or using the TDAPA, and a milestone payment by Vifor Pharma. During the term of the license agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the United States to FKC or its affiliates or to any Third Party Dialysis Organization, and we may not directly supply vadadustat to FKC or any other affiliate of Fresenius Medical Care North America, or FMCNA, or any Third Party Dialysis Organization. For more information about our license, collaboration and strategic agreements relating to vadadustat, see Part I, Item 1. Business – License, Collaboration and Other Strategic Agreements – Vadadustat.

We entered into a letter agreement on February 14, 2020, or the Letter Agreement, with Vifor Pharma, relating to Vifor Pharma'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. A PRV entitles the holder to priority review of an NDA, or a Biologics License Application for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, and could lead to expedited approval. Pursuant to the Letter Agreement, we paid Vifor Pharma \$10.0 million in connection with the closing of the PRV Purchase. Vifor Pharma is obligated to retain all rights to, and maintain the validity of, the PRV until we and Vifor Pharma (a) enter into a definitive agreement setting forth the financial and other terms by which Vifor Pharma will assign the PRV to us for use with our planned NDA for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients, or (b) make a mutual decision to sell the PRV and share the proceeds based on certain terms.

### **Our Commercial Product: Auryxia**

Auryxia (ferric citrate) is a non-calcium, non-chewable, orally-administered tablet that was approved for marketing by the 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 IDA Indication, and was commercially launched for this indication in the United States shortly thereafter.

In January 2014, our Japanese sublicensee, JT, received approval from the Japanese Ministry of Health, Labour and Welfare to market ferric citrate hydrate in Japan under the trade name Riona as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, and was commercially launched in Japan shortly thereafter. In July 2019, JT, and its subsidiary, 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. In May 2020, JT and Torii filed an application for approval of IDA as an additional indication for Riona in Japan.

In September 2015, we received approval to market ferric citrate in the European Union under the tradename Fexeric. Pursuant to the sunset clause under EU law, the European Commission'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 have licensed and sublicensed certain intellectual property rights covering Auryxia from Panion & BF Biotech, Inc., or Panion. For more information regarding our intellectual property rights to Auryxia and our license agreement with Panion see Part I, Item 1. Business – Intellectual Property – Auryxia and Part I, Item 1. Business - License, Collaboration and Other Strategic Agreements – License Agreement with Panion & BF Biotech, Inc. We have received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet), with the first having been received on October 31, 2018. We have filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with three such ANDA filers. See Part I, Item 3. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements.

### ***Market Opportunity***

#### ***Hyperphosphatemia***

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 USRDS 2020 Annual Data Report, there were approximately 556,000 adult patients in the United States with DD-CKD in 2018, 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 2018 approximately 42% 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.

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.

#### ***Iron Deficiency Anemia***

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. 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 broad 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. On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. See Part I, Item 3. Legal Proceedings for further information. 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.

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.

## **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 and clinical studies and for commercial production.

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 have redundant supply arrangements in place for the preclinical, clinical and commercial supply of vadadustat. We have entered into supply agreements with Esteve Química, S.A. and STA Pharmaceutical Hong Kong Limited, or STA, for the manufacture of vadadustat drug substance for commercial use and Patheon Inc. and STA 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 additional redundant manufacturing arrangements for both drug substance and drug product; however, the timing of such arrangements is uncertain and may occur following the launch of vadadustat, if approved.

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 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 (two approved sites) and BioVectra Inc. (one approved site), pursuant to supply agreements with pricing structured on a per-kilogram basis. Consistent with our previously disclosed plans to lower the cost of goods sold for Auryxia, BioVectra and Keryx entered into an Amended and Restated Product Manufacture and Supply and Facility Construction Agreement on

September 4, 2020. Auryxia drug product is supplied by Patheon Manufacturing Services LLC (Thermo Fisher) (three approved sites) 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 16 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data.

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.

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. 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, pursuant to which we agreed to co-exclusively collaborate with Otsuka with respect to the development and commercialization of vadadustat in the United States, subject to the approval of vadadustat by the FDA. We continue to lead the ongoing global Phase 3 development program for vadadustat, for which we reported top-line data for INNO<sub>2</sub>VATE and PRO<sub>2</sub>TECT in the second and third quarters of 2020, respectively. We and Otsuka will co-commercialize vadadustat in the United States, subject to the approval of vadadustat by the FDA.

Under the terms of the Otsuka U.S. Agreement, Otsuka paid us an upfront payment of \$125.0 million and we expect Otsuka to provide additional funding of \$352.8 million or more, depending on the actual costs incurred, toward the vadadustat global Phase 3 development program. Due to the costs incurred in completing the activities under the current global development plan exceeding a certain threshold in the second quarter of 2019, we 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, as defined below, from 52.5% to 80%, or the Otsuka Funding Option. The additional funding expected to result from having exercised the Otsuka Funding Option, or the Additional Funding, is fully creditable against future payments due to us under the arrangement, provided that future payments due to us may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. We are eligible to receive from Otsuka up to \$65.0 million in regulatory milestones and up to \$575.0 million in specified commercial milestones.

The Otsuka U.S. Agreement establishes a profit share for the commercialization of vadadustat in the United States. The parties will equally share all net sales of vadadustat in the United States, if approved, and generally each party will bear half of all costs in the United States, including medical affairs, commercialization and manufacturing costs.

Under the Otsuka U.S. Agreement, we and Otsuka will jointly conduct all medical affairs and commercialization activities pursuant to plans agreed by the parties. We will remain responsible for manufacturing vadadustat. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

#### *International Collaboration with Otsuka Pharmaceutical Co. Ltd.*

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 includes the European Union, Russia, China, Australia, Canada, the Middle East and certain other countries, or the Otsuka International Territory, but excludes Latin America and previously licensed jurisdictions. Under the Otsuka International Agreement, Otsuka is responsible

for certain development activities and commercializing vadadustat in the Otsuka International Territory, while we lead the ongoing global Phase 3 development program, for which we reported top-line data for INNO<sub>2</sub>VATE and PRO<sub>2</sub>TECT in the second and third quarters of 2020, respectively. Otsuka will fund a significant percentage of the costs of such global development program regardless of the total actual costs ultimately incurred. We and Otsuka have final decision-making authority with respect to certain matters. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

Under the terms of the Otsuka International Agreement, we expect Otsuka to pay us at least \$299.4 million, comprised of \$73.0 million that was paid upon execution of the Otsuka International Agreement and \$226.4 million or more, depending on actual costs incurred, of development funding. In addition, we are eligible to receive from Otsuka up to \$52.0 million in regulatory milestones and up to \$525.0 million in commercial milestones. Otsuka also agreed to make tiered, escalating royalty payments ranging from low double digits up to thirty percent of net sales of vadadustat within the Otsuka International Territory. In limited circumstances, upper tier royalties may be subject to reduction if the supply price charged by us to Otsuka for vadadustat exceeds certain agreed upon thresholds, and royalty payments may also be reduced if a generic product is launched, on a country-by-country basis. Otsuka may elect to conduct additional studies of vadadustat in the European Union, subject to our right to delay such studies based on our objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and we will pay its portion of the costs in the form of a credit against future amounts due to us under the Otsuka International Agreement.

#### *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. In addition, we will supply vadadustat 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.

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<sup>TM</sup>, as a treatment of anemia due to CKD for adult patients on dialysis and not on dialysis.

Under the terms of the MTPC Agreement, MTPC will make payments to us of up to \$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 is 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. For information on our royalty interest acquisition agreement with HealthCare Royalty Partners IV, L.P. with respect to royalties and sales milestones under the MTPC Agreement, see Part II, Item 9B. Other Information.

#### *Vifor Pharma License Agreement*

On May 12, 2017, we entered into a License Agreement with Vifor Pharma, or the Vifor Agreement. On April 8, 2019, we entered into an Amended and Restated License Agreement with Vifor Pharma, or the Vifor Amended Agreement, which amends and restates in full the Vifor Agreement, pursuant to which we granted Vifor Pharma an exclusive license to sell vadadustat to FKC, an affiliate of Fresenius Medical Care North America, and to Third Party Dialysis Organizations, in the United States, which would be effective upon the approval of vadadustat for DD-CKD patients by the FDA, inclusion of vadadustat in a bundled reimbursement model or that vadadustat will be reimbursed using the TDAPA, and payment by Vifor Pharma of a \$25.0 million milestone upon the occurrence of these two events. The Vifor Agreement is structured as a profit share arrangement between us and Vifor Pharma in which we will receive a majority of the profit from Vifor Pharma's sales of vadadustat to FKC and to Third Party Dialysis Organizations in the United States. We will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S. Agreement. We retain all rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka if vadadustat is approved by the FDA.

Prior and subject to FDA approval of vadadustat, we and Vifor Pharma plan to enter into a commercial supply agreement for vadadustat pursuant to which we would supply all of Vifor Pharma's commercial requirements for vadadustat in the United States. In addition, pursuant to the Vifor Agreement, Vifor Pharma will enter into supply agreements that govern the terms pursuant to which Vifor Pharma would supply vadadustat to FKC and Third Party Dialysis Organizations for use in patients at its dialysis centers, subject to FDA approval; however, FKC and the Third Party Dialysis Organizations are not obligated to utilize vadadustat in its clinics. During the term of the Vifor Agreement, Vifor Pharma will not sell to FKC, its affiliates, or Third Party Dialysis Organizations any HIF product that competes with vadadustat in the United States, and we may not directly supply vadadustat to FKC or any other affiliate of FMCNA or any Third Party Dialysis Organization.

#### *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, Janssen granted us a license for a three-year research term to conduct research on the HIF compound portfolio, which research term is now expired. During the research term, we could designate one or more compounds as candidates for development and commercialization. Once a compound was designated for development and commercialization, we were to be solely responsible for the development and commercialization of the compound worldwide at our own cost and expense.

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. In addition, Janssen could be eligible to receive up to an aggregate of \$16.5 million from us in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to \$215.0 million from us in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single 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.

Unless earlier terminated, the Janssen 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 longer of the expiration of the patents licensed under the Janssen Agreement, the expiration of regulatory exclusivity for such product, or 10 years from first commercial sale of such product. We may terminate the Janssen Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Janssen. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Janssen Agreement or in the event of certain additional circumstances.

As discussed above, we issued a Common Stock Purchase Warrant, or the Warrant, to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen, for 509,611 shares of our common stock at an exercise price of \$9.81 per share. The Warrant is exercisable by JJDC, in whole or in part, at any time prior to February 9, 2022. The Warrant and the shares issuable upon exercise of the Warrant will be sold and issued without registration under the Securities Act of 1933, as amended, or the Securities Act. We recorded the fair value of the Warrant in the amount of \$3.4 million to additional paid-in capital and research and development expense in March 2017.

#### **Auryxia**

##### *License Agreement with Panion & BF Biotech, Inc.*

Prior to the Merger, 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, effective as of April 17, 2019. 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, 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, 2020, Panion earned \$11.2 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 sublicense income to Panion under the terms of the license agreement, excluding any income under the JT and Torii sublicense.

#### *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. 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 double-digit percentage of net sales of Riona in Japan escalating up to the mid-teens, 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. In accordance with our revenue recognition policy, royalty revenues are recognized in the quarter that JT and Torii provide their written report and related information to us regarding sales of Riona, which generally will be one quarter following the quarter in which the underlying sales by JT and Torii occurred. We recorded \$5.7 million in license revenue related to royalties earned on net sales of Riona in Japan during the twelve months ended December 31, 2020. We record the associated mid-single digit percentage of net sales royalty expense due to Panion, the licensor of ferric citrate, in the same period as the royalty revenue from JT and Torii is recorded.

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.”

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 Auryxia and vadadustat 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 II, Item 3. Legal Proceedings for further information relating to these matters.

#### ***Auryxia Patent Portfolio***

Pursuant to Keryx’s license with Panion & BF Biotech, Inc., or 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 15 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 2020 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 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 2022 and 2027. To date, to our knowledge, no contested proceedings or third-party claims have been lodged against any of these Japanese patents.

We have 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), have filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with three ANDA filers. See Part II, Item 3. Legal Proceedings for further information relating to these matters.

### ***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 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, applicants are required to list with the FDA each patent whose claims cover the applicant'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 applicants 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 applicant 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 applicant 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 applicant 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 applicant 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 applicant has provided a Paragraph IV certification to the FDA, the applicant 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 applicant. 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.

On August 23, 2018, Keryx submitted a Citizen Petition requesting, *inter alia*, that FDA recognize that Auryxia is eligible for five years of NCE exclusivity based on its novel active ingredient and for three years exclusivity for the IDA Indication. On January 19, 2019, FDA responded that Auryxia is eligible for a three-year exclusivity period for the IDA Indication, which expires on November 6, 2020. FDA, however, denied the NCE exclusivity based on its determination that Auryxia contains a previously-approved active moiety (ferric cation). FDA’s decision on the Citizen Petition is subject to further review both within FDA and in the courts. On February 21, 2019, Akebia filed a Petition for Reconsideration of FDA’s decision on the NCE determination for Auryxia.

#### *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 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 applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

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, 5,753,706, 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. We have filed for and received interim patent term extension in accordance with 35 U.S.C. § 156(e)(2) for U.S. Patent No. 5,753,706, which currently has an expiration date of February 3, 2022.

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 Patents Nos. 4964585 and 4173553 will expire in November 2025 and November 2022, respectively.

## **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***

If vadadustat is approved and launched commercially, competing branded drugs may 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 Vifor Pharma in the United States and Roche Holding Ltd. outside the United States. We may also face competition from potential new anemia therapies. There are several other HIF-PHI product candidates in various stages of active 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 such companies as FibroGen, Inc., or FibroGen, Japan Tobacco International, GlaxoSmithKline plc and Bayer HealthCare AG. FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, is currently in global Phase 3 clinical development of its HIF-PHI product candidate, roxadustat. In Japan, roxadustat has launched for the treatment of anemia due to CKD in patients on dialysis, or DD-CKD. In November 2020, Astellas and Fibrogen announced the approval of roxadustat for NDD-CKD patients 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 patients not on dialysis, or NDD-CKD. FibroGen announced that the FDA has set a Prescription Drug User Fee Act, or PDUFA, date of March 20, 2021 for its NDA for roxadustat for both DD-CKD and NDD-CKD. In Japan, roxadustat, daprodustat and enarodustat are approved for 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. 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.

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 European Union, 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 our product. Several biosimilar versions of injectable ESAs are available for sale in the European Union. 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 by Vifor Pharma.

### ***Auryxia***

#### ***Hyperphosphatemia Competition***

Auryxia competes in the Hyperphosphatemia Indication in the United States with other FDA-approved phosphate binders such as Renagel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Genzyme Corporation (a wholly-owned subsidiary of 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. Many of the phosphate binders listed above are now also available in generic forms. In addition, other phosphate binders are in various phases of development, including OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets) and Ardelyx, Inc's tenapanor, that may impact the market for Auryxia.

#### *Iron Deficiency Anemia Competition*

Auryxia competes in the IDA Indication in the United States with over-the-counter oral iron, other prescription oral iron formulations, including ferrous sulfate, ferrous gluconate, ferrous fumarate, and polysaccharide iron complex, and IV 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 are available for the treatment of IDA that may impact the market for Auryxia, such as Shield Therapeutics' ferric maltol, which is currently approved in Europe as Ferracru® for IDA and more recently in the United States as Accrufer®.

#### **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. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant 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;
- 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 Studies*

Before an applicant begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations.

### *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.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its website.

### *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.

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.

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.

Under the Pediatric Research Equity Act of 2003, or PREA, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug 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. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The legislation requires the FDA to meet with drug 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 applicant, 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.

#### *Submission of an NDA to the FDA*

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. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2020 is \$2,875,842 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2021 is \$336,432. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for product candidates with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. This is known as the filing decision. 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 applicant 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. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The applicant 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 an applicant 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. For new chemical entities, or NCEs, the review clock starts after the NDA is filed with a total clock of twelve and eight months, respectively.

#### *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 transferrable 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.

#### *The FDA's Decision on an NDA*

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, analyses, or information in order for the FDA to reconsider the application. This may include the requirement to conduct another clinical study or studies. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including 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-market studies or surveillance programs. After approval, many 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.

#### *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 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 is 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.

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 and drug samples are subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, 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. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.



### *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, an applicant 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 Amendments, the FDA may not approve an ANDA 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 new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. 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, an ANDA 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 applicant 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 applicant 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 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*

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

A description of the information that the applicant must specifically certify to with respect to each patent, and the certification process as it relates to patent infringement lawsuits, is described further in Part I, Item 1. Business – Intellectual Property – The Hatch-Waxman Act.

A certification that the new 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 applicant has provided a Paragraph IV certification to the FDA, the applicant 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 after the receipt of a Paragraph IV certification automatically

prevents the FDA from approving the ANDA until the earlier 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 applicant.

#### *Pediatric Studies and Exclusivity*

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing 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) applicant 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.

#### *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*

Requirements for the conduct of clinical trials in the European Union including GCP are 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 2005/28/EC, 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 EC 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 European Union passed the new Clinical Trials Regulation (EU) No 536/2014, or the new Clinical Trials Regulation, which is set to replace the current Clinical Trials Directive. To ensure that the rules for clinical trials are identical throughout the European Union, the new EU clinical trials legislation was passed as a regulation that is directly applicable in all

EU member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive until the new Clinical Trials Regulation becomes applicable.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. 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 that will spare sponsors from submitting broadly identical information separately to various bodies and different member states.

On January 1, 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. In late 2020, the EMA indicated that it plans to focus on the findings of a system audit; improving the usability, quality and stability of the clinical trial information system; and knowledge transfer to prepare users and their organizations for the new clinical trial system. The EMA has indicated that the system will go live in December 2021.

As in the United States, there are similar requirements in the European Union for posting clinical trial information online, and in other countries as well.

#### *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, or CAT, 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.

#### *Marketing Authorization*

To obtain marketing approval of a product under EU regulatory systems, an applicant 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 Committee for Medicinal Products for Human Use, or 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 applicant 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 applicants 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 applicant, known as the reference member state. Under this procedure, an applicant 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 an applicant established in the European Union. Regulation (EC) No. 1901/2006, or Pediatric Regulation, provides that prior to obtaining a marketing authorization in the European Union, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, or PDCO, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. 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.

#### *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, applicants 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 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 new chemical entity 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 Studies and Exclusivity*

Prior to submitting a marketing authorization application in the European Union, applicants must demonstrate compliance with all measures included in an EMA approved 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 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 for 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 for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA 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. If an applicant 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.

#### *Brexit and the Regulatory Framework in the United Kingdom*

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement, the Agreement sets out certain procedures for approval and recognition of medical products in each jurisdiction.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering 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 could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom.

#### *General Data Protection Regulation*

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU 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, 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 also imposes strict rules on the transfer of personal data to countries outside the European Union, 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 evolving landscape of GDPR will continue to be 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.

#### *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 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.

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.

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. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. It is expected 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.

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.

### ***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
- the federal Health Insurance Portability and Accountability Act of 1996, or 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 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 DSCA, 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.

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. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has not been clearly defined. The Affordable Care Act provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- established the Center for Medicare and Medicaid Innovation within CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted since the Affordable Care Act 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 2% per fiscal year that started in 2013 and will stay in effect through 2029 unless additional Congressional action is taken, and 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. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed 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.

### ***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 United Kingdom, 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, 2020, we had 380 employees, 379 of whom were full-time. None of our employees is 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 believe we offer competitive compensation (including base salary, incentive bonus, and long-term equity awards tied to the value of our stock price) and benefits packages designed to attract 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 is designed to incentivize achievement of corporate goals, individual performance and adherence to our corporate values. In addition, we provide development and leadership opportunities to our employees to cultivate talent throughout the Company.

We are also focused on diversity, equality and inclusion opportunities. Three members of our Board of Directors, Maxine Gowen, Ph.D., Cynthia Smith and LeAnne M. Zumwalt, are women, and women comprise approximately 43.7% of our senior management team. We believe this structure reflects our strong endorsement of and commitment to female leadership. In addition, we have created a committee called IDEA - The Inclusion, Diversity & Equity Alliance - focused on communication and education around dimensions of diversity, such as gender, ethnicity, or other shared attributes, that we believe help build community and enable individual and corporate growth. We continue to focus on building a pipeline for talent to create more opportunities for workplace diversity.

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. We also work closely with multiple kidney patient advocacy organizations, including the National Kidney Foundation, the American Kidney Fund, the Renal Support Network and Dialysis Patient Citizens. 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](http://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 statements and future growth prospects could be materially and adversely affected.*

### Risks Related to our Financial Position and Need for Additional Capital

***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 entails upfront capital expenditures and 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, following the merger, or the Merger, whereby Keryx Biopharmaceuticals, Inc., or Keryx, became a wholly owned subsidiary of ours, commercialization. We have financed our operations primarily through sales of equity securities, our strategic collaborations and, following the Merger, product revenues, a royalty monetization transaction and debt. Prior to the Merger, 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 have incurred net losses each year since our inception, including net losses of \$383.5 million for the year ended December 31, 2020. As of December 31, 2020, we had an accumulated deficit of \$1.2 billion. We cannot guarantee when, if ever, we will become profitable. Our ability to generate product revenue and achieve profitability depends significantly on our success in many areas, including the following:

- developing, commercializing and marketing Auryxia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- obtaining marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, and the timing of such approvals, and maintaining marketing approvals for Auryxia and any other product, including those that may be in-licensed or acquired;
- developing sustainable and scalable manufacturing processes for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate products that are compliant with good manufacturing practices, or GMPs, and services 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;
- obtaining sufficient pricing and reimbursement for Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, from private and governmental payors;
- obtaining market acceptance of Auryxia, vadadustat 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;
- competing effectively with any competitive products and any disruptive technologies;
- identifying, assessing, acquiring, in-licensing and/or developing new product candidates;
- negotiating favorable terms in any transaction into which we may enter, including collaboration, merger, acquisition and licensing arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- integrating following the Merger; and
- attracting, hiring and retaining qualified personnel.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on product revenue, collaboration revenue, and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- conduct any post-marketing approval studies, Phase 4 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;

- continue our commercialization activities for Auryxia and plan for the commercialization of vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- adapt to any regulatory changes, including changes relating to reimbursement;
- adapt to any changes in reimbursement practices by third party payors;
- continue our Merger-related integration activities;
- enroll patients in our clinical trials;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, and maintain marketing approvals for Auryxia and any other product, including those that may be in-licensed or acquired;
- have Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, manufactured for clinical trials and for commercial sale;
- seek to discover and develop 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;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any delays or encounter issues with any of the above.

We also could be forced to expend significant resources in our legal proceedings, as described under Part I, Item 3. Legal Proceedings, or any other such 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.

Even if we succeed in receiving marketing approval for and are able to commercialize vadadustat in the United States and other regions, we will continue to incur substantial expenditures relating to continued commercialization and post-marketing requirements for Auryxia, vadadustat 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 U.S. Food and Drug Administration, or 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 repeat any of our clinical trials, to perform studies in addition to, different from or larger than those currently expected, or if there are any delays in completing our clinical trials. Even if vadadustat and any other product candidate, including those that may be in-licensed or acquired, are approved for commercial sale, we anticipate incurring significant costs associated with commercialization. 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 expect, 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<sup>TM</sup> 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 to become and remain profitable, and we will need to obtain additional funding to continue operations.

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

As of December 31, 2020, our cash and cash equivalents and available for sale securities were \$268.7 million. We expect to continue to expend substantial amounts of cash for the foreseeable future as we continue to commercialize Aurxyia and develop and commercialize vadadustat, if approved, and 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, if any. In addition, other unanticipated costs may arise. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amount of funding necessary to successfully complete the clinical development, including post-marketing studies, and commercialization of Aurxyia and vadadustat. Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of conducting clinical studies or any post-marketing approval requirements, Phase 4 studies or any other clinical trials for Aurxyia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired;
- the cost and timing of commercialization activities for Aurxyia, vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired, including product manufacturing, marketing, sales and distribution costs;
- the results of our meetings with the FDA, the EMA and other regulatory authorities and any consequential effects, including on study design, study size and resulting operating costs;
- Merger-related integration costs;
- difficulties or delays in enrolling patients in our clinical trials;
- the timing of, and the costs involved in obtaining, and, if approved, maintaining, marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, including to fund the preparation and filing of regulatory submissions, and the costs of maintaining marketing approvals for Aurxyia or any other product, including those that may be in-licensed or acquired;
- 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;
- the cost of securing and validating commercial manufacturing of vadadustat and any other product candidate, including those that may be in-licensed or acquired, and maintaining our manufacturing arrangements for Aurxyia 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 ability to attract, hire and retain qualified personnel;
- costs related to the creation of additional infrastructure and expansion of additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- the extent to which we engage in transactions, including strategic, merger, collaboration, acquisition and licensing transactions, pursuant to which we would develop and market commercial products, or develop other product candidates and technologies.

Furthermore, we expect to continue to incur costs associated with operating as a fully integrated, publicly traded biopharmaceutical company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. 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.

Consistent with our expectation of an NDA submission by the middle of the second quarter of 2021, we expect our cash resources to fund our current operating plan beyond the expected U.S. launch of our product candidate, vadadustat, assuming timely regulatory approval and the receipt of associated regulatory milestones. We have based these estimates on assumptions that may prove to be wrong due to a variety of factors, including due to the effects of the ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, pandemic, and we could use our available capital resources sooner than we currently expect. Furthermore, our regulatory milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic transactions, or a combination of these approaches. Even if we believe we have sufficient funds for our current or

future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic objectives.

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, vadadustat and any other products or product candidates, including those that may be in-licensed or acquired. 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, vadadustat, if approved, and any other products or product candidates, including those that may be in-licensed or acquired. Any of these events could significantly harm our business, financial condition and prospects.

***Our obligations in connection with the Loan Agreement with Pharmakon could adversely affect our financial condition and restrict our operations.***

We entered into a loan agreement, or the Loan Agreement, with funds managed by Pharmakon Advisors LP, or Pharmakon, pursuant to which senior secured term loans in an aggregate principal amount of \$100.0 million, or 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 consolidated financial statements in Part II, Item 8 – Financial Statements and Supplementary Data for additional information regarding our obligations under the Loan Agreement. Our Loan Agreement with Pharmakon contains affirmative and negative covenants applicable to us and our subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold starting in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia starting in the fourth quarter of 2020. Failure to maintain compliance with these covenants could result in an event of default under the Loan Agreement.

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, 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 Keryx's guarantee of the Term Loans, which could 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. 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, incurring certain additional indebtedness, creating certain liens, paying dividends or making certain other distributions and making certain investments;
- limiting our flexibility in planning for, or reacting to, changes in our business and our industry;
- placing us at a 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 all 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.

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

On February 25, 2021, we entered into the Royalty Agreement with HCR, pursuant to which we sold to HCR our right to receive the Royalty Interest Payments payable to us under our the MTPC Agreement, subject to the Annual Cap of \$13.0 million and the Aggregate Cap of \$150.0 million. 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 \$45.0 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and we are eligible to receive an additional \$15.0 million under the Royalty Agreement if specified sales milestones are achieved for vadamustat 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 vadamustat in the territory covered under 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.

***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 our cash needs through product revenues, public or private equity or debt transactions, payments from our collaborators, royalty transactions, strategic 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. 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 candidate, 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.

***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 acquisition of assets, businesses, or rights to products, product candidates or technologies or through strategic alliances or collaborations, similar to the Merger and our existing collaboration and license arrangements. We may not identify suitable strategic transactions, or complete such transactions in a timely manner, 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.

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 direct prior 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.

#### **Risks Related to our Merger with Keryx**

***We may fail to realize the anticipated benefits of our merger with Keryx, those benefits may take longer to realize than expected, and we may encounter significant integration difficulties and liabilities, which may have a material adverse effect on our business and financial position.***

On December 12, 2018, we completed the Merger. There can be no assurance that we will realize the full benefit of the anticipated synergies and cost savings relating to the Merger or that these benefits will be realized within the expected time frames or at all. Our ability to realize the anticipated benefits of the Merger will depend, to a large extent, on our ability to continue to integrate our business and Keryx's business and realize anticipated growth opportunities and synergies. If we are unable to successfully integrate the businesses, or integrate them in a timely fashion, we have faced, and may continue to face, adverse effects, some of which may be material, including, but not limited to (i) diversion of the attention of management and key personnel and potential disruption of our ongoing business, (ii) the loss of employees, (iii) challenges of managing a larger company, including challenges of conforming standards, controls, procedures and accounting and other policies and compensation structures, (iv) difficulties in achieving anticipated cost savings, (v) declines in our results of operations, financial condition or cash flows, (vi) a decline in the market price of our common stock, and (vii) potential liabilities, adverse consequences, increased expenses or other problems associated with our company following completion of the Merger. Many of these factors are outside of our control, and any one of them could result in increased costs, decreased expected revenues and further diversion of management time and energy, which could materially impact our business, financial statements and prospects.

In addition, following the Merger, we have become responsible for Keryx's liabilities and obligations, including with respect to legal, financial, regulatory and compliance matters, including certain post-approval regulatory requirements with respect to Auryxia and obligations under collaboration, license, supply and manufacturing agreements. These obligations have, and will continue to, result in additional cost and investment by us and, if we have underestimated the amount of these costs and investments or if we fail to satisfy any such obligations, we may not realize the anticipated benefits of the transaction. Also, due to the Merger and ongoing integration, we may forego or delay pursuit of other opportunities that may have proven to have greater commercial potential.



Further, it is possible that there may be unknown, contingent or other liabilities or problems that may arise in the future, the existence and/or magnitude of which we were previously unaware. Any such liabilities or problems could have an adverse effect on our business, financial condition or results of operations.

***Lawsuits have been filed challenging the Merger and additional lawsuits may be filed in the future. Any monetary damages, or other adverse judgment could have a material adverse effect on us.***

There is an ongoing putative class action lawsuit filed by purported Keryx shareholders challenging the disclosures made in connection with the Merger. In addition, a stockholder of Keryx filed a complaint against Keryx pursuant to Section 220 of the Delaware General Corporation Law, which sought inspection of various Keryx books and records, purportedly to investigate “possible wrongdoing,” in connection with Keryx’s negotiation and approval of the Merger, as well as the independence of former members of Keryx’s Board of Directors (some of whom are current members of our Board of Directors). See Part I, Item 3. Legal Proceedings for further information relating to the lawsuits. Additional lawsuits arising out of the Merger may be filed in the future. We could be forced to expend significant resources in the defense of these lawsuits, including but not limited to, costs associated with the indemnification of Keryx and Akebia directors and officers, and the lawsuits, regardless of outcome, could have a negative effect on our reputation, stock price and results of operations. In addition, monetary damages or other adverse judgment would have a material adverse effect on our business and financial position.

***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, 2020, we had approximately \$199.2 million 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, and 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 Centers for Medicare & Medicaid Services, or CMS, decision that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or 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 of Auryxia for the control of serum phosphorus levels in adult patients with CKD on dialysis, or 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. 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 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.

#### **Risks Related to the COVID-19 Pandemic**

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

The ongoing COVID-19 pandemic has presented a substantial public health and economic challenge around the world and continues to affect our employees, patients, healthcare providers with whom we interact, customers, collaboration partners, contract research organizations, or CROs, our contract manufacturing organizations, or CMOs, vendors, communities and business operations. The full extent to which the COVID-19 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 new information that may emerge concerning COVID-19, any resurgences or mutations of

COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets where the healthcare providers with whom we interact, our partners, our CROs, our CMOs, and our other vendors operate.

While we did not experience a significant impact from COVID-19 on our revenues during the first nine months of 2020, we believe our revenue growth was negatively impacted during the fourth quarter of 2020 primarily as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact our patient population; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future.

The majority of our office-based employees have been working from home since March 13, 2020. In addition, healthcare facilities have continued, or begun again, to restrict 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 restricted access to their clinics. As a result, we continue to primarily engage with healthcare providers and other customers virtually, where possible. The restrictions on our customer-facing employees' in-person interactions with healthcare providers could negatively impact our access to healthcare providers and, ultimately, our sales. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand for Auryxia, 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.

While most of our office-based operations can be performed remotely, there is no guarantee that we will be as effective while working remotely because our team is dispersed, many employees may have additional personal needs to attend to (such as looking after children as a result of school closures or family members who may become sick), and employees may become sick themselves and be unable to work. Further, our increased reliance on remote access to our information systems increases our exposure to potential cybersecurity breaches.

Moreover, our future success and profitability substantially depends on the management skills of our executives and certain other key employees. The unanticipated loss or unavailability of key employees due to the pandemic could harm our ability to operate our business or execute our business strategy. We may not be successful in finding and integrating suitable successors in the event of key employee loss or unavailability.

In addition, the pandemic or the response efforts to the pandemic 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. These impacts could lead to delays or disruptions in supply of our products and product candidates and have a negative effect on our inventory reserves, which could result in an increase in inventory write-offs due to expiry.

The pandemic has resulted in closures of clinical trial sites on which we rely for the completion of certain clinical trials and 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. Further, the pandemic could also potentially affect the business of the FDA, the EMA, the Japanese Pharmaceuticals and Medical Devices Agency, or the PMDA, or other governmental authorities, which could result in delays in meetings, reviews, inspections and approvals relating to our product and product candidate. Any decision by the FDA, EMA, PMDA or other governmental authorities to delay meeting with us or our collaboration partners in light of COVID-19 could have a material adverse effect on clinical trials of our product candidates or on our efforts to obtain marketing approvals for our product candidate, which could increase our operating expenses and have a material adverse effect on our financial results, including the timing and amount of future regulatory milestones we could receive from our partners.

If we or any of the third parties with whom we engage, including our collaboration partners, were to experience shutdowns, delays or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results. At this time, our third party contract manufacturing partners 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 manufacturing partners' ability to manufacture and deliver Auryxia and vadadustat (which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in delays in or disruptions to manufacturing and supply of our products. In addition, COVID-19 precautions may cause a delay in enrolling new clinical trials. We are using remote monitoring and central monitoring, where possible.

The pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, that could impact our ability to raise additional funds and has also impacted, and may continue to impact, the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. 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 any economic recession or depression that has occurred or may occur in the future.

The global impact of COVID-19 continues to rapidly evolve, and we will continue to monitor the situation closely. In particular, areas we are monitoring include possible COVID-related changes in our commercial revenue payer mix, overall product sales, and reserves and allowances, as well as negative trends that could potentially have a further significant impact on product demand and, ultimately, product revenue, or could indicate goodwill, intangible assets, and other assets to be impaired. This uncertain COVID-19 pandemic environment has presented new risks to our business. 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 extent to which COVID-19 impacts our business will depend on future developments, which are highly uncertain and the magnitude of which cannot be predicted, including new information that may emerge concerning the severity of COVID-19 and the actions to contain COVID-19 or treat its impact, among others.

### **Risks Related to Commercialization**

***Our ability to successfully commercialize any approved product, including our ability to achieve their widespread market acceptance, is critical to the success of our business.***

Our ability to generate significant product revenue will depend almost entirely on our ability to execute on our commercialization plans, the level of market adoption for, and the availability of and continued use of any approved product by physicians, hospitals, dialysis clinics, wholesalers, patients, and/or healthcare payors, including government payors, consumers, managed care organizations, pharmacy benefit managers, and pharmacies. If we are not successful in commercializing any approved product, including achieving and maintaining an adequate level of market adoption, our profitability and our future business prospects will be adversely impacted. Market acceptance of any approved product depends on a number of other factors, including:

- the availability of adequate coverage and reimbursement by 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 prevalence and severity of adverse side effects;
- adverse publicity about our products or favorable or adverse publicity about competing products;
- the availability of discounts, rebates, and price concessions;
- 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.

Market acceptance is critical to our ability to generate significant product revenue. Any product may achieve only limited market acceptance or none at all. If any of our approved products is not accepted by the market to the extent that we expect, we may not be able to generate significant product revenue and our business would suffer.

***Generic competitors are seeking approval of generic versions of Auryxia and the market entry of one or more generic competitors would limit Auryxia sales and have an adverse impact on our business and results of operation.***

Although composition and use of Auryxia are currently claimed by 15 issued patents that are listed in the FDA's Orange Book, we cannot assure that we will be successful in defending against third parties attempting to invalidate or design around our patents or assert 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 future products.

The Hatch-Waxman Act allows applicants seeking to market a generic equivalent of a drug that relies, in whole or in part, on the FDA's prior approval of a patented brand name drug, to provide notice to the holder of the New Drug Application, or NDA, for the brand name drug of its application, called a Paragraph IV certification notice, if the applicant is seeking to market its product prior to the expiration of the patents with claims directed to the brand name drug. After the introduction of a generic competitor, a significant percentage of the prescriptions written for a product may be filled with the generic version, resulting in a loss in sales of the branded product. We have received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the FDA requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet), have filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with certain such ANDA filers. See Part I, Item 3. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements. Although the United States District Court for the District of Delaware conducted a Markman hearing concerning certain claim construction issues with respect to four Orange Book-listed patents, and issued an order in favor of Keryx, we may not ultimately be successful in the ANDA litigation. Generic competition for Auryxia or any of our future products could have a material adverse effect on our sales, results of operations and financial condition.

In addition, litigation to enforce or defend intellectual property rights is complex, costly and involves significant management time. If our Orange Book-listed patents are successfully challenged by a third party and a generic version of Auryxia is approved and launched, revenue from Auryxia could decline significantly, which would have a material adverse effect on our sales, results of operations and financial condition.

***If we are unable to maintain sales, marketing and distribution capabilities or to enter into additional agreements with third parties, we may not be successful in commercializing any approved product.***

In order to market any approved product, we intend to continue to invest in sales and marketing, which will require substantial effort and significant management and financial resources. We will need to 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.

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

- potential inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- potential inability of sales personnel to obtain access to physicians;
- 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; and
- costs and expenses associated with maintaining our own sales and marketing organization.

If we are unable to maintain our own sales, marketing and distribution capabilities and our arrangements with third parties with respect to sales, marketing and distribution, or we are unsuccessful in entering into additional arrangements with third parties to sell, market and distribute or are unable to do so on terms that are favorable to us, we will not be successful in commercializing any approved product.

***Coverage and reimbursement may be limited or unavailable in certain market segments for any approved product, which could make it difficult for us or our collaboration partners to sell any approved products profitably.***

Market acceptance and sales of any approved products 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 PBM, decide which drugs they will cover, as well as establish formularies or implement other mechanisms to manage utilization of products and determine reimbursement levels. 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 private third-party payors with varying coverage and reimbursement levels for pharmaceutical products, and the timing of commencement of reimbursement by a governmental payor is 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 only under Part D. In September 2018, 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. On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. 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 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. 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. We cannot be sure that coverage or adequate reimbursement will be available for our product or any of our potential future products. Even if we obtain coverage for any 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.

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.

***If we are unable to obtain or maintain contracts with key distribution partners, our business could be materially harmed.***

We have four distributors, Fresenius Medical Care Rx, McKesson Corporation, Cardinal Health, Inc. and Amerisource Bergen Drug Corporation, that, in the aggregate, accounted for a significant percentage of our gross accounts receivable as of December 31, 2020. If we are not able to maintain our contracts 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, or

such distributors' end users' prescribing practices or clinical protocols, it would adversely impact the market opportunity for Auryxia, our product revenues and operating results.

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. In May 2017, we entered into a license agreement, which was amended and restated in April 2019, pursuant to which we granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat to Fresenius Kidney Care Group LLC, or FKC, and certain third party dialysis organizations, or the Third Party Dialysis Organizations, approved by us, in the United States. The license would be effective upon the following: FDA approval of vadadustat for anemia due to CKD in adult patients with dialysis-dependent CKD, the earlier of CMS's determination that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment, or the TDAPA, and inclusion in the bundle, and a milestone payment by Vifor Pharma. Under this amended license agreement with Vifor Pharma, or the Vifor Agreement, FKC and the Third Party Dialysis Organizations are not obligated to utilize vadadustat in their U.S. clinics. In addition, even if FKC and the Third Party Dialysis Organizations choose to utilize vadadustat in their clinics in the United States, they are not restricted from utilizing other therapies for anemia due to CKD. The Vifor Agreement restricts us from directly supplying vadadustat to FKC or any other affiliate of Fresenius Medical Care North America and the Third Party Dialysis Organizations. The Vifor Agreement does not restrict us from entering into supply agreements with other dialysis clinics, such as DaVita; however, these dialysis clinics may choose not to contract with us for vadadustat or they may choose to contract with us for a limited supply of vadadustat. If vadadustat is approved and we are not able to maintain the Vifor Agreement or enter into a supply agreement with DaVita, our business may be materially harmed.

Although we currently believe it is likely that vadadustat, if approved, will be reimbursed using the TDAPA followed by reimbursement via the bundled reimbursement model, if vadadustat is neither reimbursed under the TDAPA nor the bundled reimbursement model, then the Vifor Agreement will not become effective, and patients would 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 may take several months following approval, which would affect adoption, uptake and product revenue, for vadadustat, 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.

In addition, we may be unable to sell 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 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.

***The successful commercialization of any approved product, will depend in part on the extent to which third party payors, PBMs and governmental authorities establish adequate reimbursement levels and pricing policies.***

Third party payors are increasingly attempting to contain healthcare costs by limiting both coverage and reimbursement levels for new drugs. As a result, significant uncertainty exists as to whether and how much reimbursement third party payors will provide for newly approved drugs which, in turn, will put downward pressure on the pricing of drugs. Cost control initiatives may decrease coverage and payment levels for any drug and, in turn, the price that we will be able to charge and/or the volume of our sales. Certain third party payors require prior authorization for, or even refuse to provide, reimbursement for Auryxia, and others may do so in the future with respect to Auryxia, vadadustat and any of our other products or product candidates. In addition, certain third party payors require some form of prior authorization for the administration of ESAs for the treatment of anemia due to CKD within the non-dialysis patient population, and a similar prior authorization may be applicable to the HIF-PHI class for the treatment of anemia due to CKD within the non-dialysis patient population. Our business would be materially adversely affected if we are not able to receive approval for reimbursement from third party payors on a broad, timely or satisfactory basis; if reimbursement is subject to overly broad or restrictive prior authorization requirements; or if reimbursement is not maintained at satisfactory levels or becomes subject to prior authorization. We are unable to predict all changes to the coverage or reimbursement methodologies that will be applied by private or government payors.

In addition, in some countries, including member states of the European Union, or 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.

Recently, there has been considerable public and government scrutiny in the United States of pharmaceutical pricing and proposals to address the perceived high cost of pharmaceuticals. There have also been several recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices or price increases. Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our product candidates, if approved, and could diminish our ability to establish what we believe is a fair price for our products, ultimately diminishing our revenue for our products if they are approved.

***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 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 superior 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 Renegel® (sevelamer hydrochloride) and Renvela® (sevelamer carbonate), both marketed by Genzyme Corporation (a wholly-owned subsidiary of 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 Ardelyx, Inc.'s tenapanor (for which an NDA has been submitted to the FDA) and OPKO Health Inc.'s Alpharen™ Tablets (fermagate tablets), 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 fumarate, 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' Feraccru® (ferric maltol), which is available in Europe for the treatment of IDA and Accrufer® (ferric maltol), which is approved in the United States for the treatment of IDA.

Furthermore, Auryxia's commercial opportunities may be reduced or eliminated if our competitors develop and market products that are less expensive, more effective or safer than Auryxia. Other companies have product candidates in various stages of pre-clinical or clinical development to treat diseases and complications of the diseases for which we are marketing Auryxia.

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 Vifor Pharma in the United States and Roche Holding Ltd. outside the United States.

We and our partners may also face competition from potential new anemia therapies. There are several other HIF-PHI 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 such companies as FibroGen Inc., Japan Tobacco International, GlaxoSmithKline plc and Bayer HealthCare AG. FibroGen, together with its collaboration partners, Astellas Pharma Inc. and AstraZeneca PLC, is currently in global Phase 3 clinical development of its product candidate, roxadustat. In Japan, roxadustat has launched for the treatment of anemia due to CKD in patients on dialysis, or DD-CKD. In November 2020, Astellas and Fibrogen announced the approval of roxadustat for NDD-CKD patients 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 patients not on dialysis, or NDD-CKD. FibroGen announced that the FDA set an initial Prescription Drug User Fee Act, or PDUFA, date of December 20, 2020; however, on December 18, 2020, FibroGen shared a new PDUFA date of March 20, 2021 for its NDA for roxadustat for both DD-CKD and NDD-CKD. In Japan, roxadustat, daprodustat and enarodustat are approved for 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. 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.

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 our product. Several biosimilar versions of injectable ESAs are available for sale in the EU. 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.

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 and Roche, 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, Japan Tobacco, Inc., or 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 in Japan. We also granted Otsuka Pharmaceutical Co. Ltd., or Otsuka, exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. In Japan and certain other countries in Asia, we granted Mitsubishi Tanabe Pharma Corporation, or MTPC, exclusive rights to commercialize vadadustat, which has been approved and is being marketed by MTPC in Japan under the trade name Vafseo™. 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:



- political, regulatory, compliance and economic developments 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;
- our ability to develop relationships with qualified local distributors and trading companies;
- political and economic instability in particular foreign economies and markets;
- diminished protection of intellectual property in some countries outside of the United States;
- differing labor regulations and business practices;
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' and service providers' activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, or FCPA, the UK Bribery Act or similar local regulation;
- compliance with the EU General Data Protection Regulation, or GDPR;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- potentially negative consequences from changes in or interpretations of tax laws;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism 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 Clinical Development**

***In addition to Auryxia, we will continue to depend heavily on the success of our product candidate, vadadustat, which recently completed Phase 3 clinical development. Clinical drug development involves a lengthy and expensive process with an uncertain outcome. We will incur additional costs in connection with, and may experience delays in completing, or ultimately be unable to complete, the development and commercialization of vadadustat and any other product candidates.***

The risk of failure in drug development is high. We depend heavily on the successful commercialization of Auryxia and the successful clinical development, marketing approval and commercialization of vadadustat in the United States and other jurisdictions, which may never occur. 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. 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 clinical trial process. 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, while we announced positive top-line results from INNO<sub>2</sub>VATE and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO<sub>2</sub>TECT studies, the PRO<sub>2</sub>TECT program did not meet the primary MACE safety endpoint. 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. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay, prevent or make more challenging our ability to receive or maintain marketing approval or commercialize our product candidates. For example, the PRO<sub>2</sub>TTECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients. Our 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 for a variety of other reasons, such as:

- the costs are 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, 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;
- failure 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;
- 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;
- delay or failure in having patients complete a clinical trial or return for post-treatment follow-up;
- delay or failure in recruiting and enrolling suitable patients to participate in a clinical trial;
- 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;
- 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;
- 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;
- 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;
- the design of our clinical trials;
- failure 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
- changes in governmental regulations or administrative actions.

The COVID-19 pandemic has resulted in closures of clinical trial sites on which we rely for the completion of certain clinical trials and may delay enrollment of certain planned and ongoing clinical trials.

We may be unable to successfully complete clinical trials of Auryxia and vadadustat, 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. For example, the PRO<sub>2</sub>TECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients. 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;
- we may not obtain marketing approval for vadadustat 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 Risk Evaluation and Mitigation Strategies, or REMS, or FDA-imposed risk management plans 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 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 studies, which could delay or prevent clinical studies 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 studies is critical to our success. The timing of our clinical studies 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 studies because of concerns about adverse events observed with 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 studies 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. Finally, competition for clinical trial 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 studies 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 studies 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;
- 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 studies 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 studies;

- clinical trial sites and investigators failing to perform effectively;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical studies if we cannot enroll a sufficient number of eligible patients to participate in the clinical studies required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical studies as planned, we may need to delay, limit or terminate ongoing or planned clinical studies, any of which could have a material adverse effect on our business.

***We may not be able to conduct clinical trials in some jurisdictions outside of the United States.***

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;
- different local standards for the conduct of clinical studies;
- 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.

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

***Positive results from preclinical and clinical studies are not necessarily predictive of the results of any future clinical studies.***

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies may not be predictive of similar results in humans during clinical trials, successful results from early or small clinical trials may not be replicated in later and larger clinical trials, and successful interim results from ongoing clinical studies may not be indicative of results obtained when those studies are completed. For example, while we announced positive top-line results from INNO<sub>2</sub>VATE and vadadustat achieved the primary and key secondary efficacy endpoint in each of the two PRO<sub>2</sub>TECT studies, the PRO<sub>2</sub>TECT program did not meet the primary 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. If the results of our ongoing or future clinical trials for a product candidate are inconclusive with respect to efficacy, if we do not meet our clinical endpoints with statistical significance, or if there are safety concerns or adverse events, we may be prevented from or delayed in obtaining marketing approval a product candidate. For example, the PRO<sub>2</sub>TECT program did not meet the primary MACE safety endpoint, and we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients.

***We may not be successful in our efforts to identify, acquire, discover, develop and commercialize additional products or product candidates, which could impair our ability to grow.***

Although we continue to focus a substantial amount of our efforts on the commercialization of Auryxia and the development and potential commercialization of vadadustat, a key element of our long-term growth strategy is to acquire, 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 otherwise does not meet applicable regulatory criteria;
- 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 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 occurs, 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 would have a material adverse effect on our business.

Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential or a greater likelihood of success. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities.

Because our internal research capabilities are limited, we may be dependent upon other pharmaceutical and biotechnology companies, academic scientists, and other researchers to sell or license 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 proposing, 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, including, for example, with respect to the Merger. 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 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 products that we develop or approved products that we acquire will be manufactured profitably, 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 additional therapeutic opportunities for Auryxia or vadadustat or to acquire 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.

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

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. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of undesirable effects or unexpected characteristics.

If we or others identify undesirable effects caused by or other undesirable properties of Aurixia, vadadustat, or any other product or product candidate, including those that may be in-licensed or acquired, either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- patient recruitment could be slowed, and enrolled patients may not want to complete the clinical trial;
- we may be unable to obtain marketing approval or regulatory authorities may withdraw marketing approval;
- regulatory authorities may require warnings on the label, such as the warning on Aurixia's label regarding iron overload;
- REMS or FDA-imposed risk management plans that use restrictive risk minimization strategies, may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining marketing approval and, ultimately, market acceptance or penetration of Aurixia, vadadustat or any other product or product candidate, including those that may be in-licensed or acquired, could substantially increase our costs, and could significantly impact our ability to successfully commercialize Aurixia, 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 Aurixia 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<sub>2</sub>VATE Phase 3 program, the incidence of treatment emergent adverse events during the incident dialysis patient study (*Correction and Conversion*) 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.

With respect to the global PRO<sub>2</sub>TECT Phase 3 program, the incidence of treatment emergent adverse events during the erythropoiesis stimulating agent, or 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.

Serious adverse events considered related to vadadustat and any other product candidates could have a material adverse consequences on the development of such 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, and additional unexpected adverse events may be observed in future clinical trials or in the market. For example, we previously reported that in our Phase 2b study of vadadustat in non-dialysis patients with anemia due to CKD, one subject had a serious adverse event of an abnormal liver function test, considered a case of drug induced liver injury, or DILI, meeting the biochemical criteria of Hy's Law. Following the completion of our global Phase 3 clinical program for vadadustat, there was a review of hepatic safety across the vadadustat clinical program. The review of hepatic safety included a blinded assessment of all hepatic events in the studies by a panel of hepatic experts and analysis by an independent hepatic expert and our team. Based on this review, we concluded that the data

across the clinical program showed that the overall hepatic safety profiles of vadadustat and darbepoetin alfa appear to be similar. In addition, we concluded that there were no events across the clinical program that met the biochemical criteria for Hy's Law. More specifically, we concluded that the DILI from our Phase 2b study of vadadustat in non-dialysis patients with anemia due to CKD that we previously reported as Hy's Law did not, in fact, meet the biochemical criteria of Hy's Law. Our conclusion on this case will be reflected in our NDA for vadadustat.

The most commonly reported adverse reactions in the clinical trials that supported the approval of Auryxia for the Hyperphosphatemia Indication in the United States included diarrhea (21%), discolored feces (19%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). Gastrointestinal adverse reactions were the most common reason for discontinuing Auryxia (14%) in clinical trials for the Hyperphosphatemia Indication. The most commonly reported adverse reactions in the clinical trials that supported the approval of Auryxia in the United States for the IDA Indication included discolored feces (22%), diarrhea (21%), constipation (18%), nausea (10%), abdominal pain (5%) and hyperkalemia (5%). Diarrhea was the most common reason for discontinuing Auryxia (2.6%) in clinical trials for the IDA Indication.

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 Auryxia 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 studies. As a result, regulatory authorities, healthcare practitioners, third party payors or patients may perceive or conclude that the use of Auryxia or any other products are associated with serious undesirable effects, undermining our commercialization efforts.

Further, if we or others identify previously unknown undesirable effects, if known undesirable effects are more frequent or severe than in the past, if we or others detect and confirm unexpected safety signals for Auryxia, vadadustat, or any other product or product candidate perceived to be similar to Auryxia, vadadustat, 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:

- sales may be impaired;
- regulatory approvals may be restricted or withdrawn;
- 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 nonclinical or clinical studies, 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
- government investigations or lawsuits, including class action suits, may be brought against us.

Any of the above 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 candidate.

### **Risks Related to Regulatory Approval**

***We may not be able to obtain marketing approval for, or successfully commercialize, vadadustat, 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 continue commercialization of Auryxia or successfully develop or commercialize vadadustat or any other product or product candidate, including those that may be in-licensed or acquired.

We and Otsuka, our collaboration partner, 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 must complete Phase 3 studies and any additional preclinical or clinical studies required by the FDA, the EMA, the PMDA or other regulatory authorities. Vadadustat may not receive marketing approval. We plan to submit to the FDA an NDA for vadadustat for the treatment of anemia due to CKD in adult dialysis-dependent and non-dialysis dependent patients by the middle of the second quarter of 2021. However, as vadadustat did not meet the primary safety endpoint of the PRO<sub>2</sub>TECT program, we are remaining cautious in our outlook for potential approval of vadadustat for the treatment of anemia due to CKD in adult non-dialysis dependent patients.

Further, vadadustat may not receive marketing approval even if it is approved in other countries. For example, although vadadustat is approved in Japan for the treatment of adult patients with anemia due to CKD, such approval does not guarantee approval in the United States by the FDA.

Obtaining marketing approval in the United States and other jurisdictions 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. 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.

In February 2020, we entered into a letter agreement, or the Letter Agreement, with Vifor Pharma relating to Vifor Pharma's agreement with a third party to purchase a Priority Review Voucher issued by the FDA, or the PRV, subject to satisfaction of customary closing conditions, or the PRV Purchase. Although a PRV entitles the holder to priority review of an NDA or a Biologics License Application for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, the utilization of a PRV does not ensure a faster review or faster approval compared to products considered for approval under conventional FDA procedures, and in any event does not assure ultimate approval by FDA. Furthermore, even if utilization of the PRV enables a faster approval of vadadustat, it may not result in faster commercialization of vadadustat. For more information on risks related to commercialization of vadadustat, see "Risks Related to Commercialization". In addition, pursuant to the Letter Agreement, we paid Vifor Pharma \$10.0 million in connection with the closing of the PRV Purchase. Vifor Pharma is obligated to retain all rights to, and maintain the validity of, the PRV until we and Vifor Pharma (a) enter into a definitive agreement setting forth the financial and other terms by which Vifor Pharma will assign the PRV to us for use with our planned NDA for vadadustat for the treatment of anemia due to CKD in both dialysis-dependent and non-dialysis dependent patients, or (b) make a mutual decision to sell the PRV and share the proceeds based on certain terms. We may not come to terms with Vifor Pharma on assigning the PRV to us, and even if we do, we and Vifor Pharma may decide not to use the PRV for vadadustat and, instead, resell it. In the event of resale of the PRV at a price lower than the purchase price, our share of the proceeds from the resale would be lower than our \$10.0 million contribution.

In addition, the safety concerns associated with the current standard of care for the indications for which we are seeking marketing approval for vadadustat and any other product candidate, including those that may be in-licensed or acquired, may affect the FDA's, the EMA's, the PMDA's or other regulatory authorities' review of the safety results of our compounds in development. 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 and any other product candidate, including those that may be in-licensed or acquired, will never obtain marketing approval in certain jurisdictions or at all. The FDA may delay, limit or deny approval of vadadustat or any other product candidate, including those that may be in-licensed or acquired, 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 or that any other product candidate is safe and effective for its proposed indication(s) to the satisfaction of the FDA;
- 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 FDA for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not approve the formulation, labeling or specifications we request for vadadustat or any other product candidate;
- the FDA 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 FDA may require that we conduct additional clinical trials or repeat one or more clinical trials;
- the FDA may grant approval contingent on the performance of costly post-marketing clinical trials;
- we, or our CROs or other vendors, may fail to comply with GXP;
- the CROs that we retain to conduct our clinical trials may not perform effectively or take actions that adversely impact our clinical trials, or we may fail to communicate effectively or provide the appropriate level of oversight of our CROs;
- we or our third party manufacturers may fail to perform in accordance with the FDA'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 FDA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA 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;
- an FDA Advisory Committee or other regulatory advisory group or authority could recommend non-approval or restrictions on approval;
- the FDA's decision-making regarding vadadustat and any other product candidate may be impacted by the results of 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 FDA may not approve the manufacturing processes or facilities of third party manufacturers with whom we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requires us to amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or the PMDA or other regulatory authorities to delay, limit or deny approval of vadadustat or any other product candidate outside the United States.

If we experience delays in obtaining approval, or if we fail to obtain approval of vadadustat or any other product candidate, including those that may be in-licensed or acquired, the commercial prospects for vadadustat or any other such product candidate may be harmed and our ability to generate revenues will be materially impaired, which could have a material adverse effect on our business.

***We may be delayed in obtaining, or be unable to obtain, marketing approval or reimbursement for vadadustat or any other product candidate in certain countries outside of the United States.***

Regulatory authorities outside of the United States will require compliance with numerous and varying requirements. The approval procedures vary among jurisdictions and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, 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 FDA does not ensure approval by regulatory or reimbursement authorities outside the United States, and approval by one regulatory or reimbursement authority outside the United States does not ensure approval by the FDA or any other regulatory or reimbursement authorities. However, the failure to obtain approval or reimbursement in one jurisdiction may negatively impact our ability to obtain approval or reimbursement in another jurisdiction. The marketing approval process in countries outside of the United States may include all of the risks associated with obtaining FDA approval and, in some cases, additional risks. We may not be able to file for or obtain such

regulatory or reimbursement approvals on a timely basis, if at all. Also, favorable pricing in certain countries depends on a number of factors, some of which are outside of our control.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union 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 United Kingdom and/or the European Union 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 United Kingdom and/or the European Union for vadadustat or any other product candidate, which could significantly and 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 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, we committed to completing the post-approval pediatric study and submitting a final report to the FDA by December 31, 2019. 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 cannot guarantee that we will be able to complete these studies and submit the final reports in a timely manner. For example, with regard to the Hyperphosphatemia Indication, we did not complete and submit the post-marketing requirement pediatric clinical study report by December 31, 2019, and we received a notification of noncompliance with PREA. Our request to extend this deadline was denied, and the study is considered delayed. With regard to the IDA Indication, we did not meet a milestone relating to the 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. If we are unable to complete these studies successfully, we will need to inform the FDA, have further discussions, and if the FDA finds that we failed to comply with pediatric study requirements, it could initiate proceedings to seize or enjoin the sale of Auryxia, 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, 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 FD&C Act, 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, shareholder 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 recently 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<sup>TM</sup>, in Japan or vadadustat for commercial and clinical use.

Non-compliance with 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. Failure to comply with applicable laws could subject us to government scrutiny or government enforcement, potentially resulting in costly investigations and/or fines or sanctions, or impacting our relationships with key regulatory agencies such as the FDA, SEC or the EMA.***

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

- laws and regulations governing the conduct of preclinical and clinical studies in the United States and other countries in which we are conducting such studies;
- laws and regulations in the United States and in countries in which we are interacting with healthcare providers, patients, patient organizations and other constituencies that prohibit promoting a drug prior to approval and/or reimbursement;
- laws and regulations of countries outside the United States that prohibit pharmaceutical companies from promoting prescription drugs to the general public;
- laws, regulations and industry codes that vary from country to country and govern our relationships with healthcare providers, patients, patient organizations, and other constituencies, prohibit certain types of gifts and entertainment, establish codes of conduct and, in some instances, require disclosure to, or approval by, regulatory authorities for us to engage in arrangements with such constituencies;
- 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 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, the GDPR, and state privacy and data protection laws, such as the California Consumer Privacy Act, or CCPA, as well as state consumer protection laws;

- federal and state laws requiring the submission of accurate product prices and notifications of price increases;
- federal and state securities laws; 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.

Compliance with these and other applicable laws and regulations requires us to expend significant resources. Failure to comply with these laws and regulations may subject us to government investigations, enforcement actions by regulatory authorities, penalties, damages, fines, the restructuring of our operations, or the imposition of a clinical hold, 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.

***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, acquire or in-license 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 FD&C Act 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 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 U.S. 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, Auryxia is our first commercial product in the United States, so our implementation of our compliance program in connection with commercialization activities is still relatively new.

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.

***Efforts to pursue regulatory reform may limit the FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.***

There have been several executive actions taken, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, an executive order, applicable to all executive agencies including the FDA, was issued that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. Interim guidance issued by the Office of Information and Regulatory Affairs within the Office of Management and Budget on February 2, 2017, indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. More recently, on October 9, 2019, the prior U.S. President issued another executive order meant to ensure that agency guidance documents do not establish legally binding requirements and directing each agency to rescind guidance documents that it determines should no longer be in effect. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

***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 European Economic Area, or EEA, in May 2018. 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 with respect to sponsors with clinical trial sites 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. In addition, 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 clinical trial sites located in the EEA 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. 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.

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, is creating similar risks and obligations as those created by GDPR. 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). 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.

***Our relationships with healthcare providers, physicians and third party payors are subject to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.***

Healthcare providers, physicians and third party payors play a primary role in the recommendation and prescription of Aurixia and any other product candidates for which we obtain marketing approval. Our arrangements with healthcare providers, physicians and third party payors expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute Aurixia and vadadustat, if approved, and any other products for which we may obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by federal and state governments and by governments in foreign jurisdictions in which we conduct our business. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the FD&C Act 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 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 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, currently set at \$11,181 to \$22,363, per false claim for penalties assessed between January 29, 2018 and June 19, 2020, and \$11,665 to \$23,331, per false claim for penalties assessed after June 19, 2020, and violations of the FD&C Act, the federal government pricing laws, and the federal Anti-Kickback Statute trigger liability under the federal False Claims Act;
- HIPAA 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 and teaching hospitals;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and gift ban and transparency statutes, 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, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. 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. 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.

***Recently enacted and future legislation 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 vadaystat, or any other product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell Auryxia and vadaystat, 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.

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. Among the provisions of the ACA of potential

importance to our business including, without limitation, our ability to commercialize and the prices we obtain for Auryxia and may obtain for any of our product candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal anti-kickback statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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 2% per fiscal year which will remain in effect through 2029 unless additional congressional action is taken. The Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020, and extended the sequester by one year, through 2030. 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.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With the enactment of the Tax Cuts and Jobs Act of 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. According to the Congressional Budget Office, the repeal of the individual mandate will cause an estimated 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. The prior administration also took executive actions to undermine or delay implementation of the ACA. In addition, CMS has proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12 billion in ACA risk corridor payments to third party payors who argued that such payments were owed to them. On April 27, 2020, however, the U.S. Supreme Court reversed the federal circuit decision upholding Congress' denial of such risk corridor funding.

Further, 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 inseparable feature of the ACA and, therefore, because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The current administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The current administration has recently represented to the court of appeals considering



this judgment that it does not oppose the lower court’s ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. In those arguments, the current administration argued in support of upholding the lower court decision. However, in a subsequent filing, the U.S. Department of Justice contended that the ACA should be invalidated only in the states that are suing, rather than all states. On December 18, 2019, that court affirmed the lower court’s ruling that the individual mandate portion of the ACA is unconstitutional and it remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On March 3, 2020, the U.S. Supreme Court agreed to hear the case. On June 25, 2020, the current administration and a coalition of 18 states asked the court to strike down the entirety of the ACA. Oral argument is scheduled in the case for November 10, 2020. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business.

The costs 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.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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, on May 11, 2018, the current administration issued a plan to lower drug prices. Under this blueprint for action, the current administration indicated that HHS will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies, advance biosimilars and generics to boost price competition, evaluate the inclusion of prices in drug makers’ ads to enhance price competition, speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers, avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid, work to give Medicare Part D plan sponsors more negotiation power with drug makers, examine which Medicare Part B drug prices could be negotiated by Medicare Part D plans, improve the design of the Medicare Part B Competitive Acquisition Program, update Medicare’s drug-pricing dashboard to increase transparency, prohibit Medicare Part D contracts that include “gag rules” that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance, and require that Medicare Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. The current presidential administration’s budget proposal for fiscal year 2021 includes a \$135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs, and has issued five executive orders intended to lower the costs of prescription drug products. More recently, the prior U.S. President issued five executive orders that are intended to lower the costs of prescription drug products.

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. 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.

***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**

***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 the rights to our product, Auryxia. We have licensed and sublicensed the rights, patent or otherwise, to Auryxia from a third party, 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 the Consolidated Financial Statements contained in 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.

***We rely on third parties to conduct our clinical studies 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 optimize the commercialization of Auryxia or obtain marketing approval for or commercialize vadadustat, and our business could be substantially harmed.***

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

- if the quantity or accuracy of the data obtained by the third parties is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if the third parties otherwise fail to comply with clinical trial protocols, perform effectively or meet expected deadlines;
- if third parties experience staffing difficulties;
- if we fail to communicate effectively or provide the appropriate level of oversight;
- if third parties undergo changes in priorities or corporate structure or become financially distressed; or
- if they form relationships with other entities, some of which may be our competitors.

Any of these events could cause our preclinical 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 on 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 continued optimization of the commercialization of Auryxia and the development and commercialization of vadadustat or any other product candidates.

Even though we do not directly control the third parties on whom we rely to conduct our preclinical 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 and preclinical trials 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 on third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development, marketing approval or commercialization, resulting in additional costs and depriving us of potential product revenue.

***We rely on third parties to conduct all aspects of our product manufacturing. The loss of these manufacturers, their failure to supply us on a timely basis, or their failure to successfully carry out their contractual duties or comply with regulatory 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, including the vadadustat drug product that we supply to our collaboration partner, MTPC, for the Japanese market. Our reliance on third party manufacturers increases the risk that we will not have 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 have two suppliers of Auryxia drug substance, Siegfried Evionnaz SA (two approved sites) and BioVectra Inc. (one approved site), and one supplier of Auryxia drug product, Patheon Inc., or Patheon (three approved sites). We have entered

into supply agreements with Esteve Química, S.A. and STA Pharmaceutical Hong Kong Limited, a subsidiary of Wuxi AppTec, or STA, for the commercial manufacture of vadadustat drug substance and Patheon Inc. and STA for the commercial manufacture of vadadustat drug product. If any of the following occurs, we may not have sufficient quantities of Auryxia and/or vadadustat to support our clinical trials, commercialization, or obtaining and maintaining marketing approvals, which could materially and adversely impact our business and results of operations:

- we are unsuccessful in implementing additional redundant supply arrangements for commercial quantities of vadadustat or in maintaining our redundant supply arrangements for commercial quantities of Auryxia and vadadustat;
- our commercial supply arrangements for Auryxia or vadadustat are terminated;
- any of our third party manufacturers is unable to fulfill the terms of their agreements with us or is unable or unwilling to continue to manufacture on the manufacturing lines included in our regulatory filings; or
- any of our third party manufacturers breaches our supply agreements, does not comply with quality or regulatory requirements and guidance, is subject to regulatory review or ceases its operations for any reason.

If any of our third party manufacturers cannot or do not perform as agreed or expected, including a misappropriation of 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. 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 file to obtain 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 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.

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, PDMA 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, PMDA and other regulatory authorities prior to or after we submit our marketing applications. We do not control the 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. In addition, 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 or secure and maintain marketing approval for vadadustat.

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 Vafseo<sup>TM</sup> in Japan, we may need to find alternative manufacturing facilities, which would significantly impact our ability to continue commercializing Auryxia or develop, obtain marketing approval for or market our 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, suspension or withdrawal of approvals, license revocation, seizures or recalls of Auryxia or vadadustat, 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 recently had 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 commercial and clinical 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 any future profit margins.

***Third party manufacturers may be unable to manufacture Auryxia and vadadustat in sufficient quality and quantity, which would delay or prevent us from commercializing and developing.***

As a result of the large quantity of materials required for the production of Auryxia and vadadustat and the large quantities of tablets that are required for our commercial success, the commercial viability of Auryxia and vadadustat, if and where approved, depends on adequate supply of starting materials that meet quality, quantity and cost standards and the ability of our contract manufacturers to continually produce drug substance and finished drug product that meets all manufacturing requirements on a commercial scale. Failure to achieve and maintain these levels of supply can jeopardize and prevent the successful commercialization of Auryxia and vadadustat, if and where 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. Although this supply interruption was resolved and actions designed to prevent future interruptions in the supply of Auryxia are ongoing, any future supply interruptions, whether quality or quantity based, for Auryxia and vadadustat, if and where approved, would negatively and materially impact our reputation and financial condition.

In addition, in order to complete our development of and commercialize vadadustat, if approved in regions beyond Japan, we will need to work with third party manufacturers to manufacture vadadustat in large quantities. Our current and future third party manufacturers may be unable to successfully achieve commercial scale production of vadadustat in a timely or cost-effective manner, if at all. In addition, quality issues may arise during scale-up activities. Any changes in our manufacturing processes as a result of scaling up may result in the need to obtain additional marketing approvals. If our third party manufacturers are unable to achieve commercial scale production or there is a need for additional marketing approvals of vadadustat, the development, marketing approval and commercialization of vadadustat may be delayed or infeasible, or ongoing commercialization of Auryxia or Vafseo™ in Japan may be unsuccessful, any of which could significantly harm our business.

***We depend on collaborations with third parties for the development and commercialization of Auryxia, Riona and vadadustat. If our 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 and vadadustat, and our business could be materially harmed.***

We sublicensed the rights to commercialize Riona to JT and Torii in Japan. We entered into collaboration agreements with Otsuka to develop and commercialize vadadustat in the United States, Europe, China and certain other territories. We also entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other Asian countries. In addition, we have a license agreement with Vifor Pharma pursuant to which we granted an exclusive license to sell vadadustat to FKC and the Third Party Dialysis Organizations, approved by us, in the United States, which license would become effective only upon the satisfaction of certain conditions. 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 commercialization efforts with respect to vadadustat and any other product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies.

We may not be able to maintain our collaborations and our 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 collaborations 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 collaborations, 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 collaborations, 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, 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 or commercialization of Auryxia 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 requirements.

If any of these events occurs, the market potential of Auryxia and vadadustat, if and where approved, and any other products or product candidates, could be reduced, and our business could be materially harmed. We also cannot be certain that, following a collaboration, 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, 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 vadadustat and any other product candidates. We may decide to enter into additional collaborations for the development and commercialization of vadadustat or Auryxia. 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, or disrupt our management and 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;
- inability to negotiate collaborations on acceptable terms;

- inability to negotiate collaborations on a timely basis;
- a potential collaborator's evaluation of Aurixia, vadadustat and any other product or product candidate;
- a potential collaborator's resources and expertise; and
- restrictions due to an existing collaboration agreement.

If we are unable to enter into additional collaborations, we may have to delay or curtail the commercialization of Aurixia 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 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 Aurixia or vadadustat, in the case of commercialization, where 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.

***We may incur losses as a result of unforeseen or catastrophic events, including the emergence of a pandemic, terrorist attacks, extreme weather events or other natural disasters.***

The occurrence of unforeseen or catastrophic events, including the emergence of a pandemic, such as COVID-19 discussed above, or other widespread health emergency (or concerns over the possibility of such an emergency), terrorist attacks, extreme terrestrial or solar weather events or other natural disasters, could create economic and financial disruptions, and could lead to operational difficulties that could impair our ability to manage our businesses or result in reduced sales or delays in our clinical studies, which could have a material adverse effect on our financial results. If we or any of the third parties with whom we engage were to experience shutdowns or other business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively impacted, which could have a material adverse effect on our business and our financial results.

### **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, thus reducing any advantage of the patent. 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.

Additionally, the laws of foreign countries may not protect our intellectual property rights to the same extent as do the laws of the United States. For example, claims in a patent application directed to methods of treatment of the human body are not patentable or are restricted in many non-U.S. countries. Further, we may not pursue or obtain patent protection in all major markets. In addition, in jurisdictions outside the United States where we own or license patent rights, we may be unable to prevent unlicensed parties from selling or importing products or technologies derived elsewhere using our proprietary technology.

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, or the Act, 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.

In July 2011, a third party filed an opposition to our issued European patents, European Patent No. 2044005, or the '005 EP Patent, which covers vadadustat. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the European Patent Office decided to maintain certain claims of the patent directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division. On February 27, 2018, we withdrew the '005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia. We cannot be assured that such claims in the divisional application will be granted by the European Patent Office. If such claims are not granted, or the scope of the claims is significantly narrowed, we may not be able to adequately protect our rights, provide sufficient exclusivity, or preserve our competitive advantage.

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.

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, we share ownership and publication rights to data relating to our drug product and



technologies with our research collaborators and scientific advisors. 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.

***The intellectual property and related non-patent exclusivity that we own or have licensed relating to our product, Auryxia, is 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 not market a product for methods of use 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. In addition, any successful claim of infringement asserted against us could subject us to monetary damages or injunction, which could prevent us from making or selling Auryxia. We also may be required to obtain licenses to use the relevant technology. Such licenses may not be available on commercially reasonable terms, if at all.

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 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.

In addition to patent protection, we may utilize, if granted by the FDA, pediatric exclusivity or other provisions of the FDCA such as new chemical entity, or NCE, exclusivity, or exclusivity for a new use or new formulation, to provide non-patent exclusivity for a drug product. The FDCA provides a five-year period of non-patent exclusivity within the United States to the first applicant to gain approval of a new drug application, or 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 applicant does not own or have a legal right of reference to all the data required for approval. However, an ANDA or 505(b)(2) NDA 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, 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 applicant 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, an applicant 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 applicant.

On August 23, 2018, Keryx submitted a Citizen Petition requesting, *inter alia*, that FDA recognize that Auryxia is eligible for five years of new chemical entity, or NCE, exclusivity based on its novel active ingredient and for three years exclusivity for the IDA Indication. On January 19, 2019, FDA responded that Auryxia is eligible for a three-year exclusivity period for the IDA Indication, which expired on November 6, 2020. FDA, however, denied the NCE exclusivity based on its determination that Auryxia contains a previously-approved active moiety (ferric cation). FDA's decision on the Citizen Petition is subject to further review both within FDA and in the courts. On February 21, 2019, we filed a Petition for Reconsideration of FDA's decision on the NCE determination for Auryxia.

The FDA's determination as to whether to grant NCE exclusivity to Auryxia may also affect the timing of the 30 month stay barring FDA from granting final approval to generic versions of Auryxia. When an ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant 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 after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier 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 applicant. We have received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA, from generic drug manufacturers requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet), have filed certain complaints for patent infringement relating to such ANDAs, and have entered into settlement and license agreements with certain such ANDA filers. See Part I, Item 3. Legal Proceedings for further information relating to the ANDAs, lawsuits and settlements.

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 applicant.

We cannot assure that Auryxia or any drug candidates we may acquire or in-license 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 that Auryxia or any drug candidates we may acquire or in-license will obtain patent term extension.

***Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

Because we rely on third parties to assist with research, development and manufacture of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, services agreements, material transfer agreements, consulting agreements, research agreements or other similar agreements with our advisors, employees, third party contractors, collaborators and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such information becomes known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third party contractors, and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution with which we may collaborate will usually expect to be granted rights to publish data arising out of such collaboration. We often grant such rights, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration and remove confidential or trade secret information from any such publication. In the future, we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties or independent development or disclosure or publication of information by any of our employees, advisors, consultants, third party contractors or collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

***Litigation or third party claims of intellectual property infringement 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. In addition, third parties may have or may obtain patents in the future and claim that our product or any 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 use such products or other technologies. 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. 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 candidate. 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 candidate is in preclinical studies and clinical trials, we believe that the use of our product candidate 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. As a result of the Merger, our portfolio includes a commercial product, Auryxia. Consequently, there is an increased possibility of a patent infringement claim against us. We attempt to ensure that our product and product candidate 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.

Third parties may hold or obtain patents or other intellectual property rights and allege in the future that the use of our product or product candidate infringes these patents or intellectual property rights, or that we are employing their proprietary technology without authorization. We do not believe that there are any currently issued U.S. patents that will prevent us from commercializing Auryxia or vadadustat; nor do we make any admission that any of such patents are valid, enforceable or infringed. Under U.S. law, a party may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method. We are not aware of any valid U.S. patents issued to FibroGen, or any other person, that claim methods of using any of our product candidates for purposes of inhibiting hypoxia-inducible factor prolyl hydroxylases, or HIF-PHs, for the treatment of anemia due to CKD. For example, we are aware of certain patents that have been acquired by FibroGen directed to certain heterocyclic carboxamide compounds that are described as inhibitors of prolyl-4-hydroxylase. Those patents, however, are believed to have expired as of December 2014.

FibroGen has also filed other patent applications in the United States and other countries directed to purportedly new methods of using such 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.

There may be other patents of FibroGen or patents of other 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 candidate. 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.

Third parties, including FibroGen, may in the future claim that our product and product candidate 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, including patient selection methods, 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.

***We are currently involved in patent infringement lawsuits and opposition and invalidity proceedings and may in the future be involved in additional lawsuits or administrative proceedings to challenge the patents of our competitors or to protect or enforce our patents, which could be expensive, time consuming, and unsuccessful.***

Competitors may infringe our patents or misappropriate our trade secrets or confidential information. To counter infringement or unauthorized use, we may be required to file infringement or misappropriation claims, which can be expensive and time-consuming. 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, 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. An adverse result in any litigation or 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, 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. 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.

For example, we are currently involved in patent infringement lawsuits against several generic companies in the federal district courts. In addition, we are currently involved in opposition or invalidation proceedings in the European Patent Office, the Japan Patent Office, the Canadian Federal Court and the United Kingdom Patents Court. 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" and Part I, Item 3. Legal Proceedings of this Annual Report on Form 10-K.

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.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

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, which would have a material adverse effect on our business.

***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.

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

Filing, prosecuting and defending patents on our 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 enforcement is not as strong as in the United States. These products may compete with our product and product candidate 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 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 from the intellectual property that we develop or license.

## **Risks Related to our Business and Industry**

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

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 key employees, including employees in our commercial, development, regulatory, manufacturing and quality organizations, could impede the achievement of our research, development, regulatory and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Losing such 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 and vadadustat. Our future financial performance and our ability to develop, obtain and/or maintain market 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 personnel with sufficient experience. We may be unable to hire, train, retain or motivate these key 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 we are unable to continue to attract and retain high quality personnel, our ability to grow and pursue our business strategy will be limited.

***We may expend our limited resources to pursue a particular product, product candidate or indication and fail to capitalize on products, product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, 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 that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***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 studies, 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 cyber security 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 some 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, cyber-attack 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. Cyber-attacks 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 cyber-attacks. 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.

Likewise, 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 vulnerable to attacks against our collaborators, vendors or service providers, and we may not have adequate contractual remedies against such collaborators, vendors and service providers in 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. In the recent past, 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, inadvertent diversion of cash, divert the attention of our management and key information technology resources, disrupt key business operations, harm our reputation and deter business partners from working with us. A compromise with respect to our information security could lead to public exposure of personal information of our clinical trial patients, Auryxia patients and others, and negative publicity. Publicity about vulnerabilities and attempted or successful incursions could damage the integrity of our studies or delay their completion. If a compromise to our information security were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, any loss of clinical trial data could result in delays in our regulatory approval efforts for our product candidates and significantly increase our costs to recover or reproduce the data. In addition, such attacks could compromise our ability to protect our trade secrets and proprietary information from unauthorized access or misappropriation and a loss of, or damage to, our data or marketing applications. Inappropriate public disclosure of confidential or proprietary information could subject us to liability and cause delays in our product research, development and commercialization efforts. We currently do not maintain cybersecurity insurance to protect against losses due to security breaches.

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 Auryxia 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.***

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:

- the 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.

We are currently closing out global clinical 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 purposes of obtaining or keeping business or to obtain 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 U.S. Securities and Exchange Commission 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 are conducting clinical trials 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 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 are conducting 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 sanctions 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 people and products among 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 law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. 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 our 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 Global 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. 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 unknown or unmanaged risks or 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.

***We may encounter difficulties in managing our growth and expanding our operations successfully.***

As we commercialize Auryxia and advance vadadustat through development and, if approved, commercialization, we have expanded and may need to further expand our capabilities or contract with third parties to provide these capabilities for us. In addition, we may encounter difficulties in managing the expanded operations of a larger and more complex company following the Merger as well as challenges associated with managing an increasingly diversified 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. As our operations expand, including as they relate to vadadustat in the United States, we expect that we will need to manage additional relationships with various strategic collaborators, consultants, vendors, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management.

In addition, in connection with the Merger and our increasingly diversified business, we have experienced and may to continue to experience significant growth in our employee base. This growth has imposed and will continue to impose significant added responsibilities on members of management, including the need to recruit, hire, retain, motivate and integrate additional employees, including employees who joined us in connection with the Merger. Also, our management may have 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 activities, including the integration of Keryx's business with our business.

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. To manage our recent and anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, procedures and processes, expand our facilities and continue to recruit, train, and retain additional qualified personnel. 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 such growth. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, along with the competitive landscape for talent acquisition and retention in the biopharmaceutical industry, we may not be able to effectively manage the expansion of our operations or recruit, train, and retain additional qualified personnel. In addition, we may need to adjust the size of our workforce as a result of changes to our expectations for our business, which can result in diversion of management attention, disruptions to our business, and related expenses. The physical 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 growing our company or realizing the anticipated benefits of the Merger.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of Auryxia and 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 product testing, 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;
- loss of revenue;
- the inability to commercialize any 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 product liability risks that may arise. Consequently, a product liability claim may result in losses that could be material to 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 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 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 Global Market has ranged from a low of \$2.09 on October 30, 2020 to a high of \$31.00 on June 20, 2014. The daily closing market price for our common stock has varied between a high price of \$13.58 on June 30, 2020 and a low price of \$2.22 on October 30, 2020 in the twelve-month period ending on February 24, 2021. During this time, the price per ordinary share has ranged from an intra-day low of \$2.09 per share to an intra-day high of \$13.71 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, developments related to and results of our clinical studies, developments related to our regulatory submissions, developments related to our ability to commercialize Auryxia and vadadustat, if approved, and any other product candidates, announcements by us or our competitors of significant mergers, acquisitions, licenses, strategic collaborations, joint ventures, collaborations or capital commitments, negative publicity around Auryxia or vadadustat, the results of competitive clinical trials, products or technologies, regulatory or legal developments in the United States and other countries, developments or disputes concerning patent applications, issued patents or other proprietary rights, the recruitment or departure of key personnel, the level of expenses related to Auryxia and vadadustat or any other product or product candidate, actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts, variations in our financial results or those of companies that are perceived to be similar to us, changes in the structure of healthcare payment systems, market conditions in the biopharmaceutical sector, general economic, industry and market conditions and others beyond our control. As a result of this volatility, our shareholders 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 for information concerning

securities class action and shareholder derivative lawsuits 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 shareholders will dilute our shareholders' 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.

According to 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, BlackRock, Inc., or BlackRock, beneficially owns approximately 7.9% of our outstanding shares of common stock, State Street Corporation, or State Street, beneficially owns approximately 15.6% of our outstanding shares of common stock, Wellington Management Group LLP, or Wellington, beneficially owns approximately 8.7% of our outstanding common stock, The Vanguard Group Inc., or Vanguard, beneficially owns approximately 5.8% of our outstanding shares of common stock and our former director, Muneer Satter, beneficially owned approximately 2.1% of our outstanding common stock. Subject to certain restrictions, Mr. Satter is able to sell his shares of common stock in the public market from time to time without registering them, subject to certain limitations on the timing, amount and method of those sales imposed by Rule 144 under the Securities Act of 1933, as amended. In addition, pursuant to our Fourth Amended and Restated Investors' Rights Agreement, as amended, with Mr. Satter, he has the right, subject to certain conditions and with certain exceptions, to require us to file registration statements covering the shares common stock he owns or to include his shares in registration statements that we may file or in public offerings of our shares of common stock. Following their registration and sale under the applicable registration statement, those shares would become freely tradable. By selling a large number of shares of common stock, BlackRock, State Street, Wellington, Vanguard or Mr. Satter could cause the price of our common stock to decline.

We have a significant number of shares that are subject to outstanding options, restricted stock units and a warrant, and in the future we may issue additional options, restricted stock units, warrants or other derivative securities convertible into our common stock. The exercise or vesting of any such options, restricted stock units, warrants 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. Also, the Merger was financed by the issuance of shares of our common stock to shareholders of Keryx, comprising approximately 50.6% of our issued and outstanding shares of common stock, calculated based on our fully diluted market capitalization as of the date of signing the Agreement and Plan of Merger relating to the Merger. Keryx shareholders may decide not to hold the shares of our common stock they received in the Merger. Other Keryx shareholders, such as funds with limitations on the amount of stock they are permitted to hold in individual issuers, may be required to sell the shares of our common stock they received in the Merger. 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 certain registered securities, such as common stock, preferred stock, 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.

Sales of substantial amounts of shares of our common stock or other securities by our employees or our other shareholders 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.

***Insiders and significant stockholders could cause us to take actions that may not be, or refrain from taking actions that may be, in our best interest or in the best interest of all of our stockholders.***

As of December 31, 2020, we believe that our directors and executive officers, together with their affiliates, beneficially owned, in the aggregate, approximately 1.5% of our outstanding common stock. In addition, we have certain significant stockholders, including BlackRock, which beneficially owns approximately 7.9% of our outstanding shares of common stock, State Street, which beneficially owns approximately 15.6% of our outstanding shares of common stock, Wellington, which beneficially owns approximately 8.7% of our outstanding common stock, and Vanguard, which beneficially owns approximately 5.8% of our outstanding shares of common stock according to the most recent filings made under Section 13(d) and 13(g) of the

Exchange Act. If they were to choose to act together, they would have significant influence on all matters submitted to our stockholders for approval, as well as our management and affairs, such as:

- the composition of our Board of Directors;
- the adoption of amendments to our Ninth Amended and Restated Certificate of Incorporation, or Charter, and Amended and Restated By-Laws;
- the approval of mergers or sales of substantially all of our assets;
- our capital structure and financing; and
- the approval of contracts between us and these shareholders or their affiliates, which could involve conflicts of interest.

This concentration of ownership could harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of our company and making some transactions more difficult or impossible without the support of these stockholders, even if such transactions are beneficial to other stockholders;
- impeding a merger, consolidation, takeover or other business combination involving our company; or
- entrenching our management or our Board of Directors.

Moreover, the interests of these stockholders may conflict with the interests of other stockholders, and we may be required to engage in transactions that may not be agreeable to or in the best interest of us or other stockholders.

***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, and particularly since December 31, 2019 when we ceased to be an “emerging growth company” and December 31, 2020 when we became a “large accelerated filer”, we have and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, or the SOX Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global 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. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have and will continue to increase our legal and financial compliance costs and make some activities more time-consuming and costly.

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.

***We have identified a material weakness in our internal control over financial reporting relating to our inventory process. If we are not able to remediate this material weakness, or if we experience additional material weaknesses or other deficiencies in the future or otherwise fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting which would harm our business and the trading price of our common stock.***

Effective internal control over financial reporting is necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, is designed to prevent fraud. Any failure to maintain or implement required new or improved controls, or difficulties encountered in implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us, as and when required, conducted in connection with Section 404 of the SOX Act, or Section 404, or any testing by our independent registered public accounting firm, which became required for us as of December 31, 2019, may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. For example, as of December 31, 2019, management and our independent registered public accounting firm concluded that our internal control over financial reporting relating to our inventory process was not effective because of a material weakness due to our failure to design and maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. Despite remediation efforts we undertook during fiscal 2020 and continue to make, our management and independent registered public accounting firm have concluded that, as of December 31, 2020, our internal control over financial reporting relating to our inventory process was not effective because of a material weakness due to our failure to design and

maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. For more information about this material weakness, see Part II, Item 9A. Controls and Procedures of this Annual Report on Form 10-K. Although we have initiated remediation measures to address the material weakness, we cannot provide assurance that we will be able to correct this material weakness in a timely manner or that our remediation efforts will be adequate to allow us to conclude that our internal controls will be effective in the future. Even if this material weakness is remediated in the future, our internal control over financial reporting could in the future have additional material weaknesses, deficiencies or conditions that could require correction or remediation.

We will need to continue to dedicate internal resources, engage outside consultants and maintain a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to remediate the material weakness relating to our inventory process described above and any future control deficiencies or material weaknesses, and improve control processes as appropriate, validate through testing that controls are functioning as documented and maintain a continuous reporting and improvement process for internal control over financial reporting. If we are not able to correct material weaknesses or deficiencies in internal controls in a timely manner or otherwise comply with the requirements of Section 404 in a timely manner, our ability to record, process, summarize and report financial information accurately and within applicable time periods may be adversely affected and we could be subject to sanctions or investigations by the Securities and Exchange Commission, the Nasdaq Stock Market or other regulatory authorities as well as shareholder litigation which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

***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 Charter and Amended and Restated Bylaws 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 Amended and Restated 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 Amended and Restated 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 Amended and Restated 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 the registrant 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 Amended and Restated 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.

***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 Amended and Restated By-Laws 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 Amended and Restated By-Laws; 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.

Any provision of our Charter, our Amended and Restated By-Laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

***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 and Need for Additional Capital,” 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. A valuation allowance has been provided for the entire amount of 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 (1) any derivative action or proceeding brought on our behalf, (2) 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, (3) any action asserting a claim against us arising pursuant to any provision of the DGCL our Charter or our Amended and Restated By-Laws, or (4) 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 as described in Part I, Item 3. Legal Proceedings 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. 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. 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.

***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. 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. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. 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 the Cambridge, Massachusetts office space expires on September 11, 2026, the lease for the Cambridge, Massachusetts lab space expires on January 31, 2025, and the lease for the Boston, Massachusetts office space expires on February 28, 2023. In September 2019, Keryx entered into an agreement to sublease the Boston office space to Foundation Medicine, Inc. 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 Patents Covering Vadadustat*

In July 2011, a third party filed an opposition to our issued European Patent No. 2044005, or the '005 EP Patent, in the European Patent Office, or the EPO. During the oral proceedings, which took place on April 10, 2013, the Opposition Division of the EPO maintained the '005 EP Patent. This decision resulted in the maintenance of a claim directed to a compound chosen from a group of eight compounds, including vadadustat, as well as claims to compositions and methods for treating various diseases, including, but not limited to, anemia. Both parties appealed the decision of the Opposition Division of the EPO. On February 27, 2018, we withdrew the '005 EP Patent from appeal and filed a divisional patent application to pursue a focused claim set that includes claims for vadadustat, as well as pharmaceutical compositions and methods of treating anemia.

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

#### *Opposition and Invalidity Proceedings Against FibroGen, Inc.*

We filed an opposition in the EPO against FibroGen, Inc.'s, or 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 has appealed that decision. Likewise, we also filed an invalidity proceeding before the Japan Patent Office, or JPO, on June 2, 2014 against certain claims of FibroGen's Japanese Patent No. 4804131, or the '131 JP Patent, which is the Japanese counterpart to the '823 EP Patent, and the JPO issued a preliminary decision finding all of the challenged claims to be invalid. FibroGen subsequently amended the claims and the JPO accepted the amendments. The resulting '131 JP Patent does not cover vadadustat or any pyridine carboxamide compounds. To date, the U.S. Patent and Trademark Office has not issued FibroGen a patent covering the same claim scope as it obtained initially in Europe and Japan in the '823 EP Patent and '131 JP Patent. In the event FibroGen were to obtain such a patent in the United States, we may decide to challenge the patent as we have done in Europe and Japan.

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 related patents claim, among other things, various compounds that either stabilize HIF $\alpha$  or inhibit a HIF hydroxylase or a HIF prolyl hydroxylase, or HIF-PH, for treating or preventing various conditions, including, among other things, iron deficiency, microcytosis associated with iron deficiency, anemia of chronic disease, anemia wherein the subject has a transferrin saturation of less than 20%, anemia refractory to treatment with exogenously administered erythropoietin and microcytosis in microcytic anemia. Such 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 and our collaborators with maximum flexibility for developing vadadustat and our pipeline of investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, compounds.

Oppositions to the '155 EP Patent and the '153 EP Patent were also filed in the EPO by Glaxo Group Limited, or Glaxo, and by Bayer Intellectual Property GmbH, Bayer Pharma Aktiengesellschaft, and Bayer Animal Health GmbH, or, collectively, Bayer. Glaxo withdrew its oppositions on March 2, 2020.



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. An oral proceeding for the appeal is scheduled for February 2022.

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 is scheduled for February 2022.

Subsequently, 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. An oral proceeding for the appeal is scheduled for February 2022.

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 are scheduled for September 2021.

On February 10, 2020, we filed an opposition to FibroGen's European Patent No. 2324834 in the EPO requesting the patent to be revoked in its entirety.

On May 21, 2018, we filed a Statement of Claim in Canadian Federal Court to challenge the validity of three of FibroGen's HIF-related patents in Canada: CA 2467689, CA 2468083, and CA 2526496. On June 25, 2020, the parties agreed to dismiss the CA 2467689 patent from the lawsuit. On February 16, 2021, the parties agreed to dismiss the lawsuit in its entirety.

On June 22, 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 one of FibroGen's HIF-related patents in Japan, JP4845728. On July 20, 2018 and August 13, 2018, we and MTPC jointly filed a Request for Trial before the JPO to challenge the validity of two additional FibroGen HIF-related patents in Japan, JP5474872 and JP5474741, respectively. 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 February 10, 2020, the JPO issued a pre-notice of a trial decision for JP4845728, which invalidated all claims except two claims in amended form. On March 11, 2020, the JPO issued a pre-notice of a trial decision for JP5474872, which invalidated all claims except one claim in amended form. On April 2, 2020, the JPO issued a pre-notice of a trial decision for JP5474741, which invalidated all claims except two claims in amended form. We do not believe these decisions will prevent our collaboration partner MTPC from launching vadadustat for the treatment of anemia due to CKD in Japan.

On December 13, 2018, we and our collaboration partner, Otsuka Pharmaceutical Co. Ltd., or Otsuka, filed Particulars of Claim in the Patents Court of the United Kingdom, or the UK, 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 and Otsuka for patent infringement in the Patents Court of the UK. In September 2019, we and Otsuka 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).

### ***Legal Proceedings Relating to Auryxia***

#### ***ANDA Litigation***

On October 31, 2018, November 6, 2018, December 24, 2018 and February 4, 2019, Keryx received Paragraph IV certification notice letters regarding Abbreviated New Drug Applications, or ANDAs, submitted to the U.S. Food and Drug Administration, or FDA, by Lupin Atlantis Holdings SA, or Lupin, Teva Pharmaceuticals USA, Inc., or Teva, Chemo Research S.L., or Chemo, and Mylan Pharmaceuticals Inc., or Mylan, respectively, requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet). On December 13, 2018, Keryx and its licensors, Panion & BF Biotech, Inc., or Panion, and Chen Hsing Hsu, M.D., filed a complaint for patent infringement against Lupin and Lupin Ltd., or the Lupin Defendants, in the United States District Court for the District of Delaware, or the Delaware District Court, arising from Lupin's ANDA filing with the FDA. On December 19, 2018, Keryx and Panion filed a complaint for patent infringement against Teva and Teva Pharmaceutical Industries Limited, or the Teva Defendants, in the Delaware District Court arising from Teva's ANDA filing with the FDA. On February 1, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Chemo and Insud Pharma S.A., or the Chemo Defendants, in the Delaware District Court arising from Chemo's ANDA filing with the FDA. On March 15, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Mylan in the United States District Court for the Northern District of West Virginia arising from Mylan's ANDA filing with the FDA. On April 18, 2019, Keryx, Panion and Dr. Hsu filed a motion with the Judicial Panel on Multidistrict Litigation seeking to consolidate these four cases in the Delaware District Court for pretrial proceedings.

On March 29, 2019, April 2, 2019, and April 12, 2019, Keryx received Paragraph IV certification notice letters regarding ANDAs submitted to the FDA by Lupin Ltd., Watson Laboratories, Inc., or Watson, a wholly-owned, indirect subsidiary of Teva, and Par Pharmaceutical, Inc., or Par, an Endo International company, or Endo, respectively, requesting approval for generic versions of Auryxia tablets (210 mg iron per tablet). On May 10, 2019, Keryx, Panion and Dr. Hsu filed a complaint for patent infringement against Lupin Ltd. in the Delaware District Court arising from Lupin Ltd.'s ANDA filing with the FDA. On May 10, 2019, Keryx and Panion filed a complaint for patent infringement against Watson and the Teva Defendants, or the Watson Defendants, in the Delaware District Court arising from Watson's ANDA filing with the FDA. On May 15, 2019, Keryx and Panion filed a complaint for patent infringement against the Watson Defendants in the United States District Court for the District of Nevada, or the Nevada District Court, from Watson's ANDA filing with the FDA. On May 23, 2019, Keryx and Panion filed a complaint for patent infringement against Par in the Delaware District Court arising from Par's ANDA filing with the FDA. On May 24, 2019, Keryx and Panion filed a complaint for patent infringement against Par, in the United States District Court for the Southern District of New York, or the Southern New York District Court, arising from Par's ANDA filing with the FDA. On June 4, 2019, Keryx and Panion filed a notice of voluntary dismissal to dismiss the suit in the Nevada District Court in view of the Watson Defendants' consent to venue of the Delaware District Court. On June 26, 2019, Keryx, Panion and Dr. Hsu notified the Judicial Panel on Multidistrict Litigation of additional actions in the Delaware District Court against the Lupin Defendants and the Watson Defendants. On July 31, 2019, the Judicial Panel on Multidistrict Litigation issued an order to consolidate all of our ANDA cases in Delaware District Court for pretrial proceedings. On August 26, 2019, Keryx filed an amended complaint against the Lupin Defendants in the Delaware District Court arising from the Lupin Defendants' ANDA filings with the FDA. On September 19, 2019, the Delaware District court set a trial date for February 8, 2021. The trial has been rescheduled for June 28, 2021. On January 13, 2021, the Delaware District court vacated the deadlines for the case involving Mylan pending resolution of a discovery dispute; this order had no effect on the action against the Chemo Defendants. On February 2, 2021, the Delaware District court stayed the case involving the Chemo Defendants until March 4, 2021; this order had no effect on the action against Mylan.

On July 22, 2019, Keryx received from Teva a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 22, 2019, Keryx received from Watson a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 31, 2019, Keryx received from Lupin a supplemental Paragraph IV certification notice letter regarding its ANDA. On July 31, 2019, Keryx received from Lupin Ltd. a supplemental Paragraph IV certification notice letter regarding its ANDA. On September 17, 2019, Keryx received from Par a supplemental Paragraph IV certification notice letter regarding its ANDA. On October 16, 2019, Keryx received from Mylan a supplemental Paragraph IV certification notice letter regarding its ANDA. On May 14, 2020, Keryx received from Chemo a supplemental Paragraph IV certification notice letter regarding its ANDA.

On April 27, 2020, the Delaware District Court conducted a Markman hearing concerning certain claim construction issues with respect to four Orange Book-listed patents, and issued an order in favor of Keryx.

On August 2, 2019, Keryx and Panion entered into a settlement and license agreement with Par. This settlement resolved patent litigation brought by Keryx and Panion in response to Par's ANDA seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Par 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. Additionally, in accordance with the agreement, the parties will terminate all ongoing litigation between Keryx and Panion and Par regarding Auryxia patents pending in the Delaware District Court and the Southern New York District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On August 5, 2019, the parties filed a request to stay the litigation pending a review of the settlement and license agreement by these

regulatory authorities. On September 6, 2019 and September 9, 2019, the Southern New York District Court and the Delaware District Court, respectively, entered a stipulation and order of dismissal filed by the parties to terminate the actions against Par.

On April 30, 2020, Keryx and Panion entered into a settlement and license agreement with Teva and Watson. This settlement resolved patent litigation brought by Keryx and Panion in response to Teva and Watson's ANDAs seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Teva and Watson 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. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation between Keryx and Panion and Watson and Teva regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On May 4, 2020, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against Teva and Watson.

On September 24, 2020, Keryx, Panion and Dr. Hsu entered into a settlement and license agreement with the Lupin Defendants. This settlement resolved patent litigation brought by Keryx and Panion in response to Lupin and Lupin Ltd.'s ANDAs seeking approval to market a generic version of Auryxia tablets prior to the expiration of the applicable patents. Pursuant to the terms of the settlement, Keryx and Panion will grant Lupin and Lupin Ltd. 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. Additionally, in accordance with the agreement, the parties terminated all ongoing litigation among Keryx, Panion, the Lupin Defendants and Dr. Hsu regarding Auryxia patents pending in the Delaware District Court. The settlement and license agreement is confidential and subject to review by the U.S. Federal Trade Commission and the U.S. Department of Justice. On October 5, 2020, the Delaware District Court entered a stipulation and order of dismissal filed by the parties to terminate the action against the Lupin Defendants.

As a result of the timely filing of these lawsuits against the Chemo Defendants and Mylan in accordance with the relevant statute, a 30-month stay of approval was imposed by the FDA on Chemo's ANDA and Mylan's ANDA, absent an earlier judgment by the court in each of these lawsuits finding the patents at issue invalid, unenforceable or not infringed. We and the other plaintiffs in each of these lawsuits are seeking, among other relief, an order that the effective date of FDA approval of the ANDA be a date no earlier than the expiration of each of the patents at issue and equitable relief enjoining the Chemo Defendants and Mylan from infringing these patents. On January 13, 2021, the Delaware District court vacated the deadlines for the case involving Mylan pending resolution of a discovery dispute; this order had no effect on the action against the Chemo Defendants. On February 2, 2021, the Delaware District court stayed the case involving the Chemo Defendants until March 4, 2021; this order had no effect on the action against Mylan.

#### *CMS Litigation*

On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts, or the Massachusetts District Court, against Centers for Medicare & Medicaid Services, or CMS, the U.S. Department of Health and Human Services, Alex M. Azar II in his official capacity as Secretary of Health and Human Services, and Seema Verma in her official capacity as administrator for CMS challenging CMS's decision that Auryxia would no longer be covered by Medicare for the treatment of iron deficiency anemia, or IDA, in adult patients with CKD not on dialysis, or the IDA Indication, and imposing a prior authorization requirement for Auryxia in the treatment of adult patients with CKD on dialysis, or the Hyperphosphatemia Indication. On October 29, 2019, we filed a motion for a preliminary injunction asking the court to provide relief while the lawsuit is pending, specifically, to restore coverage of Auryxia for the IDA Indication, and to remove the prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. In the alternative, we filed a motion for summary judgment with the court asking it to decide the case on the merits. On February 4, 2020, the court denied our request for a preliminary injunction. We filed an expedited appeal with the Court of Appeals for the First Circuit challenging the district court's denial of our motion for a preliminary injunction. The First Circuit Court of Appeals held oral argument on August 14, 2020, and affirmed the district court's denial of our request for a preliminary injunction on September 30, 2020. The case is now before the district court. As a result, Auryxia remains not covered by Medicare for the IDA Indication and the prior authorization requirement for Auryxia for the Hyperphosphatemia Indication also remains in place.

#### *Shareholder Litigation Relating to Auryxia Supply*

Four putative class action lawsuits were filed against Keryx Biopharmaceuticals, Inc., or Keryx, and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur, and James Oliviero) and consolidated in the Massachusetts District Court, captioned Karth v. Keryx Biopharmaceuticals, Inc., et al. (filed October 26, 2016, with an amended complaint filed on February 27, 2017). Plaintiff sought to represent all stockholders who purchased shares of Keryx common stock between May 8, 2013 and August 1, 2016. The complaint alleges that Keryx and the named individual defendants violated Sections 10(b) and/or 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 10b-5

promulgated thereunder by making allegedly false and/or misleading statements concerning Keryx, its supplier relationships, and future prospects, and that the allegedly misleading statements were not made known to the market until Keryx's August 1, 2016 announcement of an interruption in its supply of Auryxia. By order dated July 19, 2018, the Massachusetts District Court granted in part and denied in part the defendants' motion to dismiss the complaint. On February 27, 2019, defendants filed a motion for judgment on the pleadings. On April 30, 2019, plaintiff filed a motion to further amend his complaint, and also moved for class certification. The Massachusetts District Court heard oral argument on the motions for judgment on the pleadings and class certification on June 19, 2019.

On September 23, 2019, the Massachusetts District Court issued a Memorandum and Order denying plaintiff's motion for class certification, granting defendants' motion for judgment on the pleadings, and denying plaintiff's motion for leave to further amend his Complaint. That same day, the Massachusetts District Court entered a final judgment in favor of defendants on all claims. On September 24, 2019, plaintiff filed a notice of appeal. The First Circuit Court of Appeals held oral argument on September 15, 2020, and a decision has not yet been issued.

Two stockholder derivative complaints also were filed on December 16, 2016 against Keryx and certain of its former officers (Gregory P. Madison, Scott A. Holmes, Ron Bentsur and James Oliviero) certain of its former directors (Kevin J. Cameron, Daniel P. Regan, Steven C. Gilman, Michael Rogers Michael P. Tarnok, Joseph Feczko, Jack Kaye Wyche Fowler, Jr. and John P. Butler), some of whom are current directors and officers of ours, in the Superior Court of Massachusetts, one captioned Venkat Vara Prasad Malleedi v. Keryx Biopharmaceuticals, Inc., et al., and one captioned James Anderson v. Keryx Biopharmaceuticals, Inc., et al. Each of these two complaints generally alleges breach of fiduciary duty, unjust enrichment, abuse of control, mismanagement and corporate waste. On June 27, 2017, the Superior Court of Massachusetts granted the parties' motion to consolidate and stay the derivative litigations, and that stay remains in effect. All of the complaints seek unspecified damages, interest, attorneys' fees, and other costs. It is expected that such complaints would be dismissed if the above-mentioned ruling of the Massachusetts District Court entering judgment for the defendants in the case brought under the securities laws stands; however, as discussed above, we are awaiting the outcome of the appeal of that judgment.

### ***Legal Proceedings 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. In October and November 2018, four purported shareholders of Keryx filed four separate putative class actions, or the Merger Securities Actions, against Keryx, a former officer and director of Keryx (Jodie P. Morrison), former directors of Keryx (Kevin J. Cameron, Mark J. Enyedy, Steven C. Gilman, Michael T. Heffernan, Daniel P. Regan and Michael Rogers, some of whom are current members of our Board of Directors), and, with respect to the Rosenblatt action discussed below, the Merger Sub and Akebia, challenging the disclosures made in connection with the Merger.

Three of the Merger Securities Actions were filed in the Delaware District Court: Corwin v. Keryx Biopharmaceuticals, Inc., et al. (filed October 16, 2018); Van Hulst v. Keryx Biopharmaceuticals, Inc., et al. (filed October 24, 2018); and Andreula v. Keryx Biopharmaceuticals, Inc., et al. (filed November 1, 2018). The fourth Merger Securities Action was filed in the Massachusetts District Court: Rosenblatt v. Keryx Biopharmaceuticals, Inc., et al. (filed October 23, 2018). On February 19, 2019, the plaintiff in the Rosenblatt action filed a notice of voluntary dismissal of the action without prejudice. On March 27, 2019, the plaintiff in the Van Hulst action filed a notice of voluntary dismissal of the action without prejudice.

On April 2, 2019, the Delaware District Court granted Abraham Kiswani, a member of the putative class in both the Andreula and Corwin actions, and plaintiff John Andreula's motion to consolidate the remaining two Merger Securities Actions pending in the Delaware District Court and consolidated the Corwin and Andreula cases under the caption In re Keryx Biopharmaceuticals, Inc., or the Consolidated Action. The Delaware District Court also appointed Kiswani and plaintiff Andreula as lead plaintiffs for the Consolidated Action. On June 3, 2019, the lead plaintiffs filed a consolidated amended complaint in the Consolidated Action, or the Consolidated Complaint. The Consolidated Complaint generally alleged 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 14(a) and 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and Rule 14a-9 promulgated thereunder. The alleged misstatements or omissions related to (i) certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors and (ii) any alleged negotiations that may have taken place regarding the conversion of certain convertible notes of Keryx in connection with the Merger. The Consolidated Complaint sought compensatory and/or rescissory damages, a declaration that the defendants violated Sections 14(a) and 20(a) of the Exchange Act and Rule 14a-9 thereunder, and an award of lead plaintiffs' costs, including reasonable allowance for attorneys' fees and experts' fees. The defendants in the Consolidated Action moved to dismiss the Consolidated Complaint in its entirety and with prejudice on August 2, 2019. On April 15, 2020, the Delaware District Court granted the defendants' motion and dismissed the Consolidated Action in its entirety. On July 2, 2020, lead

plaintiffs filed a second consolidated amended complaint, or the Second Consolidated Complaint. The Second Consolidated Complaint (i) asserts the same claims under the Exchange Act as the Consolidated Complaint, (ii) names the same defendants as the Consolidated Complaint, (iii) seeks the same relief as the Consolidated Complaint and (iv) as with the Consolidated Complaint, challenges as false or misleading alleged misstatements or omissions related to certain financial projections for Keryx and Akebia and certain financial analyses performed by our advisors. The defendants in the Consolidated Action moved to dismiss the Second Consolidated Amended Complaint in its entirety with prejudice on August 10, 2020. Briefing on defendants' motion to dismiss was completed on September 28, 2020, and the court has not yet issued a decision.

On December 10, 2018, a stockholder of Keryx, Michael J. Donnelly, filed a complaint against Keryx pursuant to Section 220 of the Delaware General Corporation Law in the Delaware Court of Chancery, captioned Donnelly v. Keryx Biopharmaceuticals, Inc., or the Donnelly Action. The Donnelly Action sought inspection of various Keryx books and records, purportedly to investigate "possible wrongdoing," in connection with Keryx's negotiation and approval of the Merger, as well as the independence of former members of Keryx's Board of Directors, some of whom are current members of our Board of Directors. In addition to the production of books and records, the Donnelly Action sought costs and expenses incurred in the action, including reasonable attorneys' fees. On January 31, 2019, Keryx answered the complaint in the Donnelly Action. The Delaware Court of Chancery entered a scheduling order to govern the Donnelly Action on March 28, 2019. The trial for the Donnelly Action took place on July 10, 2019. On October 24, 2019, the Delaware Chancery Court issued a written decision granting inspection, denying the plaintiff's request for costs and expenses, and directing the parties to confer on the proper scope of the inspection.

We deny any allegations of wrongdoing and intend to continue vigorously defending against the shareholder lawsuits described in this Legal Proceedings section. There is no assurance, however, that we will be successful in the defense of these lawsuits, or any associated appeals, or that insurance will be available or adequate to fund any settlement or judgment or the litigation costs of these actions. Moreover, we are unable to predict the outcome or reasonably estimate a range of possible losses at this time. A resolution of these lawsuits 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 a particular lawsuit 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 Global Market under the symbol "AKBA".

#### *Holder*

At February 22, 2021, there were approximately 30 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.

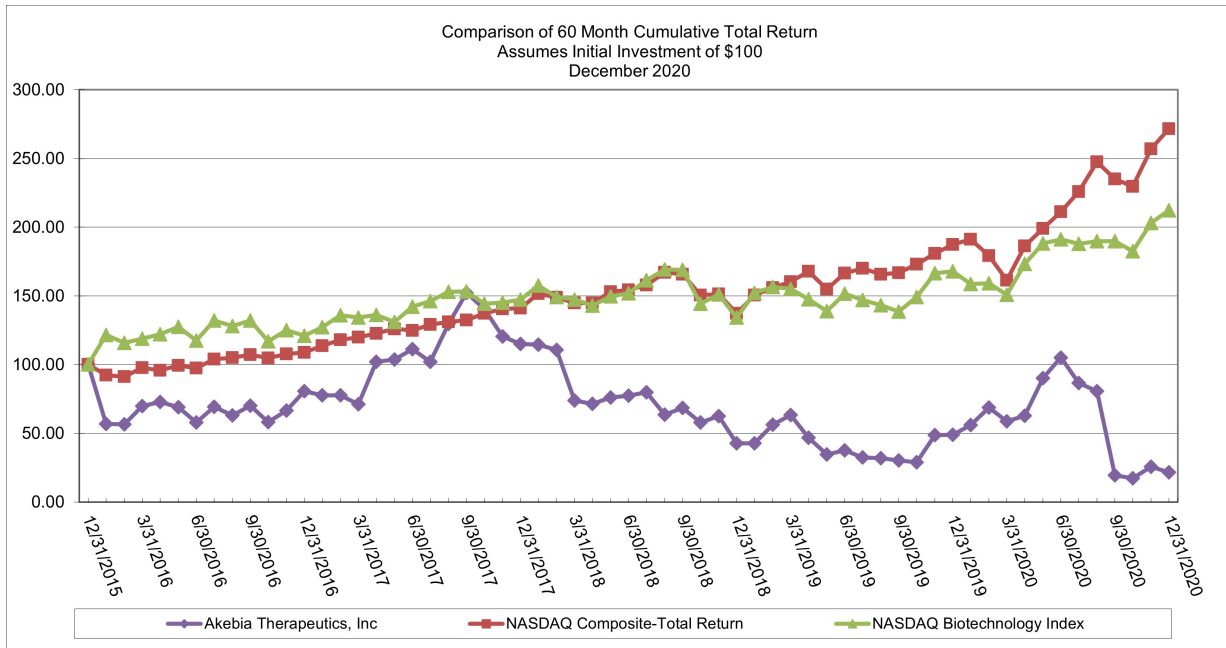
#### *Purchases of Equity Securities by the Issuer and Affiliated Purchasers*

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, 2015 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.



**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. Selected Financial Data

The selected consolidated financial data set forth below for the years ended December 31, 2020, 2019 and 2018 and as of December 31, 2020 and 2019 are derived from our audited consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The selected consolidated financial data for the years ended December 31, 2017 and 2016 and as of December 31, 2018, 2017 and 2016 are derived from our audited consolidated financial statements that are not included elsewhere in this Annual Report on Form 10-K. You should read these data together with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K under the captions “Financial Statements and Supplementary Data.” The selected financial data in this section are not intended to replace our consolidated financial statements and related notes and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year Ended December 31,				
	2020	2019	2018	2017	2016
(in thousands, except share and per share data)					
<b>Consolidated statements of operations data:</b>					
Revenues:					
Product revenue, net	\$ 128,901	\$ 111,119	\$ 6,824	\$ —	\$ —
License, collaboration and other revenue	166,406	223,882	200,918	181,227	1,535
Total revenues	295,307	335,001	207,742	181,227	1,535
Cost of goods sold	295,908	145,336	7,768	—	—
Operating expenses	375,841	475,953	378,135	257,901	137,995
Loss from operations	(376,442)	(286,288)	(178,161)	(76,674)	(136,460)
Other income (expense), net	(7,015)	(2)	6,235	3,003	713
Benefit for income taxes	—	(6,631)	(28,338)	—	—
Net loss	\$ (383,457)	\$ (279,659)	\$ (143,588)	\$ (73,671)	\$ (135,747)
Net loss per share applicable to common stockholders—basic and diluted(1)	\$ (2.77)	\$ (2.36)	\$ (2.47)	\$ (1.69)	\$ (3.60)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	138,463,152	118,395,919	58,038,252	43,500,795	37,716,949

- (1) See Note 2 of the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K for a description of the method used to calculate basic and diluted net loss per share of common stock.

	December 31,				
	2020	2019	2018	2017	2016
(in thousands)					
<b>Consolidated Balance Sheet Data:</b>					
Cash and cash equivalents and available for sale securities	\$ 268,690	\$ 147,694	\$ 321,640	\$ 317,792	\$ 260,343
Working capital	184,291	101,415	202,582	217,250	182,053
Total assets	644,139	771,201	996,540	364,257	300,216
Accumulated deficit	(1,177,511)	(794,054)	(514,395)	(370,807)	(297,136)
Total stockholders’ equity	247,618	394,757	635,928	122,574	68,120



## 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 biopharmaceutical company with the purpose of bettering the life of each person impacted by kidney disease. Since our initial public offering in 2014, we have built a business focused on developing and commercializing innovative renal therapeutics that we believe serves as a foundation for future growth. As a leader in the kidney community, we remain committed to helping patients and others where we believe our current and future products have the ability to deliver value. Our portfolio includes a late-stage product candidate and a commercial product:

- **Vadadustat** is an investigational oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which stimulates erythropoietin, or EPO, production and leads to red blood cell, or RBC, production and improved oxygen delivery to tissues. The significance of the HIF pathway was recognized by the 2019 Nobel Prize and the 2016 Albert Lasker Basic Medical Research Award, which honored the three physician-scientists who discovered the HIF pathway and elucidated this primary oxygen sensing mechanism that is essential for survival. We believe that, based on the HIF-PHI mechanism of action and clinical data to date, vadadustat has the potential to set a new oral standard of care for the treatment of anemia due to chronic kidney disease, or CKD.

We recently completed the global Phase 3 clinical development program for vadadustat, which included two separate programs, INNO<sub>2</sub>VATE and PRO<sub>2</sub>TECT. INNO<sub>2</sub>VATE evaluated vadadustat for the treatment of anemia due to CKD in adult patients on dialysis, or DD-CKD, and PRO<sub>2</sub>TECT evaluated vadadustat for the treatment of anemia due to CKD in adult patients not on dialysis, or NDD-CKD.

In May of 2020, we announced positive top-line results from our Phase 3 INNO<sub>2</sub>VATE program that showed vadadustat was non-inferior to darbepoetin alfa, an injectable erythropoiesis-stimulating agent, or ESA, with respect to hematological efficacy (change in hemoglobin concentration) and cardiovascular safety (assessed in a time to the first occurrence of a major adverse cardiovascular event (MACE) analysis, which is the composite of all-cause mortality, nonfatal myocardial infarction, or a nonfatal stroke) in treating anemia due to CKD in DD-CKD adult patients. In addition to meeting the primary endpoints of the INNO<sub>2</sub>VATE program, vadadustat met the key secondary hematological efficacy endpoint in each of the two studies in the program and also met the program's key secondary safety endpoints. The results of the INNO<sub>2</sub>VATE program were presented at American Society of Nephrology, or ASN, in October of 2020.

In September of 2020, we announced top-line results from our Phase 3 PRO<sub>2</sub>TECT program that showed vadadustat was non-inferior to darbepoetin alfa with respect to hematological efficacy in treating anemia due to CKD in NDD-CKD adult patients. While the PRO<sub>2</sub>TECT data showed that vadadustat achieved both the primary and key secondary hematological efficacy endpoints, it did not meet the program's primary cardiovascular safety (MACE) endpoint. These cardiovascular outcomes contrast with those reported within the INNO<sub>2</sub>VATE program, which evaluated vadadustat for the treatment of anemia due to CKD in DD-CKD adult patients. The results of the PRO<sub>2</sub>TECT program were presented at ASN in October of 2020. Simultaneous with the PRO<sub>2</sub>TECT ASN presentation, we presented additional analyses, conducted by Akebia, of data from the PRO<sub>2</sub>TECT program that 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.

We plan to proceed with the submission of a New Drug Application, or NDA, for vadadustat by the middle of the second quarter of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. We are also working in close collaboration with our collaboration partner, Otsuka Pharmaceutical

Co. Ltd., to prepare a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients for submission to the European Medicines Agency, or EMA, expected in 2021. However, as vadadustat did not meet the PRO<sub>2</sub>TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in NDD-CKD adult patients in the United States and Europe.

In June of 2020, we announced the first regulatory approval of vadadustat for the treatment of anemia due to CKD in DD-CKD and NDD-CKD adult patients in Japan. Our collaboration partner in Japan, Mitsubishi Tanabe Pharma Corporation, or MTPC, commenced commercial sales of vadadustat in Japan under the trade name, Vafseo<sup>TM</sup>, in August 2020.

In addition to anemia due to CKD, we believe that vadadustat has the potential to treat other serious or life-threatening conditions, including preventing and lessening the severity of acute respiratory distress syndrome, or ARDS, a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, infection. More specifically, in July of 2020, we announced an investigator-sponsored clinical study 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 lessen the severity of ARDS in up to 400 adult patients who have been hospitalized due to COVID-19. Within this randomized, double-blind, placebo-controlled study, patients will be dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. This study is being conducted under a U.S. Food and Drug Administration, or FDA, Investigational New Drug application, or IND, with UTHealth as the study sponsor and is currently enrolling patients. In January of 2021, UTHealth announced that it had been awarded \$5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at its facilities.

- **Auryxia® (ferric citrate)** is approved and marketed in the United States for two indications: (1) the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication, and (2) the treatment of iron deficiency anemia, or IDA, in adult patients with NDD-CKD, or the IDA Indication. Ferric citrate is also approved and marketed in Japan as an oral treatment for the improvement of hyperphosphatemia in patients with CKD, including DD-CKD and NDD-CKD, under the trade name Riona (ferric citrate hydrate).

## **Vadadustat**

### *Top-line Results from Global Phase 3 INNO<sub>2</sub>VATE Program within DD-CKD Adult Patients*

The two INNO<sub>2</sub>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<sub>2</sub>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<sub>2</sub>VATE program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE across both INNO<sub>2</sub>VATE studies.

### Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the INNO<sub>2</sub>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<sub>2</sub>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<sub>2</sub>VATE's *Conversion* study of 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<sub>2</sub>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 prospectively agreed to by FDA and a non-inferiority margin of 1.3 prospectively agreed to by EMA.

The INNO<sub>2</sub>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.

INNO<sub>2</sub>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<sub>2</sub>TECT Program within NDD-CKD Adult Patients

The two PRO<sub>2</sub>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<sub>2</sub>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<sub>2</sub>TECT program, defined as non-inferiority of vadadustat versus darbepoetin alfa in time to first occurrence of MACE across both PRO<sub>2</sub>TECT studies.

#### Primary and Key Secondary Efficacy Endpoint Results

Vadadustat achieved each of the PRO<sub>2</sub>TECT 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<sub>2</sub>TECT'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<sub>2</sub>TECT'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 alfa-treated patients.

#### Primary Safety Major Adverse Cardiovascular Events (MACE) Endpoint Result

The PRO<sub>2</sub>TECT program (Correction and Conversion studies) (n=3,471):

- **Primary Safety MACE Endpoint Result:** Vadadustat did not meet the PRO<sub>2</sub>TECT 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<sub>2</sub>TECT 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<sub>2</sub>TECT analysis plan was prospectively designed to analyze the effect of regional differences, most notably, well-known differences in Hb treatment targets. Within PRO<sub>2</sub>TECT, 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 using age as a dichotomous variable, 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).

In October 2020, we announced that based on these analyses and the totality of the data from our Phase 3 program, we plan to pursue regulatory approval in the United States for vadadustat for the treatment of anemia in adult NDD-CKD patients. However, as vadadustat did not meet the PRO<sub>2</sub>TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in adult NDD-CKD patients and we look forward to working with the FDA in their review of these data.

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.

## *Regulatory and Commercialization Strategy*

Based on the strength of the INNO<sub>2</sub>VATE data, the additional analyses of data from PRO<sub>2</sub>TECT conducted by Akebia and the totality of the data from our Phase 3 program, following our October 2020 pre-NDA meeting with the FDA, we plan to proceed with the submission of an NDA for vadadustat by the middle of the second quarter of 2021 for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients. We are also working in close collaboration with Otsuka Pharmaceutical Co. Ltd., to prepare a Marketing Authorization Application, or MAA, for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients for submission to the European Medicines Agency, or EMA, expected in 2021. However, as vadadustat did not meet the PRO<sub>2</sub>TECT program's primary safety endpoint, we are remaining cautious in our outlook for potential approval of vadadustat in NDD-CKD adult patients in the United States and Europe.

We are in the process of supporting MTPC's commercial launch of vadadustat in Japan, preparing for a potential commercial launch of vadadustat in the United States and supporting potential commercial launches of vadadustat in certain other markets. Our ability to launch vadadustat in the United States is dependent on the successful filing and defense of an NDA, and approval by the FDA.

We plan to commercialize vadadustat, subject to FDA approval, in the United States with our well-established, nephrology-focused commercial organization, while leveraging our collaboration with Otsuka and its U.S. nephrology commercial organization. We granted Otsuka exclusive rights to commercialize vadadustat in Europe, China and certain other markets, subject to marketing approvals. We granted MTPC exclusive rights to commercialize vadadustat in Japan, where MTPC commenced commercial sales of vadadustat under the trade name, Vafseo<sup>TM</sup>, in August 2020, and in certain other countries in Asia, subject to marketing approvals. In addition, we granted Vifor (International) Ltd., or Vifor Pharma, an exclusive license to sell vadadustat to FKC and Third Party Dialysis Organizations, which combined manage up to approximately 60% of the dialysis patients in the United States, which would be effective upon FDA approval of vadadustat, the earlier of vadadustat's reimbursement under a bundled reimbursement model or using the TDAPA, and a milestone payment by Vifor Pharma. During the term of the license agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the United States to FKC or its affiliates or to any Third Party Dialysis Organization, and we may not directly supply vadadustat to FKC or any other affiliate of Fresenius Medical Care North America, or FMCNA, or any Third Party Dialysis Organization. For more information about our license, collaboration and strategic agreements relating to vadadustat, see Part I, Item 1. Business – License, Collaboration and Other Strategic Agreements – Vadadustat.

We entered into a letter agreement on February 14, 2020, or the Letter Agreement, with Vifor Pharma, relating to Vifor Pharma'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. A PRV entitles the holder to priority review of an NDA, or a Biologics License Application, or BLA, for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, and could lead to expedited approval. Pursuant to the Letter Agreement, we paid Vifor Pharma \$10.0 million in connection with the closing of the PRV Purchase. Vifor Pharma is obligated to retain all rights to, and maintain the validity of, the PRV until we and Vifor Pharma (a) enter into a definitive agreement setting forth the financial and other terms by which Vifor Pharma will assign the PRV to us for use with our planned NDA for vadadustat for the treatment of anemia due to CKD in both DD-CKD and NDD-CKD adult patients, or (b) make a mutual decision to sell the PRV and share the proceeds based on certain terms.

### *Japan Approval and Launch*

In June 2020, we announced the first regulatory approval of vadadustat for the treatment of anemia due to CKD in DD-CKD and NDD-CKD patients in Japan. Our collaboration partner, MTPC, commenced commercial sales of vadadustat in Japan under the trade name, Vafseo<sup>TM</sup>, in August 2020. The regulatory approval triggered a \$15.0 million regulatory milestone payment from MTPC to Akebia.

### *Study in COVID-19-Related Indication*

In July 2020, we announced the initiation of an investigator-sponsored clinical study 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 lessen the severity of acute respiratory distress syndrome, or ARDS, a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, infection. The randomized, double-blind, placebo-controlled study is intended to evaluate the safety and efficacy of vadadustat in up to 400 adult patients who have been hospitalized due to COVID-19. Patients will be dosed with vadadustat or a placebo starting within 24 hours of hospital admission and continuing for up to 14 days. This study is being conducted under an FDA Investigational New Drug application with UTHealth as the study sponsor and is currently enrolling patients. In January of 2021, UTHealth announced that it had been awarded \$5.1 million in funding from the U.S. Department of Defense, or DOD, to expand this clinical trial at its facilities.

## **Auryxia**

We market Auryxia in the United States with our well-established, nephrology-focused commercial organization. Our Japanese sublicensee, Japan Tobacco, Inc., or JT, and its subsidiary, Torii Pharmaceutical Co., Ltd., or Torii, commercialize Riona in Japan.

Auryxia is our only product approved for sale in the United States and it generated approximately \$128.9 million in revenue from U.S. product sales during the year ended December 31, 2020. We have funded our operations primarily through equity offerings, strategic collaborations, product revenues and debt.

### **Operating Overview**

We have never been profitable and have incurred net losses in each year since inception. Our net losses were \$383.5 million, \$279.7 million and \$143.6 million for the years ended December 31, 2020, 2019 and 2018, 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 preparing for and conducting clinical studies of vadadustat, providing general and administrative support for these operations and protecting our intellectual property.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on product revenue, collaboration revenue, and our ability to obtain additional funding. We expect to continue to incur significant expenses if and as we:

- conduct any post-marketing approval studies, Phase 4 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;
- continue our commercialization activities for Auryxia and plan for the commercialization of vadadustat, if approved, and any other product or product candidate, including those that may be in-licensed or acquired;
- adapt to any regulatory changes, including changes relating to reimbursement;
- adapt to any changes in reimbursement practices by third party payors;
- continue our integration activities as a result of our merger, or the Merger, with Keryx Biopharmaceuticals, Inc., or Keryx;
- enroll patients in our clinical trials;
- seek marketing approvals for vadadustat and any other product candidate, including those that may be in-licensed or acquired, and maintain marketing approvals for Auryxia and any other product, including those that may be in-licensed or acquired;
- have Auryxia, vadadustat and any other product or product candidate, including those that may be in-licensed or acquired, manufactured for clinical trials and for commercial sale;
- seek to discover and develop 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;
- make royalty, milestone or other payments under our license agreements and any future license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract, hire and retain qualified personnel;
- continue to create additional infrastructure and expend additional resources to support our operations as a fully integrated, publicly traded biopharmaceutical company; and
- experience any 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, payments from our collaborators, 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, 2020, we raised approximately \$704.3 million of net proceeds from the sale of equity, including \$519.8 million from various underwritten public offerings, \$134.5 million from at-the-market offerings, or ATM offerings, pursuant to sales agreements with Cantor Fitzgerald & Co., and \$50.0 million from the sale of 3,571,429 shares of common stock to Vifor Pharma. During the year ended December 31, 2020, we completed an underwritten public offering of our common stock with aggregate net proceeds of \$142.4 million and we raised \$67.3 million of net proceeds from ATM offerings. In addition, 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 November 25, 2019, we drew down the first tranche of \$80.0 million from the Term Loans and received net proceeds of \$77.3 million. On December 10, 2020, we drew down the second tranche of \$20.0 million from the Term Loans and received net proceeds of \$20.0 million. Subsequent to December 31, 2020 and through the date of this Annual Report on Form 10-K, the Company raised \$15.9 million in net proceeds from ATM offerings. At the inception of our collaboration agreements with Otsuka and MTPC, our collaborators committed to an aggregate of approximately \$573.0 million or more in cost-share funding, which we generally continue to receive on a quarterly prepaid basis, and license payments. Of these commitments, we received approximately \$272.0 million at the onset of the collaboration agreements.

### ***Impacts of COVID-19 Pandemic***

The ongoing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), or COVID-19, pandemic has presented a substantial public health and economic challenge around the world and continues to affect our employees, patients, healthcare providers with whom we interact, customers, collaboration partners, CROs, contract manufacturing organizations, or CMOs, vendors, communities and business operations. The full extent to which the COVID-19 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 new information that may emerge concerning the COVID-19 pandemic, any resurgences or mutations of COVID-19, the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets where the healthcare providers with whom we interact, our partners, our CROs, our CMOs, and our other vendors operate.

While we did not experience a significant impact from COVID-19 on our revenues during the first nine months of 2020, we believe our revenue growth was negatively impacted during the fourth quarter of 2020 primarily as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact our patient population; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future.

The majority of our office-based employees have been working from home since March 13, 2020. In addition, healthcare facilities have continued, or begun again, to restrict 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 restricted access to their clinics. As a result, we continue to primarily engage with healthcare providers and other customers virtually, where possible. Given this uncertain environment and the disproportionate impact of the COVID-19 pandemic on CKD patients, we are actively monitoring the demand for Auryxia, including the potential for further declines or changes in prescription trends and customer orders.

At this time, our third party contract manufacturing partners 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 manufacturing partners' ability to manufacture and deliver Auryxia and vadadustat (which is currently marketed under the trade name Vafseo™ by MTPC in Japan), which may result in delays in or disruptions to manufacturing and supply of our products.

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 COVID-19 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 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 and, following the Merger, commercial sales of Auryxia 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 collaborations with Otsuka and MTPC and any other collaborations into which we may enter, as well as commercial sales of Auryxia in the United States, and royalty revenue from JT and Torii, based on net sales of Riona in Japan.

### ***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, and royalties due to the licensor of Auryxia related to the U.S. product sales recognized during the period.

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, 2020 is estimated to be six years. The fair value inventory step-up is expected to be incurred over approximately three years from the date of the Merger.

### ***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 studies;
- 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; and
- costs associated with preclinical, clinical and regulatory activities.

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 studies of Auryxia and vadadustat or if, when, or to what extent we will 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 studies 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 studies in addition to or different from those that we currently anticipate, or if we experience delays in any of our clinical studies, we could be required to expend significant additional financial resources and time on the completion of clinical development.

From inception through December 31, 2020, we have incurred \$1.3 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 and vadadustat.



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 studies, and drug substance and drug product manufacturing for clinical studies.

We recently 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 contract research organizations 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.

Prior to 2019, we did not track or record our external research and development expenses on a program-by-program basis. 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, 2020 and 2019:

	Year ended December 31,	
	2020	2019
	<i>(in thousands)</i>	
Vadadustat external costs	\$ 128,869	\$ 253,259
External costs for other programs	15,020	20,311
Total external research and development expenses	143,889	273,570
Headcount, consulting, facilities and other	74,596	49,399
Total research and development expenses	\$ 218,485	\$ 322,969

### ***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, 2020 and 2019***

	Year ended December 31,		Increase (Decrease)
	2020	2019	
	(In Thousands)		
<b>Revenues:</b>			
Product revenue, net	\$ 128,901	\$ 111,119	\$ 17,782
License, collaboration and other revenue	166,406	223,882	(57,476)
Total revenues	295,307	335,001	(39,694)
<b>Cost of goods sold:</b>			
Product	148,866	108,935	39,931
Amortization of intangibles	31,515	36,401	(4,886)
Impairment of intangible asset	115,527	—	115,527
Total cost of goods sold	295,908	145,336	150,572
<b>Operating expenses:</b>			
Research and development	218,485	322,969	(104,484)
Selling, general and administrative	153,947	149,455	4,492
License expense	3,409	3,529	(120)
Total operating expenses	375,841	475,953	(100,112)
Operating loss	(376,442)	(286,288)	(90,154)
Other expense, net	(7,015)	(2)	(7,013)
Net loss before income taxes	(383,457)	(286,290)	(97,167)
Benefit from income taxes	—	(6,631)	6,631
Net loss	\$ (383,457)	\$ (279,659)	\$ (103,798)

*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 \$128.9 million for the year ended December 31, 2020, compared to net product revenue of \$111.1 million for the year ended December 31, 2019. The increase was primarily due to an increase in units sold. While we did not experience a significant impact from COVID-19 on our revenues during the first nine months of 2020, we believe our revenue growth was negatively impacted during the fourth quarter of 2020 primarily as the kidney patient populations that we serve continue to experience both higher hospitalization and mortality rates due to COVID-19. While we are unable to quantify the impact of the COVID-19 pandemic on future revenues and revenue growth, COVID-19 continues to adversely and disproportionately impact our patient population; therefore, we expect COVID-19 to continue to have a negative impact on our revenue growth for the foreseeable future. For additional information regarding the impact that the COVID-19 pandemic has had on our company and revenue, please refer to Part I, Item 1A. Risk Factors.

In September 2018, 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. On October 15, 2019, we filed a complaint in the United States District Court for the District of Massachusetts against CMS and the U.S. Department of Health and Human Services challenging CMS's decision that Auryxia would no longer be covered by Medicare for the IDA Indication and imposing a prior authorization requirement for Auryxia in the Hyperphosphatemia Indication, or the CMS Decision. See Part I, Item 3. Legal Proceedings for further information. 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.

*License, collaboration and other revenue.* License, collaboration and other revenue was \$166.4 million for the year ended December 31, 2020, compared to \$223.9 million for the year ended December 31, 2019. We recognized \$154.3 million in collaboration revenue for the year ended December 31, 2020 from our 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 the United States, or the Otsuka International Agreement, and recognition of a milestone and royalty revenue earned under our collaboration agreement with MTPC, or the MTPC Agreement. We recognized \$216.9 million in collaboration revenue for the year ended December 31, 2019 from our cost sharing arrangement under the Otsuka U.S. Agreement and the Otsuka International Agreement and recognition of a milestone under the MTPC Agreement. The decrease in revenue between

the two periods was primarily attributable to a decrease of \$68.0 million of revenue recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement. This decrease was partially offset by an additional \$5.4 million of revenue recognized under the MTPC Agreement due to timing of milestone recognition and royalty revenue, with \$15.4 million recognized during the year ended December 31, 2020 compared to \$10.0 million during the year ended December 31, 2019. We expect our Otsuka collaboration revenue to continue to decrease in the near term as we recently completed our global Phase 3 clinical development program for vadadustat and are currently engaged in close-out activities with respect to the program.

*Cost of Goods Sold - Product.* Cost of goods sold of \$148.9 million for the year ended December 31, 2020 primarily consists of costs associated with the manufacturing of Auryxia, \$68.2 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting, \$25.1 million in non-cash charges related to an increase in the liability for excess purchase commitments as a result of reductions in the short-term and long-term Auryxia revenue sales forecast during the year ended December 31, 2020, and \$20.1 million primarily related to the write-down of inventory associated with specific lots of Auryxia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation.

Cost of goods sold of \$108.9 million for the year ended December 31, 2019 consisted primarily of costs associated with the manufacturing of Auryxia and \$70.4 million in non-cash charges related to the fair-value inventory step-up from the application of purchase accounting.

*Cost of Goods Sold - Amortization of Intangibles.* Amortization of intangibles relates to the acquired developed product rights for Auryxia. This intangible asset was being amortized using a straight-line method over its estimated useful life of approximately nine years during the six months ended June 30, 2020 and approximately seven years during the six months ended December 31, 2020. Amortization of intangibles during the years ended December 31, 2020 and 2019 was \$31.5 million and \$36.4 million, respectively. The combined effect of the lower carrying value of the Auryxia intangible asset following impairment in the second quarter of 2020, as further described below, and the corresponding adjustment to the estimated useful life of the developed product rights for Auryxia, resulted in a decrease in 2020 amortization expense compared to 2019. The Company expects the future amortization charges to increase from 2020 due to the prospective adjustment of the estimated useful life of the developed product rights for Auryxia from seven years to six years as of December 31, 2020.

*Cost of Goods Sold - Impairment of Intangible Asset.* 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 compounding impact of the CMS Decision that rescinded Medicare Part D coverage of Auryxia for the IDA Indication, and imposed a prior authorization requirement for Auryxia for the Hyperphosphatemia Indication. As a result, we recorded an impairment charge of \$115.5 million to the Auryxia intangible asset during the year ended December 31, 2020. There were no such impairment charges during the year ended December 31, 2019.

*Research and Development Expenses.* Research and development expenses were \$218.5 million for the year ended December 31, 2020, compared to \$323.0 million for the year ended December 31, 2019. The net decrease of \$104.5 million was due to the following:

	<i>(in millions)</i>
Vadadustat external development expenses	(124.4)
Other external research and development	(5.3)
Headcount, consulting and facilities	25.2
Total net decrease	<u>\$ (104.5)</u>

The decrease in the costs related to the development of vadadustat is primarily attributable to a decrease in external costs related to our global Phase 3 program (INNO<sub>2</sub>VATE and PRO<sub>2</sub>TECT), for which we reported top-line data in the second and third quarters of 2020, respectively. Although we expect our research and development expenses to continue to decrease in the near term as we recently completed our global Phase 3 clinical development program for vadadustat, we will continue to incur significant research and development expenses in future periods in support of our overall development program for vadadustat and ongoing or planned studies with respect to Auryxia, vadadustat and development of other potential product candidates.

*Selling, General and Administrative Expenses.* Selling, general and administrative expenses were \$153.9 million for the year ended December 31, 2020, compared to \$149.5 million for the year ended December 31, 2019. The increase of \$4.5 million was primarily due to increases in headcount and consulting costs. In 2021, we expect our selling, general and administrative

expenses for our ongoing commercialization of Auryxia and for support of our ongoing research and development and potential commercialization of vadadustat and other product candidates to increase modestly from 2020.

*License Expenses.* License expense related to royalties due to Panion relating to sales of Riona in Japan were \$3.4 million and \$3.5 million for the years ended December 31, 2020 and 2019, respectively.

*Other Expense, Net.* Other expense, net, was \$7.0 million for the year ended December 31, 2020, compared to \$0.1 million for the year ended December 31, 2019. Other expense, net for the year ended December 31, 2020 was primarily due to interest expense associated with our Term Loans. Other expense, net for the year ended December 31, 2019 was primarily due to interest expense associated with our former line of credit with Silicon Valley Bank, or SVB, in the first quarter of 2019, which line of credit was terminated in November 2019, and interest expense associated with our Term Loans in the fourth quarter of 2019, offset by interest income from investment balances during the year ended December 31, 2019.

*Benefit from Income Taxes.* There was no benefit from income taxes for the year ended December 31, 2020. Benefit from income taxes was \$6.6 million for the year ended December 31, 2019 due to a decrease in our deferred tax liabilities, or DTLs. During the year ended December 31, 2019, there was an increase in deferred tax assets associated with the state net operating loss generated during the period. This increase in deferred tax assets reduced our net DTLs which created a benefit from income taxes for the year ended December 31, 2019.

### Comparison of the Years Ended December 31, 2019 and 2018

	Year ended December 31,		Increase (Decrease)
	2019	2018	
	<i>(In Thousands)</i>		
Revenues:			
Product revenue, net	\$ 111,119	\$ 6,824	\$ 104,295
License, collaboration and other revenue	223,882	200,918	22,964
Total revenues	335,001	207,742	127,259
Cost of goods sold:			
Product	108,935	6,251	102,684
Amortization of intangible assets	36,401	1,517	34,884
Total cost of goods sold	145,336	7,768	137,568
Operating expenses:			
Research and development	322,969	291,007	31,962
Selling, general and administrative	149,455	87,061	62,394
License expense	3,529	67	3,462
Total operating expenses	475,953	378,135	97,818
Operating loss	(286,288)	(178,161)	(108,127)
Other income (expense), net	(2)	6,235	(6,237)
Net loss before income taxes	(286,290)	(171,926)	(114,364)
Benefit from income taxes	(6,631)	(28,338)	21,707
Net loss	\$ (279,659)	\$ (143,588)	\$ (136,071)

*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. We began recording product revenue on sales of Auryxia in the United States on December 12, 2018 following the consummation of the Merger. Net product revenue was \$111.1 million for the year ended December 31, 2019 and \$6.8 million for the period from December 12, 2018 through December 31, 2018. This increase as compared to the period from December 12, 2018 through December 31, 2018 was due to net product revenue associated with Auryxia, as there was no comparable net product revenue in the period from January 1, 2018 through December 11, 2018 prior to the Merger.

*License, collaboration and other revenue.* License, collaboration and other revenue was \$223.9 million for the year ended December 31, 2019, compared to \$200.9 million for the year ended December 31, 2018. We recognized \$216.9 million in

collaboration revenue for the year ended December 31, 2019 from our cost sharing arrangement under the Otsuka U.S. Agreement and the Otsuka International Agreement and recognition of a milestone earned under the MTPC Agreement. We recognized \$200.5 million in collaboration revenue for the year ended December 31, 2018 from our cost sharing arrangement under the Otsuka U.S. Agreement, the Otsuka International Agreement, as well as revenue recognized in connection with the MTPC Agreement. The increase in revenue between the two periods was primarily attributable to an additional \$15.7 million of revenue recognized under both the Otsuka U.S. Agreement and Otsuka International Agreement and an additional \$0.7 million of revenue recognized in connection with the MTPC Agreement. The remaining variance was primarily due to an increase in license revenue relating to our sublicense agreement with JT and Torii and includes license fees and royalties on net product sales of Riona in Japan.

*Cost of Goods Sold - Product.* Cost of goods sold of \$108.9 million for the year ended December 31, 2019 consisted primarily of costs associated with the manufacturing of Auryxia and a \$70.4 million charge related to the fair-value inventory step-up from the application of purchase accounting. Cost of goods sold of \$6.3 million for the period from December 12, 2018 through December 31, 2018 consisted primarily of costs associated with the manufacturing of Auryxia and a \$4.8 million charge related to the fair-value inventory step-up from the application of purchase accounting. This increase as compared to the period from December 12, 2018 through December 31, 2018 was due to costs associated with Auryxia, as there were no comparable costs in the period from January 1, 2018 through December 11, 2018 prior to the Merger.

*Cost of Goods Sold - Amortization of Intangibles.* Amortization of intangibles relates to the acquired developed product rights for Auryxia. For the years ended December 31, 2019 and December 31, 2018, this intangible asset was being amortized over its estimated useful life of approximately nine years using a straight-line method. Amortization of intangibles for the years ended December 31, 2019 and 2018 was \$36.4 million and \$1.5 million, respectively.

*Research and Development Expenses.* Research and development expenses were \$323.0 million for the year ended December 31, 2019, compared to \$291.0 million for the year ended December 31, 2018. The net increase of \$32.0 million was due to the following:

	<i>(in millions)</i>
Vadadustat development expenses	(5.3)
Headcount, consulting and facilities	24.1
Other research and development	13.2
Total net increase	<u>\$ 32.0</u>

The decrease in the costs related to the development of vadadustat was primarily attributable to a decrease in external costs related to other supporting clinical and preclinical activities, as well as regulatory activities, and a decrease in costs for the Japan Phase 2 studies, which were completed in 2018. There was also a decrease in external costs for the PRO2TECT and INNO<sub>2</sub>VATE Phase 3 program and a decrease in costs related to the manufacture of drug substance and drug product. The overall increase in research and development expenses was primarily impacted by increases in headcount and consulting costs to support our research and development programs.

*Selling, General and Administrative Expenses.* Selling, general and administrative expenses were \$149.5 million for the year ended December 31, 2019, compared to \$87.1 million for the year ended December 31, 2018. The increase of \$62.4 million was primarily due to commercialization costs associated with Auryxia as there were no comparable commercialization costs during the first eleven months of 2018, and an increase in costs to support our research and development programs.

*License Expenses.* License expense related to royalties due to Panion relating to sales of Riona in Japan were \$3.5 million for the year ended December 31, 2019, compared to \$67,000 for the year ended December 31, 2018. The increase of \$3.4 million was primarily due to no license expense in the period from January 1, 2018 through December 11, 2018 prior to the Merger.

*Other Expense, Net.* The decrease in other income, net of \$6.2 million was primarily due to interest expense associated with our former line of credit with SVB, in the first quarter of 2019 and interest expense associated with our Term Loans in the fourth quarter of 2019 offset by interest income from investment balances during the year ended December 31, 2018. We did not have similar income during the year ended December 31, 2019.

*Benefit for Income Taxes.* Benefit for income taxes was \$6.6 million for the year ended December 31, 2019 due to a decrease in our net DTLs. During the year ended December 31, 2019, there was an increase in deferred tax assets associated with the state net operating loss generated during the period. This increase in deferred tax assets reduced our net DTLs which created a benefit from income taxes for the year ended December 31, 2019.

## Liquidity and Capital Resources

We have incurred losses and cumulative negative cash flows from operations since our inception in February 2007, and as of December 31, 2020, we had an accumulated deficit of \$1.2 billion. We anticipate that we will continue to incur losses for the foreseeable future. We expect to continue to incur additional research and development and selling, general and administrative expenses for our ongoing research and development and potential commercialization of vadadustat and our ongoing development and commercialization of Aurixia. Consistent with our expectation of an NDA submission by the middle of the second quarter of 2021, we expect our cash resources to fund our current operating plan beyond the expected U.S. launch of our product candidate, vadadustat, assuming timely regulatory approval and the receipt of associated regulatory milestones. Although we believe we have the cash resources to fund our operating plan beyond the expected U.S. launch of vadadustat, as noted above, we expect to continue to incur significant costs and we anticipate that we will need to obtain substantial additional funding in connection with our operating plan beyond that period. We have based these estimates on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Furthermore, our regulatory milestones may not be achieved, we may not receive the anticipated funding from our collaboration partners, and we may not secure other sources of financing. The period over which our cash runway extends is also dependent on the execution of our commercial plan, which is dependent on the overall market, the competitive environment, and the execution of our reimbursement strategies.

We have funded our operations principally through sales of our common stock, payments received from our collaboration partners, and following the Merger, product sales, debt and a royalty transaction. As of December 31, 2020, we had cash and cash equivalents and available for sale securities of approximately \$268.7 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation. Accordingly, available for sale securities, consisting principally of corporate and government debt securities stated at fair value, are also available as a source of liquidity.

## 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,		
	2020	2019	2018
	<i>(In Thousands)</i>		
Net cash provided by (used in):			
Operating activities	\$ (110,388)	\$ (257,441)	\$ (97,494)
Investing activities	(40,004)	211,176	36,594
Financing activities	231,720	88,970	96,562
Net increase in cash, cash equivalents and restricted cash	<u>\$ 81,328</u>	<u>\$ 42,705</u>	<u>\$ 35,662</u>

*Operating Activities.* Net cash used in operating activities in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. Net cash used in operating activities during the year ended December 31, 2020 of \$110.4 million was largely driven by timing of payments on our Phase 3 development program for vadadustat, rebate payments and payments for inventory. These payments were partially offset by adjustments for non-cash items, including the intangible asset impairment charge of \$115.5 million, fair value step-up of inventory sold or written off of \$68.2 million, amortization of intangibles of \$31.5 million, an increase to the liability for excess purchase commitments of \$25.1 million, stock-based compensation expense of \$24.5 million, and write-downs of inventory of \$20.1 million primarily associated with specific lots of Aurixia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation. Net cash used in operating activities during the year ended December 31, 2019 of \$257.4 million was largely driven by timing of payments on our Phase 3 development program for vadadustat, payments for inventory and merger-related liabilities. These payments were partially offset by adjustments for non-cash items, including the fair value write-up of inventory sold or written off of \$70.4 million, amortization of intangibles of \$36.4 million, and stock-based compensation expense of \$11.9 million. Net cash used in operating activities during the year ended December 31, 2018 of \$97.5 million was largely driven by our Phase 3 development program for vadadustat, partially offset by receipt of cash from collaboration agreements.

*Investing Activities.* Net cash used in investing activities during the year ended December 31, 2020 of \$40.0 million was comprised primarily of purchase of available for sale securities of \$99.9 million, partially offset by proceeds from the maturities of available for sale securities of \$60.2 million. Net cash provided by investing activities during the year ended December 31, 2019 of \$211.2 million was comprised primarily of proceeds from the maturities of available for sale securities of

\$153.1 million and proceeds from the sales of available for sale securities of \$64.7 million, partially offset by purchases of equipment of \$6.7 million. Net cash provided by investing activities during the year ended December 31, 2018 of \$36.6 million was comprised primarily from the sale and maturities of available for sale securities, partially offset by purchases of available for sale securities, purchases of equipment and acquisition of the business, net of cash acquired.

*Financing Activities.* During the years ended December 31, 2020, 2019 and 2018 our net cash provided by financing activities was \$231.7 million, \$89.0 million and \$96.6 million, respectively. Net cash provided by financing activities for the years ended December 31, 2020, 2019 and 2018 consisted primarily of net proceeds from the issuance of debt, net proceeds from the public issuance of common stock, proceeds from the exercise of stock options and proceeds from the sale of stock under our employee stock purchase plan, partially offset by payments on loans payable.

### **Operating Capital Requirements**

We have one product, Auryxia, approved for commercial sale in the United States, but have not generated, and may not generate, enough product revenue from the sale of Auryxia to realize net profits from product sales. We anticipate that we will continue to generate losses for the foreseeable future, and we expect the losses to increase as we continue the development of, and seek marketing approvals for vadadustat and any other potential product candidates. We are subject to all risks incident to the development and commercialization of novel therapeutics, and we may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. We expect to continue to incur additional costs associated with operating as a public company and we anticipate that we will need substantial additional funding in connection with our continuing operations.

As of December 31, 2020, we had cash and cash equivalents and available for sale securities of approximately \$268.7 million. At the inception of our collaboration agreements with Otsuka and MTPC, our collaborators committed to an aggregate of approximately \$573.0 million or more in cost-share funding, of which we received approximately \$272.0 million at the onset of the collaborations, and the remainder of which we generally continue to receive on a quarterly prepaid basis, and through license payments.

We expect to finance future cash needs through product revenue, public or private equity or debt transactions, payments from our collaboration partners, royalty transactions, strategic transactions, or a combination of these approaches. Additionally, we will require additional capital 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. However, additional funds may not be available to us on acceptable terms or at all. 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 or product candidates, including those that may be in-licensed or acquired. If we raise additional funds through the issuance of additional debt or equity securities, it could result in dilution to our existing stockholders or increased fixed payment obligations, and any such securities may have rights senior to those of our common stock. Any of these events could significantly harm our business, financial condition and prospects.

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 risks and uncertainties, and actual results could vary as a result of a number of factors. 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. 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.

If we cannot expand our operations or otherwise capitalize on our business opportunities because we lack sufficient capital, our business, financial condition and results of operations could be materially adversely affected.

### **Contractual Obligations and Commitments**

At December 31, 2020, our future contractual obligations are as follows:

	Payments due by period (in thousands)				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating Lease Obligations	\$ 35,596	\$ 6,667	\$ 13,269	\$ 11,556	\$ 4,104
Manufacturing Agreements	215,607	130,177	44,962	31,218	9,250
Debt Obligations	128,991	9,632	55,728	63,631	—
Total	\$ 380,194	\$ 146,476	\$ 113,959	\$ 106,405	\$ 13,354

### 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 commencing in December 2021, and is subject to annual rent escalations, which commence 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, which expires on February 28, 2023. The total monthly lease payments under the base rent are approximately \$136,000 and are subject to annual rent escalations.

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 expires on February 27, 2023. Foundation is obligated to pay Keryx rent that approximates the rent due from us to Keryx's landlord with respect to the Boston Lease. 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. 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. We 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, our obligations under the Term Loans are unconditionally guaranteed by Keryx, or the Guarantee. Additionally, our and Keryx's obligations under the Term Loans and the Guarantee are secured by a first priority lien on certain assets of ours and Keryx's, including Auryxia and certain related assets, cash, and certain equity interests held by us 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. We will repay the principal under the Term Loans in equal quarterly payments starting on the 33rd-month anniversary of the applicable Funding Date or, if certain conditions are met, it will have the option to repay the principal in equal quarterly payments starting on the 48th-month anniversary of the applicable Funding Date, or collectively the Amortization Schedule. 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, we 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 us, 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 ours and our subsidiaries, including maintaining, on an annual basis, a minimum liquidity threshold starting in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. 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, 2020, we determined that no events of default had occurred.

We 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, we 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 our achieving certain regulatory and revenue conditions. We 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, we 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.

#### *Manufacturing Agreements*

As a result of the Merger, our contractual obligations include Keryx's commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or 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, collectively the BioVectra Agreement, we agreed to purchase minimum quantities of Auryxia drug substance annually at predetermined prices. On September 4, 2020, we 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 decreases 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, collectively the Amended BioVectra Agreement, requires us 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 are recorded in other assets and amortized into drug substance as inventory is released to us from BioVectra. The term of the Manufacture and Supply Agreement with BioVectra expires on December 31, 2022. The term of the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement expires on December 31, 2026, after which, it automatically renews for successive one-year terms unless either party gives notice of its intention to terminate within a specified time prior to the end of the then-current term. In addition, we and BioVectra each have the ability to terminate these agreements upon the occurrence of certain conditions. As of December 31, 2020, we are required to reimburse BioVectra for certain costs in connection with the construction of the new facility and to purchase minimum quantities of Auryxia drug substance annually for a total cost of approximately \$95.7 million through the end of the contract term.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, or the Siegfried Agreement, we have agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per kilogram will decrease with an increase in quantity above the minimum purchase quantity. The term of the Siegfried Agreement expires on December 31, 2021, after which, it automatically renews for one-year terms until terminated. The Siegfried Agreement provides us with certain termination rights prior to December 31, 2021. As of December 31, 2020, we are required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately \$47.9 million through the year ending December 31, 2021.

As part of purchase accounting, 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. The liability related to the amount of purchase commitments that exceed the current forecast was \$55.8 million and \$30.2 million as of December 31, 2020 and 2019, respectively. The \$25.6 million increase in liability, which was largely driven by reductions in the short-term and long-term Auryxia revenue sales forecast during the year ended December 31, 2020, was primarily recorded to cost of goods sold.

On February 11, 2021, Keryx and Siegfried entered into an amendment to the Siegfried Agreement, or the Siegfried Amendment. The Siegfried Agreement, as amended, includes the terms and conditions under which Siegfried will manufacture and supply finished Auryxia drug substance for commercial purposes. Siegfried currently manufactures Auryxia drug substance at two approved sites. Pursuant to the Siegfried Amendment, the term of the Siegfried Agreement was extended for one site such that the Siegfried Agreement will expire on December 31, 2022, subject to Keryx's option to extend the term for such site through December 31, 2023 by providing 12 months' prior written notice to Siegfried. The Siegfried Amendment provides for minimum annual quantity commitments and predetermined prices for the remainder of the term as well as certain other changes. Subsequent to December 31, 2020, the amount of Auryxia drug substance we have committed to purchase from Siegfried is \$45.4 million through December 31, 2022.

On April 9, 2019, we entered into a Supply Agreement with Esteve Química, S.A., or Esteve, or the Esteve Agreement. The Esteve Agreement includes the terms and conditions under which Esteve will manufacture vadaustat drug substance for commercial use. Pursuant to the Esteve Agreement, we provide rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflects our needs for vadaustat drug substance produced by Esteve over a certain number of months, represented as a quantity of vadaustat drug substance per calendar quarter. The parties have agreed to a volume-based pricing structure under the Esteve Agreement. The Esteve Agreement has an initial term of four years, beginning April 9, 2019 and ending April 9, 2023. Pursuant to the Esteve Agreement, we have agreed to purchase a certain percentage of the global demand for vadaustat drug substance from Esteve. As of December 31, 2020, we have committed to purchase \$26.0 million of vadaustat drug substance from Esteve through the second quarter of 2022. Subsequent to December 31, 2020, the amount of vadaustat drug substance we have committed to purchase from Esteve increased to \$47.6 million through the fourth quarter of 2022.

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 vadaustat 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 vadaustat 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. Pursuant to the Patheon Agreement, we have agreed to purchase a certain percentage of the global demand for vadaustat drug product from Patheon. As of December 31, 2020, we had a minimum commitment with Patheon for \$1.3 million through the third quarter of 2021.

On April 2, 2020, we 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 vadaustat 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 vadaustat 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 vadaustat drug substance from WuXi STA. As of December 31, 2020, we have committed to purchase \$44.7 million of vadaustat drug substance from WuXi STA through the first quarter of 2022.

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*

Under our agreement with IQVIA to provide contract research organization services for the PRO<sub>2</sub>TECT and INNO<sub>2</sub>VATE programs, the total remaining contract costs as of December 31, 2020 were approximately \$14.7 million, of which Otsuka reimburses a significant portion back to us. Substantive performance for the committed work with IQVIA was completed in 2020 and close out activities will be performed through the first quarter of 2021. We also contract with various other organizations to conduct research and development activities with remaining contract costs to us of approximately \$155.9 million as of December 31, 2020. 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.

#### **Off-Balance Sheet Arrangements**

As of December 31, 2020, we did not have any off-balance sheet arrangements as defined in the rules and regulations of the SEC.

#### **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, prepaid and accrued research and development expenses and stock-based compensation. 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.

#### ***Derivative Financial Instruments***

We account 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 our 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 our 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 issued by us in connection with the Janssen Pharmaceutica NV Research and License Agreement, the Janssen Agreement, is classified as equity in our consolidated balance sheet. (See Note 12 to our consolidated financial statements in Part 2, Item 8. Financial

Statements and Supplementary Data). The derivative liability recorded in connection with the Loan Agreement with Pharmakon is classified as a liability in our consolidated balance sheet. (See Note 11 to our consolidated financial statements in Part 2, Item 8. Financial Statements and Supplementary Data).

### ***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.

Prior to the regulatory approval of our product candidates, we incur expenses for the manufacture of material that could potentially be available to support the commercial launch of our products. 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, we record 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.

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.

### ***Debt***

We perform 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. We monitor, on an ongoing basis, whether events or circumstances could give rise to a change in the classification of embedded features.

### ***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.

### ***Revenue***

We generate revenues primarily from sales of Auryxia, see Note 3 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data, and from our collaborations with MTPC and Otsuka, see Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data. We recognize 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, we recognize revenue when our 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 we determine are within the scope of ASC 606, we perform 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.

We only apply the five-step model to contracts when it is probable that the entity will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We do not include a financing component in our estimated transaction price at contract inception unless we estimate that certain performance obligations will not be satisfied within one year. Additionally, we recognize the incremental costs of obtaining a contract as an expense when incurred if the amortization period of the asset that we otherwise would have recognized is one year or less.

#### *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.

#### *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 us and our Customers, health care providers, payors and other indirect customers relating to our sales of our 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 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 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 our estimates. If actual results in the future vary from our estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

*Trade Discounts and Allowances:* We generally provide Customers with discounts that include incentive fees that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we compensate (through trade discounts and allowances) our Customers for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our 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, 2020. We record 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, 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 and record this estimate as a reduction of revenue in the period the related product revenue is

recognized. 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. 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 we generally issue credits for such amounts within a few weeks of the Customer's resale of the product. 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. We estimate these rebates and record 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:* 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. 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, 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 the distribution channel at the end of each reporting period.

#### *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.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, we implement the five-step model noted above. As part of the accounting for these arrangements, 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. 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 our 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. 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. With regard to the MTPC and Otsuka collaboration agreements, we recognize 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 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. We evaluate 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, we evaluate 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. We evaluate 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 our control 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 we recognize revenues as, or when, the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we will re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our 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. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If we are 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*

We 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). We receive royalty payments from JT and Torii, based on net sales of Riona in Japan.

### *Collaborative Arrangements*

We record the elements of our 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. We consider 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 us and our collaborative partner and the transactions between us 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, we recognize our allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the Otsuka U.S. Agreement, as defined below in Note 4 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data, as a component of the related expense in the period incurred. To the extent product revenue is generated from the collaboration, we recognize our share of the net sales on a gross basis if it is deemed to be the principal in the transactions with customers, or on a net basis if it is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

### ***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, 2020 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 to our consolidated financial statements in Part II, Item 8. Financial Statements and Supplementary Data 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, 2020 and 2019 are classified as noncurrent within the income tax provision (see Note 14 to our consolidated financial statements in Part 2, Item 8. Financial Statements and Supplementary Data).

We account for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, we recognize 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, 2020 and 2019, we do not have any significant uncertain tax positions. We recognize interest and penalties related to uncertain tax positions in income tax expense.

### ***Stock-Based Compensation***

We account for 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. Our stock-based awards are comprised of stock options and RSUs. We estimate the fair value of options granted using the Black-Scholes option pricing model. We use a blend of our stock price and the quoted market price of comparable public companies to determine the fair value of restricted stock awards and common 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. Due to the lack of company-specific historical and implied volatility data for trading our stock in the public market, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to us, including stage of product development and life science industry focus. During 2017, we began to estimate our volatility by using a blend of our stock price history for the length of time we have market data for our stock and the historical volatility of similar public companies for the expected term of each grant. We are a commercial-stage biopharmaceutical company and the representative group of companies has certain similar characteristics to us. We believe the group selected has sufficient similar



economic and industry characteristics and includes companies that are most representative of us. We use 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 we do not expect substantially different exercise or post-vesting termination behavior among our employee population. For options granted to non-employees, we utilize 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 we have never paid dividends and have no current plans to pay any dividends on our common stock, which is similar to our peer group.

Our 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, we recognize expense if, and to the extent that, we estimate that achievement of the performance condition is probable. If we conclude that vesting is probable, we recognize expense from the date we reach this conclusion through the estimated vesting date.

### **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 2, Item 8. Financial Statements and Supplementary Data.

### **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, 2020 and 2019, we had cash and cash equivalents and available for sale securities of \$268.7 million and \$147.7 million, respectively, consisting primarily of money market mutual funds consisting of U.S. government debt securities, 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, 2020 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 and Vafseo<sup>TM</sup> 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, 2020, 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, 2020 by approximately \$0.3 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.**

Table of Contents

	<u>Page</u>
<a href="#">Report of Independent Registered Public Accounting Firm</a>	<a href="#">130</a>
<b>Financial Statements</b>	
<a href="#">Consolidated Balance Sheets</a>	<a href="#">133</a>
<a href="#">Consolidated Statements of Operations and Comprehensive Loss</a>	<a href="#">134</a>
<a href="#">Consolidated Statements of Stockholders' Equity</a>	<a href="#">135</a>
<a href="#">Consolidated Statements of Cash Flows</a>	<a href="#">136</a>
<a href="#">Notes to Consolidated Financial Statements</a>	<a href="#">137</a>

## 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, 2020 and 2019, 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, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020, 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, 2020, 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 February 25, 2021 expressed an adverse opinion thereon.

### Adoption of ASU No. 2016-02

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in the year ended December 31, 2019 due to the adoption of ASU No. 2016-02, *Leases (Topic 842)*, and the related amendments.

### 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 matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters 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 matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

### **Valuation of Impairment of Intangible Assets**

#### *Description of the Matter*

At December 31, 2020, the Company's definite-lived intangible asset related to developed product rights for Auryxia was \$144.2 million. As described in Note 2 and Note 9 to the consolidated financial statements, intangible assets with definite lives are assessed for recoverability whenever events or changes in circumstances indicate that the carrying amount of the assets may not be fully recoverable. The Company evaluates assets for potential impairment by comparing estimated future undiscounted net cash flows to the carrying amount of the asset group. If the carrying amount of the asset group exceeds the estimated future undiscounted cash flows, impairment is measured based on the difference between the carrying amount of the assets and fair value. In the second quarter of 2020, the Company revised its long-range plan to reduce its short-term and long-term Auryxia revenue forecast which resulted in a \$115.5 million impairment loss related to developed product rights for Auryxia.

Auditing the Company's impairment assessment involved complex judgment due to the significant judgments required to estimate the fair value of the intangible asset. The Company's model for estimating the fair value of the asset involves significant assumptions, including projected revenues and expenses related to the asset, expected contributory asset charges, and the risk-adjusted discount rate.

#### *How We Addressed the Matter in Our Audit*

We obtained an understanding, evaluated the design, and tested controls over the Company's measurement of its estimated fair value of its intangible assets, including controls over management's review of the valuation model and the significant assumptions described above. This included evaluating controls over the Company's budgetary and forecasting process used to develop the estimated future cash flows. We also tested controls over management's review of the completeness and accuracy of the data used to measure the impairment.

To test the estimated fair value of the Company's asset group and for the intangible asset with definite lives, we performed audit procedures that included, among others, assessing the methodologies used in the model and testing the significant inputs and assumptions discussed above, including the completeness and accuracy of the underlying data used by the Company in its analyses. We compared the significant assumptions used by management to current industry and economic trends, historical financial results, contractual obligations, and other relevant factors. We involved our valuation specialists to assist in the assessment of the Company's discount rate for the fair value estimate of the definite-lived intangible asset due to the carrying amount of the asset group exceeding the estimated future undiscounted cash flows. We also performed a sensitivity analysis of the significant assumptions to evaluate the change in the fair value of the intangible asset that would result from changes in underlying assumptions.

### **Valuation of Excess Purchase Commitment Liability**

#### *Description of the Matter*

At December 31, 2020, the Company's liability for excess purchase commitments related to Auryxia's executory contracts was \$55.8 million. As described in Note 5 and Note 16, the Company recorded a liability for its future firm purchase commitments that exceed the Company's current forecasts. The Company re-evaluates its excess purchase commitments each reporting period to assess whether any adjustments to its excess purchase commitments liability are necessary. This evaluation includes reviewing the contractual minimums, expiration and utilization assumptions, and sales forecasts. The Company's revised long-term and short-term Auryxia revenue forecasts, along with an amendment to supplier agreements, resulted in the Company recording an increase in its liability for excess purchase commitments of \$25.6 million during the year ended December 31, 2020.

Auditing the Company's evaluation of its excess purchase commitment liability involved complex judgment due to the significant management judgments required to estimate the value of the total excess commitment. The Company's model for estimating the liability involves significant assumptions, including projected sales volumes, which is sensitive to and affected by economic, industry and company-specific qualitative factors.

*How We Addressed  
the Matter in Our  
Audit*

We obtained an understanding, evaluated the design, and tested controls over the Company's evaluation of its excess purchase commitment liability. This included controls over the model, significant assumptions, and completeness and accuracy of the data used in the evaluation.

To test the Company's evaluation of its excess purchase commitment liability, we performed audit procedures that included, among others, testing the significant inputs and assumptions discussed above, including the completeness and accuracy of the underlying data used by the Company in its analyses. We compared the significant assumptions used by management to current industry and economic trends, historical financial results, contractual obligations, and other relevant factors. We also performed a sensitivity analysis of the significant assumptions to evaluate the change in the liability that would result from changes in underlying assumptions.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2013.

Boston, Massachusetts

February 25, 2021

**AKEBIA THERAPEUTICS, INC.**  
**Consolidated Balance Sheets**  
(in thousands, except share and per share data)

	December 31, 2020	December 31, 2019
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 228,698	\$ 147,449
Available for sale securities	39,992	245
Inventory	61,017	116,349
Accounts receivable, net	26,853	38,864
Prepaid expenses and other current assets	14,877	6,626
Total current assets	371,437	309,533
Property and equipment, net	8,622	10,380
Operating lease assets	26,876	29,038
Goodwill	55,053	55,053
Other intangible assets, net	144,170	291,212
Other assets	37,981	75,985
Total assets	\$ 644,139	\$ 771,201
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 41,308	\$ 39,217
Accrued expenses and other current liabilities	130,624	129,071
Short-term deferred revenue	15,214	39,830
Total current liabilities	187,146	208,118
Deferred revenue, net of current portion	25,345	33,120
Operating lease liabilities, net of current portion	24,621	27,528
Derivative liability	2,420	1,650
Long-term debt, net	96,378	75,805
Other non-current liabilities	60,611	30,223
Total liabilities	396,521	376,444
Commitments and contingencies (Note 16)		
Stockholders' equity:		
Preferred stock \$0.00001 par value, 25,000,000 shares authorized at December 31, 2020 and 2019; 0 shares issued and outstanding at December 31, 2020 and 2019	—	—
Common stock: \$0.00001 par value; 350,000,000 and 175,000,000 shares authorized at December 31, 2020 and 2019, respectively; 148,074,085 and 121,674,568 shares issued and outstanding at December 31, 2020 and 2019, respectively	1	1
Additional paid-in capital	1,425,115	1,188,810
Accumulated other comprehensive gain	13	—
Accumulated deficit	(1,177,511)	(794,054)
Total stockholders' equity	247,618	394,757
Total liabilities and stockholders' equity	\$ 644,139	\$ 771,201

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,		
	2020	2019	2018
<b>Revenues:</b>			
Product revenue, net	\$ 128,901	\$ 111,119	\$ 6,824
License, collaboration and other revenue	166,406	223,882	200,918
Total revenues	<u>295,307</u>	<u>335,001</u>	<u>207,742</u>
<b>Cost of goods sold:</b>			
Product	148,866	108,935	6,251
Amortization of intangibles	31,515	36,401	1,517
Impairment of intangible asset	115,527	—	—
Total cost of goods sold	<u>295,908</u>	<u>145,336</u>	<u>7,768</u>
<b>Operating expenses:</b>			
Research and development	218,485	322,969	291,007
Selling, general and administrative	153,947	149,455	87,061
License expense	3,409	3,529	67
Total operating expenses	<u>375,841</u>	<u>475,953</u>	<u>378,135</u>
Operating loss	(376,442)	(286,288)	(178,161)
<b>Other income (expense):</b>			
Interest income (expense)	(8,871)	792	6,154
Other income (expense)	1,856	(794)	81
Net loss before income taxes	<u>(383,457)</u>	<u>(286,290)</u>	<u>(171,926)</u>
Benefit from income taxes	—	(6,631)	(28,338)
Net loss	<u>\$ (383,457)</u>	<u>\$ (279,659)</u>	<u>\$ (143,588)</u>
Net loss per share - basic and diluted	<u>\$ (2.77)</u>	<u>\$ (2.36)</u>	<u>\$ (2.47)</u>
Weighted-average number of common shares - basic and diluted	<u>138,463,152</u>	<u>118,395,919</u>	<u>58,038,252</u>
<b>Comprehensive loss:</b>			
Net loss	\$ (383,457)	\$ (279,659)	\$ (143,588)
Other comprehensive gain - unrealized gain on securities	13	261	181
Total comprehensive loss	<u>\$ (383,444)</u>	<u>\$ (279,398)</u>	<u>\$ (143,407)</u>

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, 2017	47,612,619	\$ —	\$ 493,823	\$ (442)	\$ (370,807)	\$ 122,574
Keryx Merger	57,773,090	1	527,753	—	—	527,754
Issuance of Baupost Additional Share	1,497,320	—	13,386	—	—	13,386
Issuance of common stock excluding Keryx Merger, net of issuance costs	9,194,306	—	95,452	—	—	95,452
Proceeds from sale of stock under employee stock purchase plan	48,768	—	482	—	—	482
Exercise of options	178,382	—	647	—	—	647
Share-based compensation expense	—	—	19,040	—	—	19,040
Restricted stock unit vesting	583,033	—	—	—	—	—
Unrealized gain	—	—	—	181	—	181
Net loss	—	—	—	—	(143,588)	(143,588)
Balance at December 31, 2018	116,887,518	\$ 1	\$ 1,150,583	\$ (261)	\$ (514,395)	\$ 635,928
Issuance of common stock, net of issuance costs	4,068,912	—	25,785	—	—	25,785
Proceeds from sale of stock under employee stock purchase plan	87,530	—	383	—	—	383
Exercise of options	362,796	—	560	—	—	560
Retired shares	(55,324)	—	(426)	—	—	(426)
Share-based compensation expense	—	—	11,925	—	—	11,925
Restricted stock unit vesting	323,136	—	—	—	—	—
Unrealized gain	—	—	—	261	—	261
Net loss	—	—	—	—	(279,659)	(279,659)
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

See accompanying notes to consolidated financial statements.



**Akebia Therapeutics, Inc.**  
**Consolidated Statements of Cash Flows**  
(in thousands)

	Year Ended December 31,		
	2020	2019	2018
<b>Operating activities:</b>			
Net loss	\$ (383,457)	\$ (279,659)	\$ (143,588)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	2,075	2,245	899
Amortization of intangibles	31,515	36,401	1,522
Intangible asset impairment charge	115,527	—	—
Amortization of premium/discount on investments	(47)	(819)	(1,232)
Non-cash interest expense	1,534	786	28
Non-cash operating lease expense	(2,037)	(2,229)	—
Write-off of property and equipment	—	2,053	—
Non-cash merger expense(1)	—	—	13,386
Fair value step-up of inventory sold or written off	68,240	70,444	4,771
Write-down of inventory	20,072	7,112	—
Change in excess inventory purchase commitments	25,114	—	—
Stock-based compensation	24,460	11,925	19,040
Deferred income taxes	—	(6,631)	(28,338)
Change in fair value of derivative liability	286	—	—
Changes in operating assets and liabilities:			
Accounts receivable	12,011	(22,198)	33,384
Inventory	6,163	(29,142)	26
Prepaid expenses and other current assets	(8,119)	10,541	(977)
Other long-term assets	(2,779)	4,917	903
Accounts payable	3,678	1,372	13,717
Accrued expense	6,356	(27,351)	55,482
Operating lease liabilities	1,411	2,531	—
Deferred revenue	(32,391)	(39,739)	(66,935)
Deferred rent	—	—	418
Net cash used in operating activities	(110,388)	(257,441)	(97,494)
<b>Investing activities:</b>			
Acquisition of business, net of acquired cash and restricted cash	—	—	6,147
Purchase of property and equipment	(317)	(6,655)	(1,606)
Purchase of available for sale securities	(99,932)	—	(224,216)
Proceeds from the maturities of available for sale securities	60,245	153,110	243,269
Proceeds from sales of available for sale securities	—	64,721	13,000
Net cash provided by (used in) investing activities	(40,004)	211,176	36,594
<b>Financing activities:</b>			
Proceeds from the issuance of common stock, net of issuance costs	209,419	25,785	95,452
Proceeds from the sale of stock under employee stock purchase plan	1,100	383	482
Proceeds from the exercise of stock options	1,226	560	647
Retirement of treasury stock	—	(426)	—
Proceeds from the issuance of debt, net	19,975	77,668	—
Payments on debt	—	(15,000)	—
Payments on capital lease obligations	—	—	(19)
Net cash provided by financing activities	231,720	88,970	96,562
Increase in cash, cash equivalents, and restricted cash	81,328	42,705	35,662
Cash, cash equivalents, and restricted cash at beginning of the period	149,804	107,099	71,437
Cash, cash equivalents, and restricted cash at end of the period	\$ 231,132	\$ 149,804	\$ 107,099
Non-cash financing activities			
Unpaid offering costs	\$ 100	\$ —	\$ —
Fair value of shares and equity awards issued in acquisition	—	—	527,754

(1) Relates to non-cash expense associated with the fair value of the Baupost additional shares (see Note 5).  
See accompanying notes to consolidated financial statements.

**Akebia Therapeutics, Inc.**  
**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 biopharmaceutical company with the purpose of bettering the lives of people living with kidney disease. Akebia's lead investigational product candidate, vadadustat, is an oral therapy in Phase 3 development for the treatment of anemia due to chronic kidney disease, or CKD. Vadadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, or HIF-PHI, designed to mimic the physiologic effect of altitude on oxygen availability. At higher altitudes, the body responds to lower oxygen availability with stabilization of hypoxia-inducible factor, or HIF, which can lead to red blood cell, or RBC, production and improved oxygen delivery to tissues. Vadadustat is approved and marketed in Japan as a treatment for anemia due to CKD in both dialysis-dependent and non-dialysis dependent adult patients under the trade name Vafseo<sup>TM</sup>. In addition, the Company has a commercial product, Auryxia, which is currently 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 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 the improvement of hyperphosphatemia in patients with DD-CKD and NDD-CKD under the trade name Riona.

On November 11, 2019, the Company, with Keryx Biopharmaceuticals, Inc., or Keryx, as guarantor, entered into a loan agreement, or the Loan Agreement, with Biopharma Credit plc as collateral agent and lender, or the Collateral Agent, and Biopharma Credit Investments V (Master) LP as lender, pursuant to which term loans in an aggregate principal amount of \$100 million were 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 and the second tranche of \$20.0 million, or Tranche B, was drawn on December 10, 2020. Refer to Note 11 to our consolidated financial statements in Part II, Item 8 – Financial Statements and Supplementary Data for additional details on the Loan Agreement.

On December 12, 2018, the Company completed a merger with Keryx Biopharmaceuticals, Inc., or Keryx, or the Merger. Pursuant to the terms and conditions of the Agreement and Plan of Merger, or the Merger Agreement, each share of Keryx common stock, or Keryx Share, issued and outstanding immediately prior to the effective time of the Merger, or the Effective Time, was cancelled and converted into 0.37433, or the Exchange Multiplier, fully paid and non-assessable shares of Akebia common stock, or Akebia Shares, resulting in the issuance of an aggregate of 59,270,410 Akebia Shares.

Since inception, the Company has devoted most of its resources to research and development, including its preclinical and clinical development activities, 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 to the Company's Japanese partners Japan Tobacco, Inc. and its subsidiary Torii Pharmaceutical Co., Ltd., collectively JT and Torii, on December 12, 2018. Additionally, following regulatory approval of vadadustat in Japan, the Company began recognizing royalty revenues from Mitsubishi Tanabe Pharma Corporation, or MTPC, from the sale of Vafseo in August 2020. 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 or any other potential product candidate, it may be unable to achieve profitability.

The Company is subject to a number of risks including, but not limited to, the need to obtain adequate additional funding, including the resources necessary to fund the continued development and commercialization of Auryxia, and the development, regulatory activities and potential commercialization of vadadustat, risks relating to integration following the Merger, risks relating to market acceptance, coverage and reimbursement of Auryxia and vadadustat, if approved, risks related to maintaining the Company's commercial organization and capabilities, risks relating to potential generic entrants, risks of clinical trial failures, the risk of relying on third parties, the risk that the Company never achieves profitability, protection of proprietary technology, compliance with governmental regulations, and dependence on key personnel, and the impact of legal, regulatory and administrative proceedings.

In December 2015, the Company entered into a collaboration agreement with MTPC to develop and commercialize vadadustat in Japan and certain other countries in Asia, collectively, the MTPC Territory, for total payments of up to \$245.0 million,

comprised of a \$20.0 million upfront payment, up to \$50.0 million in specified development and regulatory milestones, and up to \$175.0 million in specified commercial milestones, as well as tiered royalty payments ranging from 13% to 20% on annual net sales of vadadustat in the MTPC Territory, subject to a reduction upon launch of a generic product on a country-by-country basis. The Company began receiving royalty payments from MTPC during the year ended December 31, 2020 when MTPC commenced commercial sales of vadadustat in Japan under the trade name, Vafseo™, in August 2020 (Note 4).

In December 2016, the Company entered into a collaboration and license agreement with Otsuka Pharmaceutical Co. Ltd., or Otsuka, to develop and commercialize vadadustat in the United States. In December 2016, the Company received \$125.0 million upfront payment, and in March 2017, Otsuka reimbursed the Company approximately \$33.8 million for global expenses previously incurred by us for the global development program for vadadustat in DD-CKD and NDD-CKD adult patients. The agreement also provides for additional funding for the global development program for vadadustat, totaling \$319.0 million or more, depending on the actual global development costs incurred. In addition, as of December 31, 2020, Akebia is eligible to receive from Otsuka up to \$65.0 million in specified regulatory milestones and up to \$575.0 million in specified commercial milestones. The Company will share with Otsuka the costs of developing and commercializing vadadustat in the United States and the profits from sales of vadadustat in the United States after approval by the FDA and commercial launch (Note 4).

In April 2017, the Company entered into a collaboration and license agreement with Otsuka to develop and commercialize vadadustat in Europe, Russia, China, Canada, Australia, the Middle East and certain other territories. In April 2017, the Company received a \$73.0 million upfront payment and \$0.2 million for global expenses previously incurred by the Company in implementing the current global Phase 3 development plan for vadadustat in DD-CKD and NDD-CKD adult patients in excess of a specified threshold during the quarter-ended March 31, 2017. The agreement also provides for additional funding for the global development program for vadadustat, totaling \$226.2 million or more, depending on the actual global development costs incurred. In addition, as of December 31, 2020, Akebia is eligible to receive from Otsuka up to \$52.0 million in specified regulatory milestones and up to \$525.0 million in specified commercial milestones (Note 4).

From inception through December 31, 2020, the Company has raised approximately \$704.3 million of net proceeds from the sale of equity, including \$519.8 million from several underwritten public offerings, \$134.5 million from at-the-market offerings, or ATM offerings, pursuant to sales agreements with Cantor Fitzgerald & Co. and \$50.0 million from the sale of 3,571,429 shares of common stock to Vifor (International) Ltd., or Vifor Pharma. During the year ended December 31, 2020, the Company completed an underwritten public offering of our common stock with aggregate net proceeds of \$142.4 million and raised \$67.3 million of net proceeds from ATM offerings. In November 2019, the Company received net proceeds of \$77.3 million from Tranche A of the Loan Agreement with Pharmakon. In December 2020, the Company received net proceeds of \$20.0 million from Tranche B of the Loan Agreement with Pharmakon. Subsequent to December 31, 2020 and through the date of this Annual Report on Form 10-K, the Company raised \$15.9 million in net proceeds from ATM offerings. At the inception of the Company's collaboration agreements with Otsuka and MTPC, they committed to an aggregate of approximately \$573.0 million or more in cost-share funding, of which the Company received approximately \$272.0 million at the onset of the collaborations, and the remainder of which the Company generally continues to receive on a quarterly prepaid basis, and via license payments.

The Company's management completed its going concern assessment in accordance with ASC 205-40, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASC 205-40. 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 2020 Annual Report on Form 10-K, as required by ASC 205-40. There can be no assurance, however, that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund the Company's 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. The Company will require additional capital to pursue development and commercial activities related to Auryxia and vadadustat or any additional products and product candidates, including those that may be in-licensed or acquired. The Company expects to finance future cash needs through product revenue, public or private equity or debt transactions, payments from its collaborators, royalty transactions, strategic transactions, or a combination of these approaches. However, adequate additional financing may not be available to the Company on acceptable terms, or at all. If the Company is unable to raise capital in sufficient amounts when needed or on attractive terms, it may not be able to pursue development and commercial activities related to Auryxia and vadadustat or any additional products and product candidates, including those that may be in-licensed or acquired.

## **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 June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which requires that financial assets measured at amortized cost be presented at the net amount expected to be collected. Previously, U.S. GAAP delayed recognition of the full amount of credit losses until the loss was probable of occurring. Under this ASU, the income statement will reflect an entity's current estimate of all expected credit losses. The Company adopted this new standard on January 1, 2020 using the modified retrospective approach, which requires a cumulative-effect adjustment, if any, to the opening balance of retained earnings to be recognized on the date of adoption with prior periods not restated. The cumulative-effect adjustment recorded on January 1, 2020, is not material. Please see the description of the Company's "Credit Losses" accounting policy below.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework-Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies the disclosure requirements for fair value measurements. The Company adopted this new standard on January 1, 2020 using the prospective approach for amendments applicable to the Company. The adoption of this standard did not have a material impact on the Company's consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-15, *Intangible-Goodwill and Other-Internal-Use Software (Subtopic 350-40): Customer's Accounting for Implementation Costs Incurred in a Cloud Computing Arrangement That is a Service Contract*. This standard clarifies the accounting for implementation costs in cloud computing arrangements. This standard became effective for the Company on January 1, 2020, and was adopted on a prospective basis. The adoption of this standard did not have a material impact to the Company's consolidated financial statements and disclosures.

In November 2018, the FASB issued ASU 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606*. This standard makes targeted improvements for collaborative arrangements as follows:

- Clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606, *Revenue from Contracts with Customers*, when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in ASC 606 should be applied, including recognition, measurement, presentation and disclosure requirements;
- Adds unit-of-account guidance to ASC 808, *Collaborative Arrangements*, to align with the guidance in ASC 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606; and
- Precludes a company from presenting transactions with collaborative arrangement participants that are not directly related to sales to third parties with revenue recognized under ASC 606 if the collaborative arrangement participant is not a customer.

This standard became effective for the Company on January 1, 2020, and did not have a material impact on the Company's consolidated financial statements and related disclosures.

### **New Accounting Pronouncements – Not Yet Adopted**

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*. This ASU is effective for fiscal years beginning after December 15, 2020, including interim periods therein, and is applicable to the Company in fiscal year 2021. Early adoption is permitted. ASU 2019-12 requires certain amendments to be applied using a modified retrospective approach, which requires a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption, while other amendments should be applied on a prospective basis. The Company does not expect that the adoption of this standard will 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 issued by the Company in connection with the Janssen Pharmaceutica NV Research and License Agreement, the Janssen Agreement, is classified as equity in the Company's consolidated balance sheet. (See Note 12). 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, other non-current liabilities, including the excess purchase commitment liability, stock-based compensation expense, product and collaboration revenues including various rebates and reserves related to product sales, inventories, income taxes, intangible assets and goodwill. The Company has made estimates of the impact of COVID-19 within the consolidated financial statements and there may be changes to those estimates in future periods including changes to sales, payer mix, reserves and allowances, 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.

## Credit Losses

*Available for sale debt securities.* Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. The Company classifies all securities as available for sale and includes them in current assets as they are intended to fund current operations. The Company's investment portfolio at any point in time contains investments in money market mutual funds, U.S. government debt securities, certificates of deposit and corporate debt securities. The Company segments its portfolio based on the underlying risk profiles of the securities and have a zero loss expectation for money market mutual funds, U.S. government debt securities and certificates of deposit. The Company regularly reviews the securities in an unrealized loss position and evaluates the current expected credit loss by considering factors such as historical experience, market data, issuer-specific factors, and current economic conditions. Factors considered also include whether a decline in fair value below the amortized cost basis is due to credit-related factors or noncredit-related factors, the financial condition and near-term prospects of the issuer, and our intent and ability to hold the investment to allow for an anticipated recovery in fair value. Any unrealized loss that is not credit related is recognized in other comprehensive (loss) income in the consolidated statements of operations. A credit-related unrealized loss is recognized as an allowance on the consolidated balance sheets with a corresponding adjustment to earnings in the consolidated statements of operations.

### 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, 2020, 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, 2020	December 31, 2019	December 31, 2018	December 31, 2017
Cash and cash equivalents	\$ 228,698	\$ 147,449	\$ 104,644	\$ 70,156
Prepaid expenses and other current assets	395	263	—	—
Other assets	2,039	2,092	2,455	1,281
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	<u>\$ 231,132</u>	<u>\$ 149,804</u>	<u>\$ 107,099</u>	<u>\$ 71,437</u>

### Investments

Management determines the appropriate classification of securities at the time of purchase and reevaluates such designation as of each balance sheet date. Currently, the Company classifies all securities as available for sale which are included in current assets as they are intended to fund current operations. The Company carries available for sale securities at fair value. The Company conducts periodic reviews to identify and evaluate each investment that has an unrealized loss, in accordance with the meaning of other-than-temporary impairment and its application to certain investments. When assessing whether a decline in the fair value of a security is other-than-temporary, the Company considers the fair market value of the security, the duration of the security's decline, and prospects for the underlying business. Based on these considerations, the Company did not identify any other-than-temporary unrealized losses at December 31, 2020. Unrealized losses on available for sale securities that are determined to be temporary, and not related to credit loss, are recorded in accumulated other comprehensive loss, a component of stockholders' equity. The amortized cost of debt securities in this category reflects amortization of premiums and accretion of discounts to maturity computed under the effective interest method. The Company includes this amortization in the caption "Interest income, net" within the consolidated statements of operations and comprehensive loss. The Company also includes in net investment income, realized gains and losses and declines in value determined to be other than temporary. The Company bases the cost of securities sold upon the specific identification method and includes interest and dividends on securities in interest income.

### Accounts Receivable

The Company's accounts receivable represent amounts due to the Company from product sales (see Note 3) and from its collaboration agreements with MTPC and Otsuka (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, 2020 and 2019.

### Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash, cash equivalents, investments, and accounts receivable are the only financial instruments that potentially subject the Company to concentrations of credit risk. The Company maintains its cash, cash equivalents, and investments 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,		
	2020	2019	2018
Fresenius Medical Care Rx	29 %	21 %	— %
Otsuka Pharmaceutical Co. Ltd.	29 %	45 %	90 %
AmerisourceBergen Drug Corporation	12 %	10 %	— %
McKesson Corporation	11 %	— %	— %

	Percent of Gross Accounts Receivable		
	As of December 31,		
	2020	2019	2019
AmerisourceBergen Drug Corporation	29 %	16 %	16 %
Fresenius Medical Care Rx	19 %	15 %	15 %
Cardinal Health, Inc.	14 %	15 %	15 %
McKesson Corporation	12 %	11 %	11 %
Otsuka Pharmaceutical Co. Ltd. (1)	— %	35 %	35 %

- (1) Accounts receivable from Otsuka Pharmaceutical Co. Ltd. did not represent greater than 10% of gross accounts receivable at December 31, 2020 due to timing of payments and costs incurred.

### 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, 2020 and 2019.

	Useful Life	December 31, 2020	December 31, 2019
		(in thousands)	
Computer equipment and software	3	\$ 1,010	\$ 1,010
Furniture and fixtures	5 - 7	2,086	2,086
Equipment	7	2,692	2,451
Leasehold improvements	Shorter of the useful life or remaining lease term (10 years)	8,573	8,497
		14,361	14,044
Less accumulated depreciation		(5,739)	(3,664)
Net property and equipment		\$ 8,622	\$ 10,380

Depreciation expense was approximately \$2.1 million, \$2.2 million and \$0.9 million for the years ended December 31, 2020, 2019 and 2018, respectively. For the year ended December 31, 2019, approximately \$2.1 million of certain leasehold improvements were written off in connection with the sublease of the Boston office.

## 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 adopted this new standard on January 1, 2019 using the modified retrospective approach for all leases existing at, or entered into after, the date of initial application, and elected to use the following practical expedients that are permitted under the rules of the adoption:

- The Company elected the package of transition practical expedients, which allows it to retain the lease classification and initial direct costs for any leases that existed prior to the adoption of this new standard.
- The Company did not reassess whether any contracts completed prior to the adoption are leases.

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. 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.

### **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.

### **Revenue Recognition**

The Company generates revenues primarily from sales of Auryxia, see Note 3, and from its collaborations with MTPC and 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, 2020. 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 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 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.

#### *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 partner 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 recognizes its allocation of the shared costs incurred with respect to the jointly conducted medical affairs and commercialization and non-promotional activities under the 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 it is deemed to be the principal in the transactions with customers, or on a net basis if it is instead deemed to be the agent in the transactions with customers, consistent with the guidance in ASC 606.

### **Business Combinations**

The Company accounts for the acquisition of a business in accordance with ASC Topic 805, *Business Combinations*, or ASC 805. Amounts paid for each acquisition are allocated to the assets acquired and liabilities assumed based on their fair values at the date of acquisition. The Company determines the fair value of acquired intangible assets based on detailed valuations that use certain information and assumptions provided by management, which is considered management's best estimate of inputs and assumptions that a market participant would use. The Company allocates any excess purchase price over the fair value of the net tangible and intangible assets acquired to goodwill.

Under ASC 805, transaction costs are not included as a component of consideration transferred and are expensed as incurred. Additionally, in accordance with ASC 805, a transaction entered into by or on behalf of the acquirer or primarily for the benefit of the acquirer or the combined entity, rather than primarily for the benefit of the acquiree (before the combination), is treated as separate transaction.

### **Intangible Assets**

The Company maintains 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. 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, 2020 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 for additional information).

### **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 available for sale securities and 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 remeasurements to property and equipment for the year ended December 31, 2020. During the second quarter of 2020, the Company identified indicators of impairment related to the developed product rights for Auryxia, an intangible asset measured using Level 3 inputs, and recorded an impairment charge of \$115.5 million (see Note 9 for additional information). There were no other impairments to assets measured using Level 3 inputs during the year ended December 31, 2020. There were no impairments to assets measured using Level 3 inputs during the year ended December 31, 2019.

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. Nonrefundable 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, 2020, 2019 and 2018, advertising expenses totaled \$5.0 million, \$6.0 million and \$0.5 million, respectively, all related to Auryxia. The Company

incurred advertising expenses throughout the entire fiscal years 2020 and 2019 compared to the period from December 12, 2018 through December 31, 2018 in fiscal year 2018.

### **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, 2020 and 2019 are classified as noncurrent within the income tax provision (see Note 14).

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, 2020 and 2019, 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 and RSUs. The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Company uses a blend of its stock price and the quoted market price of comparable public companies to determine the fair value of restricted stock awards and common 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. Due to the lack of company-specific historical and implied volatility data for trading the Company's stock in the public market, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is 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, which it began recording on December 12, 2018 following the consummation of the Merger. Total net product revenue was \$128.9 million and \$111.1 million for the years ended December 31, 2020 and 2019, respectively, and \$6.8 million for the period from December 12, 2018 to December 31, 2018. The following table summarizes activity in each of the product revenue allowance and reserve categories for the period from December 12, 2018 to December 31, 2018 and for the years ended December 31, 2019 and 2020 (in thousands):

	Chargebacks and Discounts	Rebates, Fees and other Deductions	Returns	Total
Balance at December 12, 2018	\$ 466	\$ 21,247	\$ 418	\$ 22,131
Provisions related to sales	415	3,869	(58)	4,226
Credits/payments made relating to sales	(365)	(2,255)	—	(2,620)
Balance at December 31, 2018	516	22,861	360	23,737
Current provisions related to sales in current year	7,822	110,866	2,008	120,696
Adjustments related to prior year sales	—	1,149	—	1,149
Credits/payments made	(7,600)	(104,324)	(2,115)	(114,039)
Balance at December 31, 2019	\$ 738	\$ 30,552	\$ 253	\$ 31,543
Current 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

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 \$21.9 million and \$23.0 million as of December 31, 2020 and 2019, respectively.



#### 4. License, Collaboration and Other Significant Agreements

During the years ended December 31, 2020, 2019 and 2018, 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, 2020:

	For the Year Ended December 31,		
	2020	2019	2018
<b>License, Collaboration and Other Revenue:</b>	(in thousands)		
MTPC Agreement	\$ 15,405	\$ 10,000	\$ 9,281
Otsuka U.S. Agreement	93,446	131,314	103,870
Otsuka International Agreement	45,451	75,614	87,320
Total Proportional Performance Revenue	\$ 154,302	\$ 216,928	\$ 200,471
JT and Torii	5,681	5,882	112
MTPC Other Revenue	6,423	1,072	335
<b>Total License, Collaboration and Other Revenue</b>	<b>\$ 166,406</b>	<b>\$ 223,882</b>	<b>\$ 200,918</b>

	December 31, 2020		
	Short-Term	Long-Term	Total
<b>Deferred Revenue:</b>	(in thousands)		
Otsuka U.S. Agreement	\$ 8,850	\$ 15,098	\$ 23,948
Otsuka International Agreement	6,364	5,568	11,932
Vifor Agreement	—	4,679	4,679
<b>Total</b>	<b>\$ 15,214</b>	<b>\$ 25,345</b>	<b>\$ 40,559</b>

The following table presents changes in the Company's contract assets and liabilities during the years ended December 31, 2020 and 2019 (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
<b>Twelve Months Ended December 31, 2020</b>				
Contract assets:				
Accounts receivable(1)	\$ 15,822	\$ 161,772	\$ (174,549)	\$ 3,045
Prepaid expenses and other current assets	\$ —	\$ 1,722	\$ —	\$ 1,722
Contract liabilities:				
Deferred revenue	\$ 72,950	\$ 122,108	\$ (154,499)	\$ 40,559
Accounts payable	\$ —	\$ 17,324	\$ (10,097)	\$ 7,227
Accrued expenses and other current liabilities	\$ —	\$ 10,615	\$ (615)	\$ 10,000
<b>Twelve Months Ended December 31, 2019</b>				
Contract assets:				
Other current assets	\$ —	\$ 10,000	\$ (10,000)	\$ —
Accounts receivable(1)	\$ 1,587	\$ 172,614	\$ (158,379)	\$ 15,822
Contract liabilities:				
Deferred revenue	\$ 112,689	\$ 167,189	\$ (206,928)	\$ 72,950
Accounts payable	\$ 13,492	\$ —	\$ (13,492)	\$ —

- (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, 2020 and 2019. 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, 2020 and 2019.

During the years ended December 31, 2020, 2019 and 2018, 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):

Revenue Recognized in the Period from:	For the Year December 31,		
	2020	2019	2018
Amounts included in deferred revenue at the beginning of the period	\$ 36,032	\$ 80,634	\$ 137,726
Performance obligations satisfied in previous periods	\$ 25,964	\$ 45,592	\$ 6,659

### ***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. In addition, the Company will supply vadadustat for both clinical and commercial use in the MTPC Territory, subject to MTPC's option to manufacture commercial drug product 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 is 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<sup>TM</sup> as a treatment of anemia due to CKD for adult patients on dialysis and not on dialysis.

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 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.

#### ***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 (the License Deliverable) in the MTPC Territory, (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<sup>TM</sup> in the third quarter of 2020 is quarterly royalties on net sales, sales milestones, and certain regulatory milestones.

As of December 31, 2020, the transaction price is 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, (vi) \$0.4 million in royalties from net sales of Vafseo. As of December 31, 2020, 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 also recognized \$0.4 million of revenue for royalties from the net sales of Vafseo during the year ended December 31, 2020. The Company recognized \$9.3 million of revenue during the year ended December 31, 2018. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2020, there is \$0.1 million in accounts receivable, no deferred revenue, and no contract assets. There were no asset or liability balances classified as long-term in the consolidated balance sheet as of December 31, 2020.

#### *Supply of Drug Product to MTPC*

In March 2020, in connection with the MTPC Agreement, the Company agreed to supply MTPC with certain vadadustat 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 passes to

MTPC and delivery has occurred. During the year ended December 31, 2020, the Company recognized \$6.2 million in revenue for drug product that was delivered during the year ended December 31, 2020. As of December 31, 2020, the Company recorded no accounts receivable, no deferred revenue, and \$4.1 million in other current liabilities and \$0.1 million in 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. The MTPC Supply Agreement includes the terms and conditions under which the Company will supply 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 will exist throughout the term of the MTPC Agreement, and the termination provisions of the MTPC Agreement govern termination of the MTPC Supply Agreement.

During the year ended December 31, 2020, the Company invoiced MTPC for \$18.6 million in up-front payments for vadadustat drug product ordered by MTPC. As of December 31, 2020, the Company recorded \$1.9 million in accounts receivable, \$13.9 million in other current liabilities and \$4.7 million in other non-current liabilities. Subsequent to December 31, 2020, the Company invoiced MTPC for an additional \$2.6 million in up-front payments for vadadustat drug product ordered by MTPC.

### ***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 is focused on the development and commercialization of vadadustat in the United States. Under the terms of the Otsuka U.S. Agreement, the Company is responsible for leading the development of vadadustat, including the ongoing Phase 3 development program, and the Company controls and retains final decision making authority with respect to certain matters, including U.S. pricing strategy and manufacturing. The Company and Otsuka will co-commercialize vadadustat in the United States, subject to the approval of vadadustat by the FDA.

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 relates to activities that will 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.

The Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan, while Otsuka may agree to perform certain activities under the global development plan from time to time as agreed by the parties. The current global development plan encompasses all activities with respect to the recently completed PRO<sub>2</sub>TECT and INNO<sub>2</sub>VATE clinical programs through the filing for marketing approval, as well as certain other studies. The Company's obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka U.S. Agreement, the parties jointly conduct all medical affairs, commercialization and non-promotional activities pursuant to underlying plans as agreed to by the parties. If approved by the FDA, Otsuka is obligated to purchase all of its supply requirements of vadadustat for commercial use from the Company pursuant to a separate supply agreement to be negotiated.

The activities under the Otsuka U.S. Agreement are governed by a joint steering committee, or JSC, formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews other detailed plans setting forth the parties' activities under the arrangement, including the medical affairs plan and commercialization and non-promotional activities plan. Additionally, the parties established a joint development committee, or JDC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities

and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a joint manufacturing committee, or JMC, which is comprised of an equal number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a joint commercialization committee, or JCC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC oversees the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. The Company has retained final decision-making authority with respect to certain matters, including U.S. pricing strategy and certain other key commercialization matters.

Under the terms of the Otsuka U.S. Agreement, the Company received a \$125.0 million up-front, non-refundable, non-creditable cash payment in December 2016. In March 2017, the Company received a payment of approximately \$33.8 million, which represented reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan through December 31, 2016. Commencing in the third quarter of 2017, whereupon the Company had incurred a specified amount of incremental costs, Otsuka began to contribute, as required by the Otsuka U.S. Agreement, a percentage of the remaining costs incurred under the current global development plan. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to December 31, 2016 will total \$319.0 million or more, depending on the actual costs incurred toward the current global development plan. The costs associated with the performance of any development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism as set forth in the Otsuka U.S. Agreement or to be determined by the parties. Costs incurred with respect to medical affairs and commercialization and non-promotional activities will generally be shared equally by the parties. In addition, due to the costs incurred in completing the activities under the current global development plan exceeding a certain threshold in the second quarter of 2019, 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, as defined below, from 52.5% to 80%, or the Otsuka Funding Option. The Company estimates the additional funding as a result of exercising the Otsuka Funding Option, or the Additional Funding, to total approximately \$122.2 million or more, depending on the actual costs incurred toward the current global development plan. The Additional Funding is fully creditable against future payments due to the Company under the arrangement, provided that future payments due to the Company may not be reduced by more than 50% in any calendar year and any remaining creditable amount above 50% in any calendar year will be applied to subsequent future payments until fully credited. As of December 31, 2020, the Additional Funding was \$88.0 million.

In addition, Otsuka is required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, as of December 31, 2020, the Company is eligible to receive up to \$65.0 million in regulatory milestone payments for the first product to achieve the associated event and up to \$575.0 million in commercial milestone payments associated with aggregate sales of licensed products. These future milestones are subject to reduction as a result of the Company's exercise of the Otsuka Funding Option, as described above. Due to the uncertainty of drug development and commercialization and the high historical failure rates associated therewith, no milestone payments may ever be received from Otsuka.

Under the Otsuka U.S. Agreement, the Company and Otsuka share the costs of developing and commercializing vadadustat in the United States and the profits from the sales of vadadustat after approval by the FDA. In connection with the profit share calculation, net sales include gross sales to third-party customers net of discounts, rebates, chargebacks, taxes, freight and insurance charges and other applicable deductions. Shared costs generally include costs attributable or reasonably allocable to the manufacture of vadadustat for commercialization purposes and the performance of medical affairs activities, non-promotional activities and commercialization activities.

Unless earlier terminated, the Otsuka U.S. Agreement will expire in the United States on a product-by-product basis on the date that one or more generic versions of vadadustat first achieves 90% market penetration. Either party may terminate the Otsuka U.S. Agreement in its entirety upon an uncured breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka U.S. Agreement in its entirety upon 12 months' prior written notice at any time after the release of the first top-line data from the global Phase 3 development program for vadadustat, which release occurred in the second quarter of 2020 with the announcement of top-line data from the INNO<sub>2</sub>VATE program. In the event of termination of the Otsuka U.S. Agreement, all rights and licenses granted to Otsuka under the Otsuka U.S. Agreement will automatically terminate and the licenses granted to the Company will become freely sublicensable. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be refunded to Otsuka.

## 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, is a customer. The Company's arrangement with Otsuka contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop, perform medical affairs activities with respect to and conduct non-promotional and commercialization activities related to vadadustat and products containing or comprising vadadustat (the License Deliverable), (ii) development services to be performed pursuant to the current global development plan (the Development Services Deliverable), (iii) rights to future intellectual property (the Future IP Deliverable), and (iv) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka U.S. Agreement. 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 Otsuka U.S. Agreement does not include a general right of return. The three performance obligations identified in connection with the Company's obligations under the Otsuka U.S. Agreement are as follows:

(i) *License and Development Services Combined (License Performance Obligation)*

The License Deliverable is not distinct from the Development Services Deliverable, due to the limitations inherent in the license conveyed. More specifically, the license conveyed to Otsuka does not provide Otsuka with the right to manufacture vadadustat and products containing or comprising vadadustat. However, the manufacturing and supply services that are conducted as part of the services to be performed pursuant to the current global development plan are necessary for Otsuka to fully exploit the associated license for its intended purpose. The value of the rights provided through the license conveyed will be realized when the underlying products covered by the intellectual property progress through the development cycle, receive regulatory approval and are commercialized. Products containing or comprising vadadustat cannot be commercialized until the development services under the current global development plan are completed. Accordingly, Otsuka must obtain the manufacturing and supply of the associated products that are included within the development services to be performed pursuant to the current global development plan from the Company in order to derive benefit from the license, which significantly limits the ability for Otsuka to utilize the License Deliverable for its intended purpose in a way that generates economic benefits.

(i) *Rights to Future Intellectual Property (Future IP Performance Obligation)*

The License and Development Services deliverables combined are distinct from the Future IP Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the receipt of any other intellectual property that may be discovered or developed in the future. The Future IP Deliverable is distinct from the Committee Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Future IP Deliverable qualifies as a separate performance obligation.

(i) *Joint Committee Services (Committee Performance Obligation)*

The License and Development Services deliverables combined are distinct from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the joint committee services. The Committee Deliverable also is distinct from the rights to Future IP Deliverable because the joint committee services have no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Committee Deliverable qualifies as a separate performance obligation.

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 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 has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company through December 31, 2016, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to December 31, 2016. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered 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 will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Otsuka 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 under ASC 606, the contract was modified in the second quarter of 2019 when the Otsuka Funding Option became effective and the Company became eligible to receive the Additional Funding amount. In connection with the modification, the Company adjusted the transaction price to include the Additional Funding amount as additional variable consideration. The Company constrains the variable consideration to an amount for which a significant revenue reversal is not probable. In the event that there is consideration received by a customer in the form of activities performed by such customer under the global development plan, such consideration is reflected as a reduction to the transaction price as contra revenue rather than as an expense because the associated services are not distinct from the License Performance Obligation.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of December 31, 2020, the transaction price totaling \$477.8 million is comprised of: (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 estimate of the net cost share consideration to be received of approximately \$319.0 million with respect to amounts incurred by the Company subsequent to December 31, 2016. As of December 31, 2020, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the years ended December 31, 2020, 2019 and 2018, the Company recognized revenue totaling approximately \$93.4 million, \$131.3 million and \$103.9 million, respectively, with respect to the Otsuka U.S. Agreement. The revenue is classified as collaboration revenue in the accompanying consolidated statements of operations. As of December 31, 2020, there is approximately \$23.9 million of deferred revenue related to the Otsuka U.S. Agreement of which \$8.9 million is classified as current and \$15.1 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2020, there are approximately \$5.0 million in contract liabilities (included in accounts payable) and \$1.2 million in prepaid expenses and other current assets in the accompanying consolidated balance sheet. As of December 31, 2019, there was approximately \$8.9 million in accounts receivable in the accompanying consolidated balance sheet.

The Company determined that the medical affairs, commercialization and non-promotional activities elements of the Otsuka U.S. Agreement represent joint operating activities in which both parties are active participants and of which both parties are exposed to significant risks and rewards that are dependent on the success of the activities. Accordingly, the Company is accounting for the joint medical affairs, commercialization and non-promotional activities in accordance with ASC No. 808, *Collaborative Arrangements* (ASC 808). Additionally, the Company has determined that in the context of the medical affairs, commercialization and non-promotional activities, Otsuka does 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 will be accounted for as a component of the related expense in the period incurred. During the years ended December 31, 2020, 2019 and 2018, the Company incurred approximately \$5.1 million, \$1.8 million and \$1.2 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement of which approximately \$2.2 million, \$0.7 million and \$0.5 million are reimbursable by Otsuka and recorded as a reduction to research and development expense during each of the years ended December 31, 2020, 2019 and 2018, respectively. During the years ended December 31, 2020, 2019 and 2018, Otsuka incurred approximately \$2.1 million, \$1.9 million and \$1.1 million, respectively, of costs related to the cost-sharing provisions of the Otsuka U.S. Agreement, of

which approximately \$1.1 million, \$1.0 million and \$0.5 million are reimbursable by the Company and recorded as an increase to research and development expense during the years ended December 31, 2020, 2019 and 2018, 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 is 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 is responsible for leading the development of vadadustat, including the ongoing global Phase 3 development program. Otsuka has 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.

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.

Pursuant to the terms of the Otsuka International Agreement, the Company is responsible for performing all activities related to the development of vadadustat as outlined in the current global development plan, while Otsuka may agree to perform certain activities under the global development plan from time to time as agreed by the parties. Under the Otsuka International Agreement, the Company controls and retains final decision-making authority with respect to certain matters. Per the terms of the Otsuka International Agreement, Otsuka is generally responsible for the conduct of any development activities that may be required for marketing approvals in the Otsuka International Territory or otherwise performed with respect to the Otsuka International Territory that are incremental to those included in the current global development plan. The Company's obligations related to the conduct of the current global development plan include the associated manufacturing and supply services for vadadustat.

Under the Otsuka International Agreement, Otsuka is to be solely responsible for the conduct of all medical affairs and commercialization activities in the Otsuka International Territory pursuant to underlying plans as reviewed and discussed by the parties. If approved by the relevant jurisdictional regulatory health authorities in the Otsuka International Territory, the Company will provide vadadustat to Otsuka for commercialization pursuant to a separate supply agreement to be negotiated. Additionally, the parties agreed not to promote, market or sell any competing product in the territory covered by the agreement.

The activities under the Otsuka International Agreement are governed by a JSC formed by an equal number of representatives from the Company and Otsuka. The JSC coordinates and monitors the parties' activities under the collaboration. Among other responsibilities, the JSC manages the overall strategic alignment between the parties, oversees the current global development plan and reviews other detailed plans setting forth any other development activities that may be conducted under the arrangement. Additionally, the parties established a JDC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JDC shares information related to, and reviews and discusses activities and progress under, the current global development plan and any other development that may be conducted pursuant to the collaboration. The Company and Otsuka also established a JMC, which is comprised of an equal number of representatives from each of the parties. Among other responsibilities, the JMC oversees the manufacturing plan and related manufacturing activities. In support of the potential commercialization of vadadustat, the parties established a JCC, which is comprised of an equal number of representatives from the Company and Otsuka. Among other responsibilities, the JCC manages the activities and progress under the commercialization and non-promotional activities plan and all other sales and marketing activities. The Company has retained final decision-making authority with respect to certain matters. Otsuka has retained final decision-making authority with respect to all commercialization matters, other than decisions related to certain marketing matters.

Under the terms of the Otsuka International Agreement, the Company received a \$73.0 million up-front, non-refundable, non-creditable cash payment. The Company also received a payment of approximately \$0.2 million which represents reimbursement for Otsuka's share of costs previously incurred by the Company in implementing the current global development plan in excess of a specified threshold during the quarter ended March 31, 2017. Commencing in the second quarter of 2017, Otsuka began to contribute, as required by the Otsuka International Agreement, a percentage of the remaining costs incurred under the current global development plan. The Company estimates that Otsuka's funding of the current global development plan costs subsequent to March 31, 2017 will total roughly \$226.2 million or more, depending on the actual current global development plan costs incurred. The costs associated with the performance of any mutually agreed upon development activities in addition to those outlined in the current global development plan will be subject to a cost sharing or reimbursement mechanism as set



forth in the Otsuka International Agreement or to be determined by the parties. Otsuka may elect to conduct additional studies of vadadustat in the EU, subject to the Company's right to delay such studies based on its objectives outside the Otsuka International Territory. Otsuka will pay a percentage of the costs of any such studies, and the Company will pay its portion of the costs in the form of a credit against future amounts due to the Company under the Otsuka International Agreement. The costs incurred related to any other development activities, which are pursued solely for obtaining or maintaining marketing approval in the Otsuka International Territory or otherwise performed solely with respect to the Otsuka International Territory that are incremental to the development activities included in the current global development plan, will be borne in their entirety by Otsuka. Otsuka will pay costs incurred with respect to medical affairs and commercialization activities in the Otsuka International Territory.

In addition, Otsuka would be required to make certain milestone payments to the Company upon the achievement of specified development, regulatory and commercial events. More specifically, as of December 31, 2020, the Company is eligible to receive up to \$52.0 million in regulatory milestone payments for the first licensed product to achieve the associated event. Moreover, the Company is eligible for up to \$525.0 million in commercial milestone payments associated with aggregate sales of all licensed products. Additionally, to the extent vadadustat is commercialized, the Company would be entitled to receive tiered royalty payments ranging from the low double digits to the low thirties based on a percentage of net sales. Royalties are due on a country-by-country basis from the date of the first commercial sale of a licensed product in a country until the latest to occur of: (i) the expiration date in such country of the last to expire valid claim within the intellectual property covering the licensed product, (ii) the date of expiration of data 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 pharmaceutical development and the high historical failure rates associated therewith, no milestone or royalty payments may ever be received from Otsuka. There are no cancellation, termination or refund provisions in the Otsuka International Agreement that contain material financial consequences to the Company.

Unless earlier terminated, the Otsuka International Agreement will expire upon the expiration of the royalty term in the last country in the Otsuka International Territory. Either party may terminate the Otsuka International Agreement in its entirety upon an uncured material breach or insolvency on the part of the other party. Otsuka may terminate the Otsuka International Agreement in its entirety or for a specific region in the Otsuka International Territory upon 12 months' prior written notice at any time after the release of the first top-line data from the global Phase 3 development program for vadadustat, which release occurred in the second quarter of 2020 with the announcement of top-line data from the INNO<sub>2</sub>VATE program. In the event of termination of the Otsuka International Agreement, all rights and licenses granted to Otsuka under the Otsuka International Agreement will automatically terminate, and the licenses granted to the Company will become freely sublicensable, but potentially subject to a future royalty. In addition, the upfront payment, all development costs and milestone payments received by the Company prior to such termination will not be eligible for refund to Otsuka.

#### *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 relate to the respective territories. Accordingly, the Company has 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 has 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, is a customer. The Company's arrangement with Otsuka related to the Otsuka International Territory contains the following material promises under the contract at inception: (i) license under certain of the Company's intellectual property to develop and commercialize (including the associated packaging) vadadustat and products containing or comprising vadadustat and development services to be performed pursuant to the current global development plan (the License and Development Services Deliverable), (ii) rights to future intellectual property (the Future IP Deliverable) and (iii) joint committee services (the Committee Deliverable).

The Company has identified three performance obligations in connection with its obligations under the Otsuka International Agreement. Factors considered in making this assessment of which material promises will be accounted for as a separate performance obligation 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 Otsuka International Agreement does not include a general right of return. The three performance obligations identified in connection with the Company's obligations under the Otsuka International Agreement are as follows:

- (i) *License and Development Services Combined (License Performance Obligation)*

The Company has determined that the license granted to Otsuka pursuant to the Otsuka International Agreement will be accounted for as component of the development services as opposed to a separately identified promise. Although the rights granted under the license are effective throughout the entire term of the arrangement, the Company will not be providing significant additional contributions of study data, regulatory submissions and regulatory approvals beyond the point that services under the current global development plan are conducted. Therefore, the period and pattern of recognition would be the same for both the license and the development services. Consequently, the Company has concluded that the license will effectively be treated as an inherent part of the associated development services promise instead of as a separate promise. As a result, the License and Development Services Deliverable will be treated as a single performance obligation (the License Performance Obligation).

(i) *Rights to Future Intellectual Property (Future IP Performance Obligation)*

The License and Development Services Deliverable is distinct from the Future IP Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development services without the receipt of any other intellectual property that may be discovered or developed in the future. The Future IP Deliverable is distinct from the Committee Deliverable because the Committee Deliverable has no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Future IP Deliverable qualifies as a separate performance obligation.

(i) *Joint Committee Services (Committee Performance Obligation)*

The License and Development Services Deliverable is distinct from the Committee Deliverable because Otsuka can obtain the value of the license using the clinical trial materials implicit in the development service without the joint committee services. The Committee Deliverable is distinct from the Future IP Deliverable because the Committee Deliverable has no bearing on the value to be derived from the rights to potential future intellectual property. As a result, the Committee Deliverable qualifies as a separate performance obligation.

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 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 has concluded that a change in the key assumptions used to determine the best estimate of standalone selling price for each performance obligation would not have a significant impact on the allocation of arrangement consideration.

The transaction price at inception was comprised of: (i) the up-front payment, (ii) the cost share payment with respect to amounts incurred by the Company during the quarter ended March 31, 2017, and (iii) an estimate of the cost share payments to be received with respect to amounts incurred by the Company subsequent to March 31, 2017. No development or regulatory milestones were included in the transaction price at inception, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including whether the receipt of the milestone payment 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 Otsuka 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. In the event that there is consideration received by a customer in the form of activities performed by such customer under the global development plan, such consideration is reflected as a reduction to the transaction price as contra revenue rather than as an expense because the associated services are not distinct from the License Performance Obligation.

No amounts were allocated to the Future IP Performance Obligation because the associated best estimate of standalone selling price was determined to be immaterial. Due to the similar performance period and recognition pattern between the License Performance Obligation and the Committee Performance Obligation, the transaction price has been allocated to the License

Performance Obligation and the Committee Performance Obligation on a combined basis. Accordingly, the Company will recognize revenue related to the allocable arrangement consideration on a proportional performance basis as the underlying development services are performed pursuant to the current global development plan which is commensurate with the period and consistent with the pattern over which the Company's obligations are satisfied for both the License Performance Obligation and the Committee Performance Obligation. Effectively, the Company has treated the arrangement as if the License Performance Obligation and the Committee Performance Obligation are a single performance obligation.

As of December 31, 2020, the transaction price totaling \$299.4 million is comprised of: (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) an estimate of the net cost share consideration to be received with respect to amounts incurred by the Company subsequent to March 31, 2017 of \$226.2 million. As of December 31, 2020, no development or regulatory milestones have been assessed as probable of being reached and thus have been fully constrained.

During the years ended December 31, 2020, 2019 and 2018, the Company recognized revenue totaling approximately \$45.5 million, \$75.6 million, and \$87.3 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, 2020, there is approximately \$11.9 million of deferred revenue related to the Otsuka International Agreement of which \$6.4 million is classified as current and \$5.6 million is classified as long-term in the accompanying consolidated balance sheet based on the performance period of the underlying obligations. Additionally, as of December 31, 2020, there are approximately \$2.3 million in contract liabilities (included in accounts payable) and \$0.5 million in prepaid expenses and other current assets in the accompanying consolidated balance sheet. As of December 31, 2019, there was approximately \$4.0 million in accounts receivable in the accompanying 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, Janssen granted to the Company a license for a three-year research term to conduct research on the HIF compound portfolio, which research term is now expired. During the research term, the Company could designate one or more compounds as candidates for development and commercialization. Once a compound was designated for development and commercialization, the Company was to be solely responsible for the development and commercialization of the compound worldwide at its own cost and expense.

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. In addition, Janssen could be eligible to receive up to an aggregate of \$16.5 million from the Company in specified development milestone payments on a product-by-product basis. Janssen will also be eligible to receive up to \$215.0 million from the Company in specified commercial milestones as well as tiered, escalating royalties ranging from a low to mid-single 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.

Unless earlier terminated, the Janssen 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 longer of the expiration of the patents licensed under the Janssen Agreement, the expiration of regulatory exclusivity for such product, or 10 years from first commercial sale of such product. The Company may terminate the Janssen Agreement in its entirety or only with respect to a particular licensed compound or product upon 180 days' prior written notice to Janssen. The parties also have customary termination rights, subject to a cure period, in the event of the other party's material breach of the Janssen Agreement or in the event of certain additional circumstances.

As discussed above, the Company issued a Common Stock Purchase Warrant, or the Warrant, to Johnson & Johnson Innovation – JJDC, Inc., or JJDC, an affiliate of Janssen, for 509,611 shares of the Company's common stock at an exercise price of \$9.81 per share. The Warrant is exercisable by JJDC, in whole or in part, at any time prior to February 9, 2022. The Warrant and the shares issuable upon exercise of the Warrant will be sold and issued without registration under the Securities Act of 1933, as amended, or the Securities Act. The Company recorded the fair value of the Warrant in the amount of \$3.4 million to additional paid-in capital and research and development expense in March 2017.

## ***Vifor Pharma License Agreement***

### *Summary of Agreement*

On May 12, 2017, the Company entered into a License Agreement, or the Vifor Agreement, with Vifor (International) Ltd., or Vifor Pharma, pursuant to which the Company granted Vifor Pharma an exclusive license to sell vadadustat solely to Fresenius Kidney Care Group LLC, or FKC, an affiliate of Fresenius Medical Care North America, or FMCNA, in the United States. On April 8, 2019, the Company and Vifor Pharma entered into an Amended and Restated License Agreement, or the Vifor Amended Agreement, which amended and restated in full the Vifor Agreement.

Pursuant to the Vifor Amended Agreement, the Company granted Vifor Pharma an exclusive license to sell vadadustat to FKC and to certain third party dialysis organizations approved by the Company, or Third Party Dialysis Organizations, in the United States.

The license granted under the Vifor Amended Agreement will become effective upon (i) the approval of vadadustat for DD-CKD adult patients by the FDA, (ii) the earlier of a determination by the Centers for Medicare & Medicaid Services, or CMS, that vadadustat will be reimbursed using Medicare's bundled reimbursement model or that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment, and (iii) payment by Vifor Pharma of a \$25.0 million milestone upon the occurrence of (i) and (ii).

The Vifor Amended Agreement is structured as a profit share arrangement between the Company and Vifor Pharma in which the Company will receive a majority of the profit, after deduction of certain amounts relating to Vifor Pharma's costs, from Vifor Pharma's sales of vadadustat to FKC and the Third Party Dialysis Organizations in the United States. The Company will share the milestone payment and the revenue from the profit share with Otsuka pursuant to the Otsuka U.S. Agreement. The Company currently retains rights to commercialize vadadustat for use in the NDD-CKD market and in other dialysis organizations in the United States, which will be done in collaboration with Otsuka following FDA approval.

The Vifor Amended Agreement provides that the Company and Vifor Pharma will enter into a commercial supply agreement for vadadustat pursuant to which the Company will supply all of Vifor Pharma's requirements for vadadustat in the United States. In addition, Vifor Pharma will enter into supply arrangements with FKC and the Third Party Dialysis Organizations that will govern the terms pursuant to which Vifor Pharma will supply vadadustat to FKC and the Third Party Dialysis Organizations for use in patients at its dialysis centers in the United States. During the term of the Vifor Amended Agreement, Vifor Pharma is not permitted to sell any HIF product that competes with vadadustat in the United States to FKC or its affiliates or to any Third Party Dialysis Organization, and the Company may not directly supply vadadustat to FKC or any other affiliate of FMCNA or any Third Party Dialysis Organization.

Unless earlier terminated, the Vifor 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 United States. Vifor Pharma may terminate the Vifor Amended Agreement in its entirety upon 12 months' prior written notice after the release of the first top-line data in the vadadustat global Phase 3 program for DD-CKD adult patients, which release occurred in the second quarter of 2020 with the announcement of top-line data from the INNO<sub>2</sub>VATE program. In addition, either party may, subject to a cure period, terminate the Vifor Amended Agreement in the event of the other party's uncured material breach or bankruptcy. The Company may terminate the Vifor Amended Agreement (or suspend the license) upon the occurrence of certain events, such as for specific violations of the Vifor Amended Agreement, Vifor Pharma's failure to achieve certain sales levels, or if there are changes in Vifor Pharma's relationship with FKC or in applicable laws and regulations related to the reimbursement of drugs like vadadustat at dialysis clinics, or if Vifor Pharma contests the validity or enforceability of any patent controlled by the Company that covers vadadustat. The Vifor Amended Agreement also includes a standstill provision and customary representations and warranties.

### *Investment Agreement*

In connection with the Vifor Agreement, in May 2017, the Company and Vifor Pharma entered into an investment agreement, or the Investment Agreement, pursuant to which the Company sold an aggregate of 3,571,429 shares of the Company's common stock, or the Shares, to Vifor Pharma 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. As the parties' rights under the Vifor Agreement are conditioned upon (a) the approval of vadadustat for DD-CKD adult patients by the FDA; (b) the earlier of a determination by CMS that vadadustat will be reimbursed using Medicare's bundled reimbursement model or that vadadustat will be reimbursed using the Transitional Drug Add-On Payment Adjustment; and (c) payment by Vifor Pharma of a \$25.0 million milestone upon the occurrence of (a) and (b), in accordance with ASC 606, the Company has determined that the full

transaction price is fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including clinical and regulatory risks that must be overcome in order for the parties' rights to become effective and the probability of the \$25.0 million milestone being achieved. Accordingly, the \$4.7 million continues to be recorded as deferred revenue in the accompanying consolidated balance sheets. Upon the satisfaction of the aforementioned conditions, revenue will be recognized as the Company supplies vadadustat to Vifor Pharma using a proportional performance method.

Vifor Pharma agreed to a lock-up restriction such that it agreed not to sell the Shares for a period of time following the effective date of the Investment Agreement as well as a customary standstill agreement. In addition, the Investment Agreement contains voting agreements made by Vifor Pharma with respect to the Shares. The 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 Rule 506 promulgated thereunder.

#### *Priority Review Voucher Letter Agreement*

On February 14, 2020, the Company entered into a letter agreement, or the Letter Agreement, with Vifor Pharma relating to Vifor Pharma'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. A PRV entitles the holder to priority review of a New Drug Application, or NDA, or a Biologics License Application for a new drug, which reduces the target FDA review time to six months after official acceptance of the submission, and could lead to expedited approval. Pursuant to the Letter Agreement, Akebia paid Vifor Pharma \$10.0 million in connection with the closing of the PRV Purchase. Vifor Pharma is obligated to retain all rights to, and maintain the validity of, the PRV until Akebia and Vifor Pharma (a) enter into a definitive agreement setting forth the financial and other terms by which Vifor Pharma will assign the PRV to Akebia for use with Akebia's planned NDA for vadadustat for the treatment of anemia due to CKD in both dialysis-dependent and non-dialysis dependent patients, or (b) make a mutual decision to sell the PRV and share the proceeds based on certain terms.

During the quarter ended March 31, 2020, the \$10.0 million payment to Vifor Pharma was recorded to research and development expense in the consolidated statement of operations and as an operating cash outflow in the unaudited condensed consolidated statement of cash flows.

#### ***License Agreement with Panion & BF Biotech, Inc.***

As a result of the Merger, 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, effective as of April 17, 2019. 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. Consistent with the Panion License Agreement, 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, 2020 and 2019 and for the period from December 12, 2018 to December 31, 2018, the Company incurred approximately \$11.2 million, \$10.2 million and \$0.4 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, as the Company is required to pay a mid-single digit percentage of net sales of ferric citrate in the Company's licensed territories to Panion under the terms of the Panion Amended License Agreement.

#### ***Sublicense Agreement with Japan Tobacco, Inc. and its subsidiary, Torii Pharmaceutical Co., Ltd.***

##### *Summary of Agreement*

As a result of the Merger, 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.

Ferric citrate hydrate is currently approved by the Japanese Ministry of Health, Labour and Welfare for manufacturing and marketing in Japan for the treatment of hyperphosphatemia in patients with CKD. Ferric citrate hydrate is being marketed in Japan by Torii, under the brand name Riona. During the three months ended June 30, 2020, JT and Torii announced the filing of a supplemental NDA with the Pharmaceuticals and Medical Devices Agency seeking an additional indication for Riona to treat adult patients with IDA in Japan. The Company is eligible to receive royalty payments based on a tiered double-digit percentage of net sales of Riona in Japan escalating up to the mid-teens, subject to certain reductions upon expiration or termination of the Amended and Restated License Agreement between Keryx and Panion, by 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 us. 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, including 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, 2020 and 2019 and for the period from December 12, 2018 to December 31, 2018, the Company recognized \$5.7 million, \$5.9 million and \$0.1 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.

## 5. Business Combination

On December 12, 2018, the Company completed the Merger with Keryx. Keryx's proprietary product, Auryxia, is approved by the FDA for two indications: (1) the control of serum phosphorus levels in adult patients with DD-CKD, or the Hyperphosphatemia Indication and (2) the treatment of iron deficiency anemia in adult patients with NDD-CKD, or the IDA Indication.

Pursuant to the terms and conditions of the Merger Agreement, each outstanding Keryx Share, excluding the Baupost Additional Shares, as defined below, and each outstanding Keryx equity award were converted into Akebia Shares and substantially similar Akebia equity awards, respectively, at an exchange ratio of 0.37433 for a total fair value consideration of \$527.8 million consisting of the following (in thousands):

Fair value of 57,773,090 Akebia Shares	\$	516,492
Fair value of 602,752 Akebia RSUs		304
Fair value of 3,967,290 Akebia stock options		10,958
Total consideration	\$	527,754

Immediately prior to the Merger, Baupost Group Securities, L.L.C., or Baupost, agreed to convert its \$164.7 million of Keryx's Convertible Notes into 35,582,335 Keryx Shares, in accordance with the terms of the governing indenture agreement, in exchange for an additional 4,000,000 Keryx Shares, or the Baupost Additional Shares. The aggregate 39.6 million Keryx Shares were then converted into Akebia Shares at the 0.37433 exchange ratio. The fair value of the Baupost Additional Shares, on an as-converted basis, of \$13.4 million has been excluded from the purchase price and recorded within selling, general and administrative expenses in the Company's consolidated financial statements, as the issuance of those shares by Keryx is considered to be a separate transaction under ASC 805, since it was entered into by or on behalf of the acquirer or primarily for the benefit of the acquirer or the combined entity.

The Company allocated the \$527.8 million purchase price to the identifiable assets acquired and liabilities assumed in the business combination at their fair values as of December 12, 2018 as follows (in thousands):

Cash and cash equivalents	\$	5,257
Inventory		235,597
Trade accounts receivable, net		15,834
Prepaid expenses and other current assets		8,399
Goodwill		55,053
Intangible assets:		
Developed product rights for Auryxia		329,130
Other intangible assets		545
Property and equipment, net		3,646
Other assets		14,441
Accounts payable		(17,570)
Accrued expenses		(42,972)
Deferred tax liability		(35,096)
Debt		(15,000)
Fair value of unfavorable executory contract		(29,510)
Total purchase price	\$	527,754

In performing the purchase price allocation, the Company considered, among other factors, the intended future use of acquired assets, analysis of historical financial performance and estimates of future performance of Keryx's business.

As part of the purchase price allocation, the Company identified developed product rights for Auryxia as the primary intangible asset. The fair value of the developed product rights for Auryxia was determined using the multi-period excess earnings method which is a variation of the income approach, and is a valuation technique that provides an estimate of the fair value of an asset based on the principle that the value of an intangible asset is equal to the present value of the incremental after-tax cash flows attributable to the asset, after taking charges for the use of other assets employed by the business. Key estimates and assumptions used in this model were projected revenues and expenses related to the asset, estimated contributory asset charges, and a risk-adjusted discount rate of 20.0% used to calculate the present value of the future expected cash inflows from the asset. The intangible asset is being amortized on a straight-line basis over its estimated useful life, which at the time of the Merger was estimated to be nine years. 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 and made a corresponding adjustment to the estimated useful life of the developed product rights for Auryxia from nine years to seven years. As part of the Company's routine forecasting process during the fourth quarter of 2020, the Company 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 (see Note 9 for additional information).

The Company also 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. As of the acquisition date, the fair value of the off-market element was \$29.5 million. During the year ended December 31, 2020, the Company recorded a \$25.6 million increase to the liability for excess purchase commitments, and a corresponding charge to cost of goods sold largely driven by reductions in the short-term and long-term Auryxia revenue sales forecast. As of December 31, 2020 and 2019, the Company's liability for excess purchase commitments was \$55.8 million and \$30.2 million (see Note 16 for additional information).

The goodwill represents the excess of the purchase price over the estimated fair value of net assets acquired. The factors contributing to the recognition of goodwill were based on several strategic and synergistic benefits that were expected to be realized from the Merger. These benefits included the expectation that the combined company would establish itself as a leading renal company with enhanced position and large market opportunity, synergistic utilization of Keryx's commercial organization, and strengthening the combined company's financial profile. Such goodwill is not deductible for tax purposes.

In connection with the Merger, the Company identified a deferred tax liability of \$35.1 million as a result of the difference in the book basis and tax basis related to the identifiable inventory, other intangible assets, net and other liability. In determining the deferred tax liability to be recorded the Company elected to first consider the recoverability of the deferred tax assets acquired in the acquisition before considering the recoverability of the acquirer's existing deferred tax assets.

## 6. Available For Sale Securities

Available for sale securities at December 31, 2020 and 2019 consist of the following:

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
	(in thousands)			
<b>December 31, 2020</b>				
Cash and cash equivalents	\$ 228,698	\$ —	\$ —	\$ 228,698
Available for sale securities:				
U.S. government debt securities	\$ 39,979	\$ 13	\$ —	\$ 39,992
Total available for sale securities	\$ 39,979	\$ 13	\$ —	\$ 39,992
Total cash, cash equivalents, and available for sale securities	\$ 268,677	\$ 13	\$ —	\$ 268,690



	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
(in thousands)				
<b>December 31, 2019</b>				
Cash and cash equivalents	\$ 147,449	\$ —	\$ —	\$ 147,449
Available for sale securities:				
Certificates of deposit	\$ 245	\$ —	\$ —	\$ 245
Total available for sale securities	\$ 245	\$ —	\$ —	\$ 245
Total cash, cash equivalents, and available for sale securities	\$ 147,694	\$ —	\$ —	\$ 147,694

The estimated fair value of the Company's available for sale securities balance at December 31, 2020, by contractual maturity, is as follows (in thousands):

Due in one year or less	\$ 39,992
Due after one year	—
Total available for sale securities	\$ 39,992

There were no realized gains or losses on available for sale securities for the years ended December 31, 2020 or 2019. Additionally, the Company did not have any available for sale securities that were in an unrealized loss position as of December 31, 2020 or 2019. As such, the Company did not recognize any credit losses during the year ended December 31, 2020.

## 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, 2020 and 2019 are summarized below:

	Fair Value Measurements Using			Total
	Level 1	Level 2	Level 3	
(in thousands)				
<b>December 31, 2020</b>				
Assets:				
Cash and cash equivalents	\$ 228,698	—	—	\$ 228,698
U.S. government debt securities	—	39,992	—	39,992
	\$ 228,698	\$ 39,992	\$ —	\$ 268,690
Liabilities:				
Derivative liability	—	—	\$ 2,420	\$ 2,420
	\$ —	\$ —	\$ 2,420	\$ 2,420

	Fair Value Measurements Using			Total
	Level 1	Level 2	Level 3	
(in thousands)				
<b>December 31, 2019</b>				
Assets:				
Cash and cash equivalents	\$ 147,449	—	—	\$ 147,449
Certificates of deposit	—	245	—	245
	<u>\$ 147,449</u>	<u>\$ 245</u>	<u>\$ —</u>	<u>\$ 147,694</u>
Liabilities:				
Derivative liability	—	—	\$ 1,650	\$ 1,650
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,650</u>	<u>\$ 1,650</u>

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 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 events of default include maintaining, on an annual basis, a minimum liquidity threshold starting 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 \$2.4 million and \$1.7 million as of December 31, 2020 and 2019, respectively. The Company classified the derivative liability as a non-current liability on the balance sheet at December 31, 2020 and 2019. The estimated fair value of the derivative liability on both December 31, 2020 and 2019 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. Probabilities surrounding clinical development success were derived using industry benchmarks. 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, 2019	\$ 1,650
Initial fair value of derivative liability for Tranche B, recorded as debt discount	484
Change in fair value of derivative liability, recorded as other expense	286
Balance at December 31, 2020	<u>\$ 2,420</u>

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, 2020 and 2019.

Investment securities are exposed to various risks such as interest rate, market and credit risks. When the Company holds investment securities, due to the level of risk associated with certain investment securities and the level of uncertainty related to changes in the value of investment securities, the Company considers if changes in risks in the near term would result in material changes in the fair value of investments.

## 8. Inventory

The components of inventory, inclusive of step-up as a result of bringing Keryx's inventory onto Akebia's books in connection with the Merger, are summarized as follows:

	December 31, 2020	December 31, 2019
	(in thousands)	
Raw materials	\$ 2,542	\$ 2,278
Work in process	64,076	137,858
Finished goods	19,691	42,096
Total inventory	<u>\$ 86,309</u>	<u>\$ 182,232</u>

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, 2020	December 31, 2019
	(in thousands)	
<b>Balance Sheet Classification:</b>		
Inventory	\$ 61,017	\$ 116,349
Other assets	25,292	65,883
Total inventory	<u>\$ 86,309</u>	<u>\$ 182,232</u>

Inventory amounts written down as a result of excess, obsolescence, scrap or other reasons and charged to cost of goods sold totaled \$20.1 million and \$7.1 million during the years ended December 31, 2020 and 2019, respectively, in addition to related step-up charges of \$11.4 million and \$17.1 million during the years ended December 31, 2020 and 2019, respectively. There were no inventory write-offs during the period from December 12, 2018 through December 31, 2018. The increase for the year ended December 31, 2020 was primarily related to the write-down of inventory associated with specific lots of Auryxia because it was determined that these lots were not manufactured in conformance with the FDA's GMP guidance relating to validation. This write-down was largely related to a previously disclosed manufacturing quality issue related to Auryxia.

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, 2020				
	Gross Carrying Value	Accumulated Amortization	ASC 842 Adjustment	Total	Estimated useful life
<b>Acquired intangible assets:</b>					
Developed product rights for Auryxia	\$ 213,603	\$ (69,433)	\$ —	\$ 144,170	6 years
Favorable lease	545	(5)	(540)	—	N/A
Total	<u>\$ 214,148</u>	<u>\$ (69,438)</u>	<u>\$ (540)</u>	<u>\$ 144,170</u>	
	December 31, 2019				
	Gross Carrying Value	Accumulated Amortization	ASC 842 Adjustment	Total	Estimated useful life
<b>Acquired intangible assets:</b>					
Developed product rights for Auryxia	\$ 329,130	\$ (37,918)	\$ —	\$ 291,212	9 years
Favorable lease	545	(5)	(540)	—	N/A
Total	<u>\$ 329,675</u>	<u>\$ (37,923)</u>	<u>\$ (540)</u>	<u>\$ 291,212</u>	

On December 12, 2018, the Company completed the Merger, whereby it acquired certain definite-lived intangible assets, including the developed product rights for Auryxia and a favorable lease. The Company amortizes its definite-lived intangible assets acquired as part of the Merger using the straight-line method, which is considered the best estimate of economic benefit, over its estimated useful life. As a result of the adoption of ASC 842 on January 1, 2019, the Company reclassified the remaining balance of the favorable lease intangible asset into the operating lease asset. The Company recorded \$31.5 million, \$36.4 million and \$1.5 million in amortization expense related to the developed product rights for Auryxia during the years ended December 31, 2020, 2019 and 2018, respectively. Estimated future amortization expense for the intangible asset as of December 31, 2020 is as follows (in thousands):

	<b>Total</b>
2021	\$ 36,042
2022	36,043
2023	36,042
2024	36,043
2025	—
Thereafter	—
	<u>\$ 144,170</u>

#### *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.

As part of the Company's routine forecasting process, as of December 31, 2020, 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, 2020 and 2019, derived as follows (in thousands):

Total Merger consideration	\$	527,754
Less: Fair value of identified acquired assets and liabilities, net		(472,701)
Goodwill	\$	<u>55,053</u>

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. There were no impairments of goodwill during the years ended December 31, 2020, 2019 and 2018.

## 10. Accrued Expenses

Accrued expenses are as follows:

	December 31, 2020	December 31, 2019
	(in thousands)	
Product revenue allowances	\$ 38,049	\$ 30,552
Accrued clinical	28,986	61,815
Accrued payroll	14,402	12,604
MTPC - Supply of Commercial Drug Product	13,887	—
Otsuka PRV contribution	10,000	—
Lease liability	5,286	4,989
MTPC - Supply of Validation Drug Product	4,090	—
Professional fees	3,271	3,444
Royalties	2,998	2,713
Accrued commercial manufacturing	514	2,680
Accrued severance	497	725
Accrued other	8,644	9,549
Total accrued expenses	<u>\$ 130,624</u>	<u>\$ 129,071</u>

## 11. Debt

Future principal payments on the Term Loans (as defined below) as of December 31, 2020 are as follows (in thousands):

	Principal Payments
	(in thousands)
2021	\$ —
2022	7,140
2023	33,474
2024	59,386
2025	—
Thereafter	—
Total before unamortized discount and issuance costs	100,000
Less: unamortized discount and issuance costs	(3,622)
Total term loans	<u>\$ 96,378</u>

## 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, if certain conditions are met, it will have the option to repay the principal in equal quarterly payments starting on the 48th-month anniversary of the applicable Funding Date, or collectively the Amortization Schedule. 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 starting in 2021, and on a quarterly basis, a minimum net sales threshold for Auryxia which started in the fourth quarter of 2020. 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, 2020, the Company determined that no events of default had occurred.

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 \$2.4 million and \$1.7 million as of December 31, 2020 and 2019, respectively. The Company classified the derivative liability as a non-current liability on the balance sheet at December 31, 2020.

The Company recognized approximately \$8.9 million and \$0.9 million of interest expense related to the Loan Agreement during the years ended December 31, 2020 and 2019, respectively.

#### *Revolving Line of Credit*

Keryx, the Company's wholly owned subsidiary following the Merger, had a \$40.0 million revolving line of credit, or the Line of Credit, under its Loan and Security Agreement with Silicon Valley Bank, or SVB. On July 31, 2019, Keryx entered into a Waiver and First Amendment to Loan and Security Agreement, or the Loan Amendment. Pursuant to the Loan Amendment, certain revisions were made to the Loan and Security Agreement, including requiring Keryx to maintain, from and after December 31, 2019, subject to certain exceptions, a certain amount of funds to which the Company had unrestricted access in one or more asset management accounts with SVB or SVB's affiliate and revising certain of the representations and warranties and covenants in the Loan and Security Agreement. In addition, pursuant to the Loan Amendment, SVB waived the then-existing events of default.

On August 7, 2019, the Company executed and delivered to SVB an Unconditional Guaranty, or the Guaranty, pursuant to which the Company guaranteed the prompt and complete payment and performance when due of all of the obligations and liabilities of Keryx under the Loan and Security Agreement, as amended by the Loan Amendment, or the Amended Loan Agreement. In addition, the Company entered into a Security Agreement with SVB effective August 7, 2019, or the Security Agreement, pursuant to which the Company granted to SVB a continuing first priority security interest in substantially all of the Company's personal property, other than the Company's intellectual property, to secure the payment and performance of the Company's obligations under the Guaranty. The Company's obligations under the Guaranty were independent of Keryx's obligations, and separate actions were able to be brought against the Company.

Availability under the Line of Credit was subject to a borrowing base comprised of eligible receivables and eligible inventory of Keryx as set forth in the Loan and Security Agreement. As of December 31, 2020 and 2019, there was \$0 outstanding under the Line of Credit and the Company had \$0 in available borrowing base as of December 31, 2020 and 2019, as the Line of Credit was terminated in November 2019.

The principal amount outstanding under the Loan and Security Agreement bore interest at a floating rate per annum equal to the greater of (i) 2.00% above the "prime rate," as reported in The Wall Street Journal and (ii) 6.75%, which interest was payable monthly. Principal amounts borrowed under the Line of Credit were able to be repaid and, prior to the maturity date, re-borrowed, subject to the terms and conditions set forth in the Loan and Security Agreement. Upon entry into the Loan and Security Agreement (payable in installments and subject to certain conditions), and at the one year anniversary of the effective date of the Loan and Security Agreement (or, if earlier, upon termination of or an event of default under the Loan and Security Agreement), Keryx paid to SVB a fee equal to 1.00% of the Line of Credit. Keryx was also required to pay on a quarterly basis a fee equal to 0.25% per annum of the average unused portion of the Line of Credit. Pursuant to the terms of the Loan and Security Agreement, Keryx was required to pay a termination fee of 2.00% of the Line of Credit, if the Loan and Security Agreement was terminated prior to the maturity date, subject to certain exceptions. The Company terminated the Loan and Security Agreement, the Unconditional Guaranty, and the Security Agreement on November 7, 2019, and Keryx paid SVB a termination fee of \$0.8 million.

During the years ended December 31, 2020 and 2019 and for the period from December 12, 2018 through December 31, 2018, the Company recognized approximately \$0, \$0.5 million and \$65,000, respectively, of interest expense related to the Line of Credit. The Company did not incur any amortization expense related to the origination fee and other additional fees noted above as such fees were included in the fair value of the Line of Credit as of December 12, 2018, the date on which the Merger was consummated, in accordance with ASC 805.

## **12. Warrant**

In connection with the Janssen Agreement, in February 2017, the Company issued a warrant to purchase 509,611 shares of the Company's common stock at an exercise price of \$9.81 per share. The warrant was fully vested upon issuance and exercisable in whole or in part, at any time prior to February 9, 2022. The warrant satisfied the equity classification criteria of ASC 815, and is therefore classified as an equity instrument. The fair value at issuance of \$3.4 million was calculated using the Black-Scholes option pricing model and was charged to research and development expense as it represented consideration for a

license for which the underlying intellectual property was deemed to have no alternative future use. As of December 31, 2020, the warrant remains outstanding and expires on February 9, 2022.

### **13. 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, 2020, the authorized capital stock of the Company included 350,000,000 shares of common stock, par value \$0.00001 per share, of which 148,074,085 and 121,674,568 shares were issued and outstanding at December 31, 2020 and 2019, 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, 2020 and 2019.

#### ***At-the-Market Facility***

In May 2016, the Company established an at-the-market, or ATM, equity offering program pursuant to which it was able to offer and sell up to \$75.0 million of its common stock at the then current market prices from time to time. Through December 31, 2018, the Company sold 1,775,214 shares of common stock under this program with net proceeds of \$22.6 million, of which 694,306 shares were sold in the year ended December 31, 2018 for net proceeds of approximately \$10.5 million. Additionally, the Company sold 1,384,520 shares in the six months ended June 30, 2019 for net proceeds (after deducting commissions and other offering expenses) of approximately \$9.4 million.

On November 12, 2019, the Company entered into an Amended and Restated Controlled Equity Offering<sup>SM</sup> Sales Agreement with Cantor Fitzgerald & Co. for the offer and sale of common stock at the then current market prices in amounts to be determined from time to time. Also, on November 12, 2019, the Company filed a prospectus supplement pursuant to which it was able to offer and sell up to \$75.0 million of its common stock at the then current market prices from time to time. In December 2019, the Company commenced sales under this program. Through December 31, 2019, the Company sold 2,684,392 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of \$16.8 million. During the three months ended March 31, 2020, the Company sold 7,973,967 shares of common stock under this program with net proceeds (after deducting commissions and other offering expenses) of \$56.7 million.

On March 12, 2020, the Company filed an additional prospectus supplement, pursuant to which it is able to offer and sell up to \$65.0 million of its common stock at current market prices from time to time. During the year ended 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. Subsequent to December 31, 2020 and through the date of this Annual Report on Form 10-K, 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.

#### ***Equity Offering***

In March 2018, the Company completed a follow-on public equity offering, whereby the Company sold 8,500,000 shares of common stock at a public offering price of \$10.50 per share. The aggregate net proceeds received by the Company from the offering were approximately \$84.8 million, net of underwriting discounts and commissions and estimated offering expenses payable by the Company. The Company did not have any follow-on public equity offerings during the year ended December 31, 2019.

In May 2020, the Company sold 12,650,000 shares of its common stock in a public offering at a price of \$12.00 per share, including 1,650,000 shares from the full exercise of the underwriters' option to purchase additional shares. The aggregate net proceeds received by the Company from the offering were \$142.4 million, net of underwriting discounts and commissions and offering expenses payable by the Company.

#### ***Shares Issued and Awards Assumed in Connection with Business Combination***

On December 12, 2018, the Company completed the Merger. Pursuant to the terms and conditions of the Merger Agreement, each Keryx Share issued and outstanding as of the Effective Time was cancelled and converted into 0.37433 fully paid and non-assessable Akebia Shares. As a result, in December 2018, the Company issued 57,773,090 shares of common stock to Keryx shareholders, and 1,497,320 shares issued as part of the Baupost Additional Shares which has been excluded from the business combination purchase price (see Note 5).



Additionally, in connection with the Merger, the Company converted outstanding and unexercised options to purchase Keryx Shares into 3,967,290 options to purchase Akebia Shares, as adjusted to reflect the Exchange Multiplier, of which 3,733,336 are service-based stock options and 233,954 are performance-based stock options. The Company also converted outstanding Keryx Restricted Shares into 602,752 Akebia RSUs, of which 486,709 are service-based RSUs and 116,043 are performance-based RSUs.

### ***Acceleration of Equity Awards***

In connection with the closing of the Merger, certain executives of Keryx were terminated and as a result, the Company accelerated in full the vesting of all of the outstanding equity awards for each such executive, consistent with his or her existing employment agreements. Additionally, subject to limited exceptions, all outstanding equity awards held by certain officers of Akebia also had the vesting of their outstanding equity awards accelerated in full upon consummation of the Merger as a result of the change in control provision included in each such officer's award agreements and their Executive Severance Agreements. As a result, the Company recognized \$9.7 million of stock-based compensation expense related to the acceleration of awards during the year ended December 31, 2018.

### ***Equity Plans***

On February 28, 2014, the Company's Board of Directors adopted its 2014 Incentive Plan and its 2014 Employee Stock Purchase Plan, or the 2014 ESPP, which were subsequently approved by its shareholders and became effective upon the closing of the Company's initial public offering on March 25, 2014. The Company's 2014 Incentive Plan was subsequently amended on December 11, 2018, which amendment did not require shareholder approval. The Company's 2014 Incentive Plan, as amended, is referred to as the 2014 Plan. 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 shareholders 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 shareholder approval, or the Inducement Award Program. During the year ended December 31, 2020, the Company granted 1,113,250 options to purchase shares of the Company's common stock to new hires under the Inducement Award Program, of which 1,064,550 options to purchase Akebia Shares remained outstanding at December 31, 2020.

The 2014 Plan allows for the granting of stock options, stock appreciation rights, or SARs, restricted stock, unrestricted stock, 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 Akebia 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 Shares, 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, 2020, the Company granted 1,714,800 options to purchase Akebia Shares to employees under the 2014 Plan, 1,113,250 options to purchase Akebia Shares to employees under the Inducement Award Program, 2,465,950 Akebia RSUs to employees under the 2014 Plan, 515,500 Akebia PSUs to employees under the 2014 Plan, 220,900 options to purchase Akebia Shares to directors under the 2014 Plan, and 95,900 Akebia RSUs to directors under the 2014 Plan.

The ESPP provides for the issuance of options to purchase shares of the Company's common stock to participating employees at a discount to their fair market value. As noted above, the Company's stockholders approved the ESPP, which amended and restated the Company's 2014 ESPP, on June 6, 2019. The maximum aggregate number of shares at December 31, 2020 of the

Company's common stock available for future issuance under the ESPP is 5,480,334. 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, 2020	December 31, 2019
Common stock options and RSUs outstanding (1)	14,108,828	12,195,031
Shares available for issuance under Akebia equity plans (2)	3,468,080	2,983,256
Warrant to purchase common stock	509,611	509,611
Shares available for issuance under the ESPP (3)	5,480,334	5,715,992
<b>Total</b>	<b>23,566,853</b>	<b>21,403,890</b>

- (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, 2021, January 1, 2020 and January 1, 2019, the shares reserved for future grants under the 2014 Plan increased by 4,880,775, 4,031,376 and 3,801,198 shares, respectively, pursuant to the 2014 Plan Evergreen Provision. On January 30, 2019, the Company's Board of Directors approved 3,150,000 shares for issuance as option awards in fiscal year 2019 under the Inducement Award Program.
- (3) On June 6, 2019, the shares reserved for future issuance under the ESPP increased by 5,200,000 shares upon shareholder approval of the Amended and Restated 2014 Employee Stock Purchase Plan. On February 28, 2018 and February 28, 2017, the shares reserved for future issuance under the 2014 ESPP remained unchanged. There were no increases in the shares reserved for future issuance pursuant to the evergreen provision under the ESPP in 2017 and 2018 as the maximum aggregate number of shares available for purchase under the 2014 ESPP had reached its cap of 739,611 on February 28, 2016.

### **Stock-Based Compensation**

#### **Stock Options**

##### *Service-Based Stock Options*

On February 28, 2020, as part of the Company's annual grant of equity, the Company issued 1,714,800 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 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 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 \$8.5 million, \$5.4 million and \$11.9 million of stock-based compensation expense related to stock options granted during fiscal years 2020, 2019 and 2018, respectively.

On December 12, 2018, pursuant to the Merger Agreement, each outstanding and unexercised option to acquire Keryx Shares granted under a Keryx equity plan converted into an option to acquire Akebia Shares, with the number of shares and exercise price adjusted by the Exchange Multiplier. As a result, the Company assumed 3,733,336 service-based options related to the Merger. The vesting schedule for these options is consistent with the vesting schedule noted above.

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,								
	2020			2019			2018		
Risk-free interest rate	0.32%	-	1.38%	1.42%	-	2.57%	2.54%	-	3.01%
Dividend yield	—%			—%			—%		
Volatility	69.56%	-	75.92%	61.4%	-	64.1%	61.65%	-	77.04%
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, 2020:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2019	7,624,109	\$ 9.77		\$ 3,173,101
Granted	3,048,950	\$ 8.91		
Exercised	(166,633)	\$ 7.36		\$ 438,337
Forfeited	(1,117,751)	\$ 11.59		\$ 853,732
Expired/cancelled	(18,302)	\$ 10.48		
Outstanding, December 31, 2020	9,370,373	\$ 9.31	7.37	\$ 387,596
Options exercisable, December 31, 2020	4,606,431	\$ 10.63	5.89	\$ 347,576
Vested and expected to vest, December 31, 2020	9,370,373	\$ 9.31		

The weighted-average grant date fair values of options granted in the years ended December 31, 2020, 2019, and 2018 were \$5.63, \$3.85, and \$7.12 per share, respectively. The total intrinsic value of options exercised during the years ended December 31, 2020, 2019, and 2018 were \$0.4 million, \$1.3 million, and \$1.2 million, respectively. The fair value of options that vested during the years ended December 31, 2020, 2019, and 2018 were \$6.8 million, \$4.3 million, and \$13.6 million, respectively. As of December 31, 2020, there was approximately \$19.5 million of unrecognized compensation cost related to stock options 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 2.66 years.

#### Performance-Based Stock Options

On December 12, 2018, pursuant to the Merger Agreement, each outstanding and unexercised performance-based option to acquire Keryx Shares granted under a Keryx equity plan converted into a service-based option or performance-based option to acquire Akebia Shares, with the number of shares and exercise price adjusted by the Exchange Multiplier. As a result, the Company issued 233,954 performance-based options related to the Merger. The Company did not have any performance based-options outstanding in fiscal year 2018 prior to the Merger. The Company did not issue any performance-based options during the years ended December 31, 2020 and 2019. As of December 31, 2020, the Company had no performance-based options outstanding compared to 46,790 performance-based options outstanding at December 31, 2019.

The following table summarizes the Company's performance-based option activity for the year ended December 31, 2020:

	Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding, December 31, 2019	46,790	\$ 15.77	6.83	\$ —
Granted	—	\$ —		
Exercised	—	\$ —		\$ —
Forfeited/cancelled	(46,790)	\$ 15.77		
Outstanding, December 31, 2020	—	\$ —	0	\$ —

The Company did not record any stock-based compensation expense related to performance-based options during 2020, 2019 and 2018. There were no performance-based options that vested during fiscal year 2020, 46,790 performance-based options that vested during fiscal year 2019, and no performance-based options that vested during fiscal year 2018. As of December 31,

2020, 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, 2020, as part of the Company's annual grant of equity, the Company issued 2,268,000 restricted stock units, or RSUs, to employees. In addition, the Company 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 either the first or the third anniversary of the grant date, (ii) one third of each RSU grant vests on the first, second and third anniversaries of the grant date, subject, in each case, to the individual's continued service through the applicable vesting date, or (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. 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 \$14.6 million, \$6.2 million and \$5.8 million of stock-based compensation expense related to employee RSUs in 2020, 2019 and 2018, respectively.

On December 12, 2018, pursuant to the Merger Agreement, each Keryx Share that was subject to a Keryx restricted share award, other than those Keryx restricted shares that accelerated or lapsed as a result of the completion of the Merger, was converted into an RSU award of Akebia, covering the number of Akebia Shares determined in accordance with the Exchange Multiplier. As a result, the Company issued 486,709 service-based RSUs in substitution for Keryx restricted share awards in connection with the Merger. These RSUs vest either (i) in 3 equal annual installments beginning after the one year anniversary of the grant date or (ii) one third on the one year anniversary of the grant date with the remaining RSUs vesting on the first day of each calendar quarter over the next two years thereafter.

### Performance-Based Restricted Stock Units

During the year ended December 31, 2020, the Company issued 515,500 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 and regulatory milestones. The PSUs also feature a time-based vesting component. 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 and regulatory milestones. The Company recorded approximately \$0.5 million, \$0 and \$0 of stock-based compensation expense related to employee PSUs in 2020, 2019 and 2018, respectively.

A following table summarizes the Company's RSU and PSU activity for the year ended December 31, 2020:

	Shares	Weighted-Average Grant Date Fair Value
Unvested balance, December 31, 2019	4,511,030	\$ 5.25
Granted	3,077,350	\$ 8.75
Vested	(1,863,878)	\$ 5.00
Forfeited	(999,149)	\$ 6.31
Unvested balance, December 31, 2020	4,725,353	\$ 7.43

The total amount of RSUs and PSUs that vested during 2020, 2019 and 2018 (measured on the date of vesting) was \$9.4 million, \$2.7 million, and \$7.4 million, respectively. As of December 31, 2020, there was approximately \$20.1 million of unrecognized compensation cost related to RSUs and PSUs, which is expected to be recognized over a weighted average period of 1.71 years.

There are 13,102 performance-based RSUs, issued in connection with the Merger, outstanding at December 31, 2020.

### Employee Stock Purchase Plan

The first offering period under the ESPP opened on January 2, 2015. The Company issued 235,658 shares during the year ended December 31, 2020. The Company recorded approximately \$0.8 million, \$0.3 million and \$0.2 million of stock-based compensation expense related to the ESPP during 2020, 2019 and 2018, respectively.

### Compensation Expense Summary

The Company has classified its stock-based compensation expense related to share-based awards as follows:

	Years ended December 31,		
	2020	2019	2018
	(in thousands)		
Research and development	\$ 6,113	\$ 3,544	\$ 5,755
Selling, general and administrative	18,347	8,381	13,285
Total	<u>\$ 24,460</u>	<u>\$ 11,925</u>	<u>\$ 19,040</u>

Compensation expense by type of award:

	Years ended December 31,		
	2020	2019	2018
	(in thousands)		
Stock options	\$ 8,517	\$ 5,421	\$ 12,114
Restricted stock units	15,103	6,240	6,731
Employee stock purchase plan	840	264	195
Total	<u>\$ 24,460</u>	<u>\$ 11,925</u>	<u>\$ 19,040</u>

Included in the compensation expense of stock options and RSUs for the year ended December 31, 2018, is approximately \$1.1 million related to awards assumed under the Merger and acceleration of the vesting for awards of certain officers of Keryx.

### 14. 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. At December 31, 2018 the Company recorded a tax benefit of \$28.3 million as a result of the Merger with Keryx. As part of purchase accounting, the Company recorded a deferred tax liability that is a source of income for which the Company can benefit from its tax attributes. The use of the Company's tax attributes resulted in a release of the corresponding valuation allowance associated with this benefit. At December 31, 2019 the Company recorded an additional tax benefit of \$6.6 million as a result of additional losses incurred during the year. There was no current or deferred income tax expense or benefit for the year ended December 31, 2020 due to the Company's net losses and increases in its valuation allowance against its deferred tax assets.

The provision for income taxes for each of the years ended December 31, 2020, 2019 and 2018 consisted of the following:

	Year ended December 31,		
	2020	2019	2018
<b>Current:</b>			
Federal	—	—	23
State	—	—	104
Foreign	—	—	—
<b>Total Current:</b>	—	—	127
<b>Deferred:</b>			
Federal	—	—	(16,383)
State	—	(6,631)	(12,082)
Foreign	—	—	—
<b>Total Deferred:</b>	—	(6,631)	(28,465)
<b>Total Income Taxes</b>	—	(6,631)	(28,338)

Our effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2020, 2019 and 2018:

	Year ended December 31,		
	2020	2019	2018
Federal tax at statutory rate	21.0 %	21.0 %	21.0 %
State and local tax at statutory rate	3.0	5.5	4.1
Research and development tax credits	0.1	2.0	5.0
Equity compensation	—	—	—
Alternative minimum tax	—	—	—
Change in valuation allowance	(21.5)	(22.4)	16.3
Impact of US tax reform	—	—	—
Non-deductible transaction costs	—	—	(3.1)
Other permanent differences	(0.4)	(0.3)	(0.7)
Reduction in deferred tax assets for change in ownership	—	(1.6)	(26.1)
Effect of rate changes	0.8	(1.4)	—
Provision to Return Adjustment	(1.5)	—	—
Prior Period Adjustment to State NOL DTA	(1.5)	—	—
Other	—	(0.5)	—
<b>Effective tax rate</b>	— %	2.3 %	16.5 %

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 \$82.5 million and \$64.0 million, during the years ended December 31, 2020 and 2019, respectively. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2020	2019
(in thousands)		
Deferred tax assets:		
Accrued expenses	\$ 3,079	\$ 2,933
Deferred revenue	9,091	18,678
Stock based compensation	10,014	10,136
Research and development credits	4,620	9,601
Other non-current liabilities	17,015	8,049
Net operating loss carryforward	262,532	242,167
ASC 842 lease liability	6,776	8,382
Fixed assets	700	806
UNICAP	2,132	—
Inventory Reserve	8,260	—
Derivative Liability	542	—
Other	2,535	4,018
Total deferred tax assets	327,296	304,770
Less valuation allowance	(277,941)	(195,418)
Total deferred tax assets, net of valuation allowance	49,355	109,352
Deferred tax liabilities:		
Fixed assets	—	—
Intangible assets	(34,178)	(75,940)
Inventory	(8,479)	(25,494)
ASC 842 ROU asset	(6,101)	(7,495)
Derivative liability	(597)	(423)
Total deferred tax liabilities	(49,355)	(109,352)
Net deferred tax liability	\$ —	\$ —

At December 31, 2020 and 2019, the Company has approximately \$0.4 million (after amortization of \$1.6 million) and \$0.5 million (after amortization of \$1.4 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, 2020 and 2019, the Company has approximately \$1,128.3 million and \$1,014.8 million, respectively, of federal NOL carry-forwards which expire through 2037. Included in the \$1,128.3 million of federal NOLs are losses of \$546.4 million that will carry forward indefinitely as a result of the Tax Cuts and Jobs Act. Additionally, at December 31, 2020 and 2019, the Company has approximately \$1,620.7 million and \$1,374.0 million, respectively, of state NOL carry-forwards which expired through 2040. The Company also has approximately \$2.4 million of federal research and development tax credit carryforwards which expire through 2040 and \$2.8 million of state research and development tax credit carryforwards which expire through 2035.

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 NOL's 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 2019, 2018 and 2017 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 2020, 2019 and 2018. 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.

## **15. 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 \$1.6 million, \$1.3 million and \$0.3 million were made during the years ended December 31, 2020, 2019 and 2018, respectively.

## **16. 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 commencing in December 2021, and is subject to annual rent escalations, which commence in December 2022.

Additionally, as a result of the Merger, the Company has a lease for 27,300 square feet of office space in Boston, Massachusetts, or the Boston Lease, which expires in February 2023. The total monthly lease payments under the base rent are approximately \$136,000 and are subject to annual rent escalations.

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 February 28, 2023, 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 was 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 \$6.7 million and \$6.6 million for the years ended December 31, 2020 and 2019. Cash paid for amounts included in the measurement of operating lease liabilities were \$7.0 million and \$6.9 million for the years ended December 31, 2020 and 2019.

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 expires 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 and \$0.2 million in sublease rental income from Foundation during the years ended December 31, 2020 and 2019, respectively.



The Company has not entered into any material short-term leases or financing leases as of December 31, 2020.

The total security deposit in connection with the Cambridge Lease is \$1.6 million as of December 31, 2020. Additionally, the Company recorded \$0.8 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 in prepaid expenses and other current assets in the Company's consolidated balance sheet as of December 31, 2020.

As of December 31, 2020, 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)		
2021	\$ 6,667	\$ 1,797	\$ 4,799
2022	7,322	1,824	5,267
2023	5,947	307	4,911
2024	5,739	—	5,040
2025	5,817	—	5,116
Thereafter	4,104	—	8,818
<b>Total</b>	<b>\$ 35,596</b>	<b>\$ 3,928</b>	<b>\$ 33,951</b>

In arriving at the operating lease liabilities, the Company applied incremental borrowing rates ranging from 6.22% to 6.94%, 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, 2020, the remaining lease terms ranged from 2.16 years to 5.70 years. As of December 31, 2020, 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	\$ 35,596
Present value adjustment using incremental borrowing rate	(5,672)
<b>Operating lease liabilities</b>	<b>\$ 29,924</b>

The Company recorded approximately \$3.7 million in rent expense for the year ended December 31, 2018.

#### *Manufacturing Agreements*

As a result of the Merger, the Company's contractual obligations include Keryx's commercial supply agreements with BioVectra Inc., or BioVectra, and Siegfried Evionnaz SA, or 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, collectively the BioVectra Agreement, 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 decreases 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, collectively the Amended BioVectra Agreement, requires 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 are recorded in other assets and amortized into drug substance as inventory is released to the Company from BioVectra. The term of the Manufacture and Supply Agreement with BioVectra expires on December 31, 2022. The term of the Amended and Restated Product Manufacture and Supply and Facility Construction Agreement expires on December 31, 2026, after which it automatically renews for successive one-year terms unless either party gives notice of its intention to terminate within a specified time prior to the end of the then-current term. In addition, the Company and BioVectra each have the ability to terminate these agreements upon the occurrence of certain conditions. As of December 31, 2020, the Company is required to

reimburse BioVectra for certain costs in connection with the construction of the new facility and to purchase minimum quantities of Auryxia drug substance annually for a total cost of approximately \$95.7 million through the end of the contract term.

Pursuant to the Siegfried Master Manufacturing Services and Supply Agreement, or the Siegfried Agreement, the Company has agreed to purchase a minimum quantity of drug substance of Auryxia at predetermined prices. The price per kilogram will decrease with an increase in quantity above the minimum purchase quantity. The term of the Siegfried Agreement expires on December 31, 2021, after which, it automatically renews for one-year terms until terminated. The Siegfried Agreement provides for certain termination rights prior to December 31, 2021 for the Company. As of December 31, 2020, the Company is required to purchase a minimum quantity of drug substance for Auryxia annually at a total cost of approximately \$47.9 million through the year ending December 31, 2021.

As part of purchase accounting, 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. The liability related to the amount of purchase commitments that exceed the current forecast was \$55.8 million and \$30.2 million as of December 31, 2020 and 2019, respectively. The \$25.6 million increase in liability, which was largely driven by reductions in the short-term and long-term Auryxia revenue sales forecast during the year ended December 31, 2020, was primarily recorded to cost of goods sold.

On February 11, 2021, Keryx and Siegfried entered into an amendment to the Siegfried Agreement, or the Siegfried Amendment. The Siegfried Agreement, as amended, includes the terms and conditions under which Siegfried will manufacture and supply finished Auryxia drug substance for commercial purposes. Siegfried currently manufactures Auryxia drug substance at two approved sites. Pursuant to the Siegfried Amendment, the term of the Siegfried Agreement was extended for one site such that the Siegfried Agreement will expire on December 31, 2022, subject to Keryx's option to extend the term for such site through December 31, 2023 by providing 12 months' prior written notice to Siegfried. The Siegfried Amendment provides for minimum annual quantity commitments and predetermined prices for the remainder of the term as well as certain other changes. Subsequent to December 31, 2020, the amount of Auryxia drug substance the Company has committed to purchase from Siegfried is \$45.4 million through December 31, 2022.

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 includes the terms and conditions under which Esteve will manufacture vadadustat drug substance for commercial use. Pursuant to the Esteve Agreement, the Company provides rolling forecasts to Esteve on a quarterly basis, or the Esteve Forecast. The Esteve Forecast reflects 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 have agreed to a volume-based pricing structure under the Esteve Agreement. The Esteve Agreement has an initial term of four years, beginning April 9, 2019 and ending April 9, 2023. Pursuant to the Esteve Agreement, the Company has agreed to purchase a certain percentage of the global demand for vadadustat drug substance from Esteve. As of December 31, 2020, the Company has committed to purchase \$26.0 million of vadadustat drug substance from Esteve through the second quarter of 2022. Subsequent to December 31, 2020, the amount of vadadustat drug substance the Company has committed to purchase from Esteve increased to \$47.6 million of through the fourth quarter of 2022.

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. 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, 2020, the Company had a minimum commitment with Patheon for \$1.3 million through the third quarter of 2021.

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, 2020, the Company has committed to purchase \$44.7 million of vadadustat drug substance from WuXi STA through the first quarter of 2022.

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*

Under the Company's agreement with IQVIA to provide contract research organization services for the PRO<sub>2</sub>TECT and INNO<sub>2</sub>VATE programs, the total remaining contract costs as of December 31, 2020 were approximately \$14.7 million, of which Otsuka reimburses a significant portion back to the Company. Substantive performance for the committed work with IQVIA was completed in 2020 and close out activities will be performed through the first quarter of 2021. The Company also contracts with various other organizations to conduct research and development activities with remaining contract costs to the Company of approximately \$155.9 million at December 31, 2020. 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, 2020, 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.

## 17. 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,		
	2020	2019	2018
Warrants	509,611	509,611	509,611
Outstanding stock options	9,386,517	7,670,899	8,346,888
Unvested restricted stock units	4,722,311	4,524,132	962,316
Total	14,618,439	12,704,642	9,818,815

## 18. Quarterly Results (unaudited)

	Three Months Ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
	(in thousands, except per share data) (unaudited)			
Product revenue, net	\$ 29,209	\$ 30,696	\$ 34,392	\$ 34,604
License, collaboration and other revenue	\$ 59,269	\$ 59,446	\$ 25,596	\$ 22,095
Cost of goods sold	\$ 27,713	\$ 174,616	\$ 30,345	\$ 63,234
Operating expenses	\$ 119,890	\$ 89,345	\$ 87,738	\$ 78,868
Loss from operations	\$ (59,125)	\$ (173,819)	\$ (58,095)	\$ (85,403)
Other expense, net	\$ (1,622)	\$ (1,932)	\$ (1,864)	\$ (1,597)
Benefit for income taxes	\$ —	\$ —	\$ —	\$ —
Net loss	\$ (60,747)	\$ (175,751)	\$ (59,959)	\$ (87,000)
Net loss per share:				
basic and diluted	\$ (0.47)	\$ (1.28)	\$ (0.42)	\$ (0.60)
Weighted-average number of common shares:				
basic and diluted	128,395,163	136,906,968	143,314,729	145,111,415

	Three Months Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(in thousands, except per share data) (unaudited)			
Product revenue, net	\$ 23,111	\$ 29,089	\$ 30,004	\$ 28,915
License, collaboration and other revenue	\$ 49,555	\$ 71,714	\$ 61,973	\$ 40,640
Cost of goods sold	\$ 31,257	\$ 37,669	\$ 38,263	\$ 38,147
Operating expenses	\$ 117,378	\$ 122,657	\$ 109,619	\$ 126,299
Loss from operations	\$ (75,969)	\$ (59,523)	\$ (55,905)	\$ (94,891)
Other income (expense), net	\$ 791	\$ 508	\$ 43	\$ (1,344)
Benefit for income taxes	\$ (2,757)	\$ (845)	\$ (1,277)	\$ (1,752)
Net loss	\$ (72,421)	\$ (58,170)	\$ (54,585)	\$ (94,483)
Net loss per share:				
basic and diluted	\$ (0.62)	\$ (0.49)	\$ (0.46)	\$ (0.79)
Weighted-average number of common shares:				
basic and diluted	117,063,352	118,268,832	118,863,063	119,358,081

## 19. Subsequent Events

On February 25, 2021, the Company entered into a royalty interest acquisition agreement, or the Royalty Agreement, with HealthCare Royalty Partners IV, L.P., or HCR, pursuant to which the Company sold to HCR its right to receive all royalties and sales milestones for vadadustat, collectively the Royalty Interest Payments, in each case, payable to the Company under its 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. 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 \$45.0 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and the Company is eligible to receive 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 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.

The Royalty Agreement requires the Company to take certain actions, including actions with respect to the Royalty Interest Payments, the MTPC Agreement, the Company's agreement with MTPC for the commercial supply of vadadustat drug product, 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.

### 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, 2020, our management, with the participation of 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, 2020, our disclosure controls and procedures were not effective because of a material weakness in our internal control over financial reporting relating to our inventory process which is described in more detail below.

#### *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, 2020 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 the material weakness in our internal control over financial reporting relating to our inventory process as reported in our Annual Report on Form 10-K for the year ended December 31, 2019 remains un-remediated as of December 31, 2020 and that, our internal control activities over financial reporting as of December 31, 2020 was not effective due to the following material weakness: the Company did not design and maintain effective controls over the completeness, accuracy and presentation and disclosure of inventory. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis. Specifically, we did not maintain effective controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing and (iii) the periodic assessment of excess and obsolete inventory related reserves.

Although during 2020 we strengthened our controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing and (iii) the periodic assessment of excess and obsolete inventory related reserves, further remediation is needed. The control deficiencies described above resulted in certain accounting errors, including in our internal preliminary consolidated financial statements for the year ended December 31, 2020 that were corrected prior to the issuance of such annual consolidated financial statements. Management has taken actions to remediate the deficiencies in its internal control over financial reporting and implemented additional processes and controls designed to address the underlying causes associated with the material weakness. Management is committed to finalizing the remediation of the material weakness during 2021. Management's internal control remediation efforts include the following:

- We have designed and implemented more robust controls throughout 2020 and will continue to improve the precision of our controls in 2021.
- We provided training to individuals with internal control responsibilities, including review documentation requirements, during 2020, and will continue to do so in 2021.
- We designed controls to address the completeness and accuracy of any key reports utilized in the execution of internal controls.
- We reported regularly during 2020, and will continue to report regularly in 2021, to the audit committee on the progress and results of control remediation.
- We engaged an outside firm to assist with performing sufficient testing in 2020 and executed upon a monitoring protocol to allow the Company to validate the operating effectiveness of certain controls over financial reporting to gain assurance that such controls are present and functioning as designed. We will continue to engage an outside firm in 2021 to assist management with performing sufficient testing throughout the year to validate the operating effectiveness of certain controls over financial reporting.

As management continues to evaluate and work to improve its internal control over financial reporting, management may determine it is necessary to take additional measures to address the material weakness. Until the controls have been operating for a sufficient period of time and management has concluded, through testing, that these controls are operating effectively, the material weakness described above will continue to exist.

Management will monitor the progress of the remediation plan and report regularly to the audit committee on the progress and results of the remediation plan, including the identification, status and resolution of internal control deficiencies.

### ***Changes in Internal Control over Financial Reporting***

During the quarter ended December 30, 2020, we implemented certain internal controls in connection with our remediation efforts described above. Except 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 2020, 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, 2020. 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, 2020, 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, because of the effect of the material weakness described below on the achievement of the objectives of the control criteria, Akebia Therapeutics, Inc. (the "Company") has not maintained effective internal control over financial reporting as of December 31, 2020, based on the COSO criteria.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management's assessment. We identified deficiencies in internal controls included within the Company's inventory process. Specifically, the Company did not maintain effective controls related to (i) the review of inventory reconciliations, (ii) the validation of the inventory costing and (iii) the periodic assessment of excess and obsolete inventory related reserves.

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, 2020 and 2019, 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, 2020, and the related notes. This material weakness was considered in determining the nature, timing and extent of audit tests applied in our audit of the 2020 consolidated financial statements, and this report does not affect our report dated February 25, 2021, which 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  
February 25, 2021

### **Item 9B. Other Information**

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 receive all royalties and sales milestones for vada dustat, 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. 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 \$45.0 million from HCR (net of certain transaction expenses) under the Royalty Agreement, and we are eligible to receive an additional \$15.0 million under the Royalty Agreement if specified sales milestones are achieved for vada dustat in the territory covered by the MTPC Agreement, subject to the satisfaction of certain customary conditions. We retain the right to receive all potential future regulatory milestones for vada dustat 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 us of an amount equal to the Aggregate Cap minus the aggregate amount of all Royalty Interest Payments actually received by HCR.

The Royalty Agreement requires us to take certain actions, including actions with respect to the Royalty Interest Payments, the MTPC Agreement, our agreement with MTPC for the commercial supply of vada dustat drug product, and our 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, we granted HCR a precautionary security interest in connection with the Royalty Interest Payments. This summary of the Royalty Agreement does not purport to be complete and is subject to, and qualified in its entirety by, the full text of the Royalty Agreement, a copy of which we plan to file as an exhibit to our Quarterly Report on Form 10-Q for the quarter ending March 31, 2021.

The foregoing information is included for the purpose of providing the disclosures required under "Item 1.01 – Entry into a Material Definitive Agreement," of Current Report on Form 8-K.

## **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 2021 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 2021 Annual Meeting of Stockholders and 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 2021 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 2021 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 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

## PART IV

### Item 15. Exhibits, 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 (Deficit)

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**	<a href="#">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, filed on June 28, 2018)</a>
2.2	<a href="#">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, filed on October 1, 2018)</a>
3.1	<a href="#">Ninth Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, filed on March 28, 2014)</a>
3.2	<a href="#">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, filed on June 9, 2020)</a>
3.3	<a href="#">Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K, filed on March 28, 2014)</a>
4.1	<a href="#">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)</a>
4.2	<a href="#">Fourth Amended and Restated Investors' Rights Agreement, dated March 5, 2014 (incorporated by reference to Exhibit 4.4 to the Company's 10-K for the year ending December 31, 2014 and filed on March 4, 2015)</a>
4.3#	<a href="#">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, filed on March 12, 2018)</a>
4.4#	<a href="#">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, filed on August 8, 2017)</a>
4.5	<a href="#">Common Stock Purchase Warrant between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q, filed on May 9, 2017)</a>
4.6*	<a href="#">Description of Registrant's Securities</a>
10.1†	<a href="#">Form of Director and Officer Indemnification Agreement (incorporated by reference to Exhibit 10.1 to the Company's Annual Report on Form 10-K, filed on March 12, 2018)</a>
10.2	<a href="#">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)</a>
10.3	<a href="#">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 10-K for the year ending December 31, 2014 and filed on March 4, 2015)</a>
10.4	<a href="#">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 10-K for the year ending December 31, 2015 and filed on March 14, 2016)</a>
10.5	<a href="#">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, filed on November 9, 2016)</a>
10.6	<a href="#">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 10-K for the year ending December 31, 2017, filed on March 12, 2018)</a>

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
10.7	<a href="#">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, filed on August 8, 2018)</a>
10.8*	<a href="#">Sixth Amendment to Office Lease Agreement Between CLPF-Cambridge Science Center, LLC and Akebia Therapeutics, Inc. dated November 30, 2020</a>
10.9	<a href="#">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, filed on March 1, 2017)</a>
10.10	<a href="#">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, filed on November 12, 2019)</a>
10.11†	<a href="#">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)</a>
10.12†	<a href="#">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)</a>
10.13†	<a href="#">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)</a>
10.14†	<a href="#">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 filed on August 10, 2020)</a>
10.15†	<a href="#">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)</a>
10.16†	<a href="#">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)</a>
10.17†	<a href="#">Amended and Restated Non-Employee Director Compensation Program, effective January 1, 2018 (incorporated by reference to Exhibit 10.13 to the Company's 10-K for the year ending December 31, 2017 and filed on March 12, 2018)</a>
10.18†	<a href="#">Amended and Restated Non-Employee Director Compensation Program, effective January 30, 2019 (incorporated by reference to Exhibit 10.31 to the Company's Annual Report on Form 10-K, filed on March 26, 2019)</a>
10.19†	<a href="#">Non-Employee Director Compensation Program, effective January 26, 2021</a>
10.20†	<a href="#">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)</a>
10.21†	<a href="#">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)</a>
10.22†	<a href="#">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, filed on January 25, 2019)</a>
10.23†	<a href="#">2014 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.30 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)</a>
10.24†	<a href="#">Amended and Restated 2014 Employee Stock Purchase Plan (incorporated by reference to Appendix A to the Company's Definitive Proxy Statement, filed with the Securities and Exchange Commission on April 26, 2019)</a>

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
10.25†	<a href="#"><u>Cash Incentive Plan (incorporated by reference to Exhibit 10.31 to the Company's Registration Statement on Form S-1/A (333-193969), filed on March 4, 2014)</u></a>
10.26†	<a href="#"><u>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, filed on March 12, 2018)</u></a>
10.27†	<a href="#"><u>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, filed on March 26, 2019)</u></a>
10.28†	<a href="#"><u>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)</u></a>
10.29†	<a href="#"><u>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)</u></a>
10.30†	<a href="#"><u>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, filed on March 21, 2003)</u></a>
10.31†	<a href="#"><u>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, filed on April 29, 2004)</u></a>
10.32†	<a href="#"><u>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, filed on August 9, 2006)</u></a>
10.33†	<a href="#"><u>Keryx Biopharmaceuticals, Inc. 2007 Incentive Plan, (incorporated by reference to Annex D to Keryx Biopharmaceuticals, Inc.'s Definitive Proxy Statement on Schedule 14A, filed on April 30, 2007)</u></a>
10.34†	<a href="#"><u>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, filed on May 27, 2016)</u></a>
10.35†	<a href="#"><u>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, filed on June 29, 2018)</u></a>
10.36†	<a href="#"><u>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, filed on November 9, 2016)</u></a>
10.37†	<a href="#"><u>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, filed on March 26, 2019)</u></a>
10.38†	<a href="#"><u>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, filed on May 27, 2016)</u></a>
10.39†	<a href="#"><u>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 for the quarter ended June 30, 2014, filed on August 7, 2014)</u></a>
10.40†	<a href="#"><u>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, filed on March 26, 2019)</u></a>
10.41†	<a href="#"><u>Master Consulting Services Agreement by and between the Company and Jason A. Amello, dated August 7, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on November 5, 2020)</u></a>
10.42#	<a href="#"><u>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, filed on August 11, 2015)</u></a>

Exhibit Number	Description of Exhibit
10.43#	<a href="#">Collaboration Agreement between Akebia Therapeutics, Inc. and Mitsubishi Tanabe Pharma Corporation, dated December 11, 2015 (incorporated by reference to Exhibit 10.29 to the Company's 10-K for the year ending December 31, 2015 and filed on March 14, 2016)</a>
10.44#	<a href="#">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, filed on November 8, 2017)</a>
10.45#	<a href="#">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 10-K for the year ending December 31, 2016 and filed on March 6, 2017)</a>
10.46#	<a href="#">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, filed on August 8, 2017)</a>
10.47#	<a href="#">Research and License Agreement between Akebia Therapeutics, Inc. and Janssen Pharmaceutica NV, dated February 9, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on May 9, 2017)</a>
10.48!	<a href="#">Amended and Restated License Agreement, dated April 8, 2019, by and between Akebia Therapeutics, Inc. and Vifor (International) Ltd. (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2019)</a>
10.49	<a href="#">Amended and Restated Controlled Equity Offering<sup>SM</sup> Sales Agreement, dated November 12, 2019, by and between Akebia Therapeutics, Inc. and Cantor Fitzgerald &amp; Co. (incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K, filed on November 12, 2019)</a>
10.50	Reserved
10.51	Reserved
10.52!	<a href="#">Second Amended and Restated License Agreement dated April 17, 2019, by and between Akebia Therapeutics, Inc. and Panion &amp; BF Biotech, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2019)</a>
10.53#	<a href="#">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, filed on November 7, 2017)</a>
10.54#	<a href="#">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 10.12 to Keryx Biopharmaceuticals, Inc.'s Annual Report on Form 10-K, filed on March 1, 2017)</a>
10.55#	<a href="#">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, filed on November 7, 2017)</a>
10.56#	<a href="#">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, filed on February 21, 2018)</a>
10.57*	<a href="#">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.</a>
10.58*	<a href="#">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.</a>

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
10.59*!	<a href="#">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.</a>
10.60#	<a href="#">Exclusive Distribution Agreement between Keryx Biopharmaceuticals, Inc. and Cardinal Health 105, Inc., dated October 16, 2014 and 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, filed on March 26, 2019)</a>
10.61#	<a href="#">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, filed on March 26, 2019)</a>
10.62!	<a href="#">Supply Agreement, dated as of April 9, 2019, by and between Akebia Therapeutics, Inc. and Esteve Química, S.A. (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q, filed on August 8, 2019)</a>
10.63!	<a href="#">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, filed on March 12, 2020)</a>
10.64!	<a href="#">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, filed on March 12, 2020)</a>
10.65!	<a href="#">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 filed on May 5, 2020)</a>
10.66!	<a href="#">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 filed on August 10, 2020)</a>
10.67!	<a href="#">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, filed on September 11, 2020)</a>
21.1*	<a href="#">List of Subsidiaries</a>
23.1*	<a href="#">Consent of Ernst &amp; Young LLP</a>
31.1*	<a href="#">Certification of Principal Executive Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended</a>
31.2*	<a href="#">Certification of Principal Financial Officer Required Under Rule 13a-14(a) of the Securities Exchange Act of 1934, as amended</a>
32.1*	<a href="#">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</a>
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

<b>Exhibit Number</b>	<b>Description of Exhibit</b>
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: February 25, 2021

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: February 25, 2021	By: <u>/s/ John P. Butler</u> John P. Butler <i>Director, President and Chief Executive Officer (Principal Executive Officer)</i>
Date: February 25, 2021	By: <u>/s/ David A. Spellman</u> David A. Spellman <i>Senior Vice President, Chief Financial Officer and Treasurer (Principal Financial Officer)</i>
Date: February 25, 2021	By: <u>/s/ Violetta Cotreau</u> Violetta Cotreau <i>Senior Vice President, Chief Accounting Officer (Principal Accounting Officer)</i>
Date: February 25, 2021	By: <u>/s/ Adrian Adams</u> Adrian Adams <i>Chairperson</i>
Date: February 25, 2021	By: <u>/s/ Mark J. Enyedy</u> Mark J. Enyedy <i>Director</i>
Date: February 25, 2021	By: <u>/s/ Steven C. Gilman</u> Steven C. Gilman <i>Director</i>
Date: February 25, 2021	By: <u>/s/ Maxine Gowen</u> Maxine Gowen <i>Director</i>
Date: February 25, 2021	By: <u>/s/ Michael T. Heffernan</u> Michael T. Heffernan <i>Director</i>
Date: February 25, 2021	By: <u>/s/ Michael Rogers</u> Michael Rogers <i>Director</i>
Date: February 25, 2021	By: <u>/s/ Cynthia Smith</u> Cynthia Smith <i>Director</i>
Date: February 25, 2021	By: <u>/s/ Myles Wolf</u> Myles Wolf <i>Director</i>
Date: February 25, 2021	By: <u>/s/ LeAnne M. Zumwalt</u> LeAnne M. Zumwalt <i>Director</i>

## DESCRIPTION OF CAPITAL STOCK

The following description of capital stock of Akebia Therapeutics, Inc. (“us,” “our,” “we” or the “Company”) is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, as amended, our amended and restated bylaws, and applicable provisions of Delaware corporate law. You should read our certificate of incorporation, as amended, and our amended and restated bylaws, which are incorporated by reference as Exhibit 3.1, Exhibit 3.2 and Exhibit 3.3, respectively, to the Annual Report on Form 10-K of which this Exhibit 4.6 is a part, for the provisions that are important to you.

### General

Our authorized capital stock consists of 350,000,000 shares of our common stock, par value \$0.00001 per share, and 25,000,000 shares of undesignated preferred stock, par value \$0.00001 per share.

### Common Stock

*Dividend Rights.* Subject to preferences that may apply to shares of preferred stock outstanding at the time, holders of outstanding shares of common stock are entitled to receive dividends out of assets legally available at the times and in the amounts as the Board of Directors may from time to time determine.

*Voting Rights.* Each outstanding share of common stock is entitled to one vote on all matters submitted to a vote of stockholders. Holders of shares of our common stock shall have no cumulative voting rights.

*Conversion or Redemption Rights.* Our common stock is neither convertible nor redeemable.

*Liquidation Rights.* Upon our liquidation, dissolution or winding up, the holders of our common stock will be entitled to receive pro rata our assets which are legally available for distribution, after payment of all debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then-outstanding shares of preferred stock.

*Rights and Preferences.* Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

### Preferred Stock

Under our certificate of incorporation, we are authorized to issue up to 25,000,000 shares of preferred stock at \$0.00001 par value per share. The preferred stock may be issued in one or more series, and the Board of Directors is expressly authorized (i) to fix the descriptions, powers, preferences, rights, qualifications, limitations and restrictions with respect to any series of preferred stock and (ii) to specify the number of shares of any series of preferred stock.

### Anti-Takeover Effects of Our Certificate of Incorporation and Our Bylaws

Our certificate of incorporation and bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the Board of Directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of our company unless such takeover or change in control is approved by the Board of Directors.

These provisions include:

*Classified Board.* Our certificate of incorporation provides that, subject to the special rights of the holders of any series of Preferred Stock to elect directors, our Board of Directors is divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our Board of Directors is elected each year. The classification of directors has the effect of making it more difficult for stockholders to change the composition of our Board. Our certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors shall be fixed exclusively pursuant to a resolution adopted by our Board of Directors.

*Action by Written Consent; Special Meetings of Stockholders.* Our certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our certificate of incorporation and the bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the Board of Directors pursuant to a resolution adopted by a majority of the total number of directors. Stockholders are not permitted to call a special meeting or to require the Board of Directors to call a special meeting.

*Removal of Directors.* Subject to the special rights of the holders of any series of Preferred Stock to elect directors, our certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our Board.

*Advance Notice Procedures.* Our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the Board of Directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the Board of Directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the bylaws do not give the Board of Directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of our company.

*Super Majority Approval Requirements.* The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. A majority vote of our Board of Directors or the affirmative vote of holders of at least 75% of the total votes of the outstanding shares of capital stock of our company entitled to vote with respect thereto, voting together as a single class, are required to amend, alter, change or repeal the bylaws. In addition, the affirmative vote of the holders of at least 85% of the total votes of the outstanding shares of capital stock of our company entitled to vote with respect thereto, voting together as a single class, are required to amend, alter, change or repeal, or to adopt any provisions inconsistent with, any of the provisions in our certificate of incorporation relating to decreasing the number of authorized shares of common stock, issuing or changing the number of authorized shares of preferred stock, the Board of Directors, limitation of director liability, meetings of stockholders, exclusive jurisdiction for certain actions and amendments to our certificate of incorporation and bylaws. This requirement of a supermajority vote to approve amendments to our bylaws and certificate of incorporation could enable a minority of our stockholders to exercise veto power over any such amendments.

*Authorized but Unissued Shares.* Our authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital and corporate acquisitions. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or

discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

*Exclusive Forum.* The certificate of incorporation provides that, subject to limited exceptions, and to the fullest extent permitted by law, 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 shareholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Under our certificate of incorporation, this exclusive forum provision will not apply to claims which 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 certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law and federal securities laws for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

### **Section 203 of the Delaware General Corporation Law**

We are subject to Section 203 of the Delaware General Corporation Law, or Section 203, which prohibits a Delaware corporation from engaging in business combinations with an interested stockholder. An interested stockholder is generally defined as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation or any entity or person affiliated with or controlling or controlled by such entity or person, or an interested stockholder. Section 203 provides that an interested stockholder may not engage in business combinations with the corporation for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the Board of Directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the Board of Directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines business combinations to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;

- any sale, lease, transfer, pledge or other disposition of 10% or more of the assets of the corporation to or with the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loss, advances, guarantees, pledges or other financial benefits by or through the corporation.

SIXTH AMENDMENT TO LEASE

This SIXTH AMENDMENT TO LEASE (this “**Amendment**”) is entered into as of November 30, 2020 (the “**Effective Date**”), by and between CLPF-CAMBRIDGE SCIENCE CENTER, LLC, a Delaware limited liability company (“**Landlord**”), and AKEBIA THERAPEUTICS, INC., a Delaware corporation (“**Tenant**”).

RECITALS

A. MA-Riverview/245 First Street, L.L.C. (the “**Original Landlord**”) and Tenant entered into that certain Office Lease Agreement dated as of December 3, 2013 (the “**Original Lease**”), as amended by that certain First Amendment to Lease dated December 15, 2014, that certain Second Amendment to Lease dated November 23, 2015, that certain Third Amendment to Lease dated July 25, 2016, that certain Fourth Amendment to Lease, dated May 1, 2017, and that certain Fifth Amendment to Lease dated April 9, 2018 (collectively, the “**Lease**”), respecting certain premises consisting of approximately 59,216 rentable square feet on the 11<sup>th</sup>, 12<sup>th</sup> and 14<sup>th</sup> floors of the office building (the “**Original Premises**”) located at 245 First Street, Cambridge, Massachusetts (the “**Building**”) and approximately 5,951 rentable square feet on the 1<sup>st</sup> floor of the adjacent lab building (the “**First Floor Premises**”) (collectively, the “**Premises**”), which buildings together comprise the Cambridge Science Center.

B. Landlord is the successor in interest to the Original Landlord.

C. Tenant has an appurtenant right to use, in common with others, the PH System Room (as defined in the Third Amendment to Lease) located in the Building, for which the Tenant pays the Tank Fee (as defined in the Third Amendment to Lease) to Landlord.

D. The First Floor Premises Term (as defined in the Third Amendment to Lease) is scheduled to expire on November 30, 2021.

E. Landlord and Tenant wish to enter into this Amendment to (i) extend the First Floor Premises Term, and (ii) amend certain other terms and conditions of the Lease.

NOW, THEREFORE, in consideration of the mutual covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant agree to amend the Lease as follows:

1. Recitals; Capitalized Terms. All of the foregoing recitals are true and correct. Unless otherwise defined herein, all capitalized terms used in this Amendment shall have the meaning ascribed to them in the Lease, and all references to the Lease or “this Lease” or “herein” or “hereunder” or similar terms or to any sections thereof shall mean the Lease, or such section thereof, as amended by this Amendment.

2. First Floor Premises Extension Term. The First Floor Premises Term is hereby extended for a period commencing on December 1, 2021 and expiring on January 31, 2025 (the “**Extended First Floor Premises Termination Date**”) on the terms and conditions set forth

below. All terms and provisions of the Lease, as amended hereby, shall apply to Tenant’s leasing of the First Floor Premises and during the First Floor Premises Term, except to the extent expressly provided otherwise in this Amendment.

3. Rent for the First Floor Premises Extension Term. Tenant shall have no obligation to pay Base Rent with respect to the First Floor Premises for the period from December 1, 2020 through January 31, 2021. Commencing on December 1, 2021, in addition to Base Rent payable for the Original Premises and Additional Rent due under the Lease, Tenant shall pay Base Rent to Landlord with respect to the First Floor Premises in the amount and on the schedule outlined in the following table:

RENTAL PERIOD	ANNUAL BASE RENT	MONTHLY PAYMENT
December 1, 2021 – November 30, 2022	\$581,710.25	\$48,475.85
December 1, 2022 - November 30, 2023	\$599,146.68	\$49,928.89
December 1, 2023 - November 30, 2024	\$617,118.70	\$51,426.56
December 1, 2024 - January 31, 2025	N/A	\$52,970.88

4. Tank Fee for the Extension Term. Commencing on December 1, 2021, in addition to Base Rent payable for the First Floor Premises, Tenant shall pay as Additional Rent, the Tank Fee in connection with its use of the PH System Room, to Landlord in the amount and on the schedule outline in the following table. Tenant shall have no obligation to pay the Tank Fee for the period from December 1, 2020 through January 31, 2021.

RENTAL PERIOD	ANNUAL TANK FEE	MONTHLY PAYMENT
December 1, 2021 - November 30, 2022	\$4,398.75	\$366.56
December 1, 2022 - November 30, 2023	\$4,530.60	\$377.55
December 1, 2023 - November 30, 2024	\$4,666.50	\$388.88
December 1, 2024 - January 31, 2025	N/A	\$400.55

5. First Floor Premises Contribution. Tenant intends to perform certain improvements to the First Floor Premises (“**Tenant’s First Floor Premises Work**”) subject to and in accordance with the provisions of Sections 1.B(ii) and 1.B(iii) of the Third Amendment to Lease, incorporated herein by reference. Landlord shall reimburse Tenant for certain costs incurred by Tenant with respect to Tenant’s First Floor Premises Work, subject to and in accordance with the terms and conditions of Sections 1.C and 1.D of the Third Amendment to Lease, incorporated herein by reference, except that:

- i. The “**Maximum Contribution**” shall be \$89,265.00;
- ii. The “**Outside Requisition Date**” shall be November 30, 2022;



iii. For purposes of this Section 5, “Tenant’s First Floor Premises Work” as used in Section 1 of the Third Amendment to Lease shall refer to “Tenant’s First Floor Premises Work” as defined in this Amendment;

iv. Landlord shall have no obligation to reimburse Tenant for the costs of a test fit plan;

v. Landlord shall receive a construction management fee equal to one percent (1%) of the Landlord’s First Floor Premises Contribution (as defined in the Third Amendment to Lease); and

vi. Section 1.D(iii) is hereby deleted in its entirety and replaced with the following: “Tenant shall be entitled to apply any unused portion of the Maximum Contribution towards Base Rent due hereunder.”

a. Extension Option. The First Floor Premises Extension Option set forth in Section 4 of the Third Amendment to Lease shall remain in full force and effect to further extend the First Floor Premises Term beyond the Extended First Floor Premises Termination Date set forth in this Amendment, except that (a) the First Floor Premises Option Term shall commence on February 1, 2025 and shall expire on September 11, 2026; and (b) Section 4.A(iii) of the Third Amendment to Lease shall be amended such that it shall be a condition that no more than twenty percent (20%) of the First Floor Premises is sublet (other than pursuant to a Business Transfer, as defined in Article 11 of the Lease) at the time that Tenant delivers its Extension Notice or at the time Tenant delivers its Acceptance Notice, if any.

b. Brokerage. Each party represents to the other that it has not dealt with any broker in connection with this Amendment other than CBRE. Tenant shall indemnify and hold Landlord harmless from and against any claim or claims for brokerage or other commissions relating to this Amendment asserted by any broker, agent or finder engaged by Tenant or with whom Tenant has dealt other than CBRE. Landlord shall indemnify and hold Tenant harmless from and against any claim or claims for brokerage or other commissions relating to this Amendment asserted by any broker, agent or finder engaged by Landlord or with whom Landlord has dealt. Any commission due in connection with this Amendment shall be paid by Landlord pursuant to a separate agreement between Landlord and CBRE.

c. Ratification. Except as expressly modified by this Amendment, the Lease shall remain in full force and effect, and as further modified by this Amendment, is expressly ratified and confirmed by the parties hereto. This Amendment shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, subject to the provisions of the Lease regarding assignment and subletting.

d. Governing Law; Interpretation and Partial Invalidity. This Amendment shall be governed and construed in accordance with the laws of the Commonwealth of Massachusetts. If any term of this Amendment, or the application thereof to any person or circumstances, shall to any extent be invalid or unenforceable, the remainder of this Amendment, or the application of such term to persons or circumstances other than those as to which it is invalid or unenforceable,

shall not be affected thereby, and each term of this Amendment shall be valid and enforceable to the fullest extent permitted by law. The titles for the paragraphs are for convenience only and are not to be considered in construing this Amendment. This Amendment contains all of the agreements of the parties with respect to the subject matter hereof, and supersedes all prior dealings between them with respect to such subject matter. No delay or omission on the part of either party to this Amendment in requiring performance by the other party or exercising any right hereunder shall operate as a waiver of any provision hereof or any rights hereunder, and no waiver, omission or delay in requiring performance or exercising any right hereunder on any one occasion shall be construed as a bar to or waiver of such performance or right on any future occasion.

e. Successors. This Amendment shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns.

f. Counterparts and Authority. This Amendment may be executed in multiple counterparts, each of which shall be deemed an original and all of which together shall constitute one and the same document. Landlord and Tenant each warrant to the other that the person or persons executing this Amendment on its behalf has or have authority to do so and that such execution has fully obligated and bound such party to all terms and provisions of this Amendment.

[Signature Pages Follow]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment as of the day and year first above written.

**LANDLORD:**

**CLPF-CAMBRIDGE SCIENCE CENTER, LLC,**  
a Delaware limited liability company

By: Clarion Lion Properties Fund Holdings, L.P.,  
a Delaware limited partnership,  
its Sole Member

By: CLPF-Holdings, LLC,  
a Delaware limited liability company,  
its General Partner

By: Clarion Lion Properties Fund Holdings REIT, LLC,  
a Delaware limited liability company,  
its Sole Member

By: Clarion Lion Properties Fund, LP,  
a Delaware limited partnership,  
its Managing Member

By: Clarion Partners LPF GP, LLC,  
a Delaware limited liability company,  
its General Partner

By: Clarion Partners, LLC,  
a New York limited liability company,  
its Sole Member

By: /s/ Brian Collins

Name: Brian Collins

Title: Authorized Signatory

**TENANT:**

**AKEBIA THERAPEUTICS, INC.,**  
a Delaware corporation

By: /s/ David Spellman

Name: David Spellman

Title: SVP, CFO and Treasurer

**AKEBIA THERAPEUTICS, INC.**  
**NON-EMPLOYEE**  
**DIRECTOR COMPENSATION PROGRAM**

**Effective January 26, 2021**

Non-employee members of the Board of Directors (the “**Board**”) of Akebia Therapeutics, Inc. (the “**Company**”) shall be eligible to receive cash and equity compensation as set forth in this Non-Employee Director Compensation Program (this “**Program**”). The cash and equity compensation described in this Program shall be paid or be made, as applicable, automatically and without further action of the Board, to each member of the Board who is not an employee of the Company or any parent or subsidiary of the Company (each, a “**Non-Employee Director**”) who is eligible to receive such cash or equity compensation, unless such Non-Employee Director declines the receipt of such cash or equity compensation by written notice to the Company. This Program shall remain in effect until it is revised or rescinded by further action of the Board. This Program shall be reviewed by the Board periodically and may be amended, modified or terminated by the Board at any time in its sole discretion and nothing herein should be construed as a guarantee to any Non-Employee Director of any particular level of cash or equity compensation. The terms and conditions of this Program shall supersede any prior cash and/or equity compensation arrangements for service as a member of the Board between the Company and any of its Non-Employee Directors. This Program shall become effective on the date set forth above (the “**Effective Date**”).

1. Cash Compensation.

(a) Annual Retainers. Each Non-Employee Director shall be eligible to receive an annual retainer of \$45,000 for service on the Board.

(b) Additional Annual Retainers. In addition to the annual retainer payable pursuant to Section 1(a) above, a Non-Employee Director shall be eligible to receive the following annual retainers:

(i) Chairperson of the Board. A Non-Employee Director serving as Chairperson of the Board shall be eligible to receive an additional annual retainer of \$35,000 for such service; provided, that, in the event that a Non-Employee Director is one of two concurrently serving Chairpersons of the Board, the additional annual retainer payable to such Non-Employee Director pursuant to this Section 1(b)(i) shall be \$17,500.

(ii) Audit Committee. A Non-Employee Director serving as Chairperson of the Audit Committee of the Board (the “Audit Committee”) shall be eligible to receive an additional annual retainer of \$20,000 for such service. A Non-Employee Director

serving as a member of the Audit Committee (other than the Chairperson of the Audit Committee) shall be eligible to receive an additional annual retainer of \$10,000 for such service.

(iii) Compensation Committee. A Non-Employee Director serving as Chairperson of the Compensation Committee of the Board (the "Compensation Committee") shall be eligible to receive an additional annual retainer of \$15,000 for such service. A Non-Employee Director serving as a member of the Compensation Committee (other than the Chairperson of the Compensation Committee) shall be eligible to receive an additional annual retainer of \$7,500 for such service.

(iv) Nominating and Corporate Governance Committee. A Non-Employee Director serving as Chairperson of the Nominating and Corporate Governance Committee of the Board (the "NCG Committee") shall be eligible to receive an additional annual retainer of \$10,000 for such service. A Non-Employee Director serving as a member of the NCG Committee (other than the Chairperson of the NCG Committee) shall be eligible to receive an additional annual retainer of \$5,000 for such service.

(v) Research and Development Committee. A Non-Employee Director serving as Chairperson of the Research and Development Committee of the Board (the "R&D Committee") shall be eligible to receive an additional annual retainer of \$10,000 for such service. A Non-Employee Director serving as a member of the R&D Committee (other than the Chairperson of the R&D Committee) shall be eligible to receive an additional annual retainer of \$5,000 for such service.

(c) Payment of Retainers. The annual retainers described in Sections 1(a) and 1(b) shall be earned on a quarterly basis based on a calendar quarter and shall be paid in cash by the Company in arrears not later than the fifteenth day following the end of each calendar quarter. In the event a Non-Employee Director does not serve as a Non-Employee Director, or in the applicable positions described in Section 1(b), for an entire calendar quarter, the retainer paid to such Non-Employee Director shall be prorated for the portion of such calendar quarter actually served as a Non-Employee Director, or in such position, as applicable.

2. Equity Compensation. Non-Employee Directors shall be granted the equity awards described below. Each award described below shall be granted under and shall be subject to the terms and provisions of the Company's 2014 Incentive Plan, as amended, or any other successor Company equity incentive plan under which awards are permitted to be made to Non-Employee Directors (the "**Equity Plan**") and (i) for option awards, a non-qualified stock option award agreement, including attached exhibits, in substantially the form of award agreement applicable to Non-Employee Directors most recently approved by the Board and/or the Compensation Committee, as applicable, and (ii) for restricted stock unit awards, a restricted stock unit award agreement, including attached exhibits, in substantially the form of award agreement applicable to Non-Employee Directors most recently approved by the Board and/or the Compensation Committee, as applicable. All applicable terms of the Equity Plan apply to this Program as if fully set forth herein. For the avoidance of doubt, if there is any conflict between the terms of

the Equity Plan (including the applicable award agreements thereunder) and this Program, the Equity Plan (including the applicable award agreements thereunder) shall control.

(a) Initial Awards. Each Non-Employee Director who is initially elected or appointed to the Board after the Effective Date shall be eligible to receive, on the date of such initial election or appointment, an option to purchase 80,200 shares of the Company's common stock (subject to adjustment as provided in the Equity Plan). The awards described in this Section 2(a) shall be referred to as "**Initial Awards**." No Non-Employee Director shall be granted more than one Initial Award.

(b) Subsequent Awards. A Non-Employee Director who (i) has been serving on the Board for at least six months as of the date of any annual meeting of the Company's stockholders after the Effective Date and (ii) will continue to serve as a Non-Employee Director immediately following such meeting, shall be automatically granted, on the date of such annual meeting, an option to purchase 20,100 shares of the Company's common stock (subject to adjustment as provided in the Equity Plan) and 13,700 restricted stock units of the Company. The option awards described in this Section 2(b) shall be referred to as "**Subsequent Options**", the restricted stock unit awards described in this Section 2(b) shall be referred to as "**Subsequent RSUs**", and the Subsequent Options and Subsequent RSUs shall together be referred to as the "**Subsequent Awards**." For the avoidance of doubt, a Non-Employee Director elected for the first time to the Board at an annual meeting of the Company's stockholders shall only receive an Initial Award in connection with such election, and shall not receive any Subsequent Award on the date of such meeting as well.

(c) Termination of Service of Employee Directors. Members of the Board who are employees of the Company or any parent or subsidiary of the Company who subsequently terminate their service with the Company and any parent or subsidiary of the Company and remain on the Board will not receive an Initial Award pursuant to Section 2(a) above, but to the extent that they are otherwise eligible, will be eligible to receive, after termination from service with the Company and any parent or subsidiary of the Company, Subsequent Awards as described in Section 2(b) above.

(d) Terms of Awards Granted to Non-Employee Directors.

(i) Purchase Price. The per share exercise price of each option granted to a Non-Employee Director shall equal the fair market value (as determined pursuant to the Equity Plan) of a share of the Company's common stock on the date the option is granted.

(ii) Vesting. Each Initial Award shall vest and become exercisable in accordance with the following schedule, subject to the Non-Employee Director remaining in continuous Employment (as such term is defined in the Equity Plan) through each such vesting date: 33 1/3% of the Initial Award shall vest on the one-year anniversary of the date of grant and 66 2/3% shall vest ratably on the first day of each calendar quarter between the one-year anniversary of the date of grant and the third anniversary of the date of grant. Each Subsequent Option shall vest and become exercisable in full on the first anniversary of the date of grant subject to the Non-Employee Director remaining in continuous Employment (as such term is

defined in the Equity Plan) through such vesting date. Each Subsequent RSU shall vest in full on the first anniversary of the date of grant subject to the Non-Employee Director remaining in continuous Employment (as such term is defined in the Equity Plan) through such vesting date.

(iii) Term. The term of each option granted to a Non-Employee Director shall be ten (10) years from the date the option is granted.

3. Reimbursements. The Company shall reimburse each Non-Employee Director for all reasonable, documented, out-of-pocket travel and other business expenses incurred by such Non-Employee Director in the performance of such Non-Employee Director's duties to the Company in accordance with the Company's applicable expense reimbursement policies and procedures, as in effect from time to time. To the extent that any reimbursement under this Program provides for a deferral of compensation under Section 409A of the Internal Revenue Code of 1986, as amended: (a) the amount eligible for reimbursement in one calendar year may not affect the amount eligible for reimbursement in any other calendar year; (b) the right to reimbursement is not subject to liquidation or exchange for another benefit; and (c) any such reimbursement of an expense must be made on or before the last day of the calendar year following the calendar year in which the expense was incurred.

**AMENDMENT NO. 1 TO  
MASTER MANUFACTURING SERVICES AND SUPPLY AGREEMENT**

This Amendment No. 1 to Master Manufacturing Services and Supply Agreement (“Amendment No. 1”) is made effective and entered into on December 21, 2020 (the “Amendment Effective Date”) by and between **Siegfried Evionnaz SA**, with principal offices located at Route du Simplon 1, 36, 1902 Evionnaz, Switzerland (together with its Affiliates and subsidiaries “Vendor”); and **Keryx Biopharmaceuticals, Inc.**, with its offices at 245 First Street, Cambridge, Massachusetts, USA 02142 (“Keryx”).

WHEREAS, Vendor and Keryx entered into a Master Manufacturing Services and Supply Agreement dated December 20, 2017 (“Agreement”) under which Vendor manufactures Product for purchase by Keryx; and

WHEREAS, on December 12, 2018, Keryx merged with Akebia Therapeutics, Inc. (“Akebia”) and, pursuant to such merger, Akebia assumed all of Keryx’s rights and obligations under the Agreement. Keryx continues to operate as a wholly owned subsidiary of Akebia, and Akebia is an Affiliate of Keryx; and

WHEREAS, Vendor and Keryx wish to amend the Agreement as herein provided.

NOW THEREFORE, Vendor and Keryx hereto mutually agree as follows:

1. The text of Section 16.1 of the Agreement is be deleted and is hereby replaced by the following:

16.1 The term of this Agreement (the “Term”) shall commence as of the Agreement Date and, subject to earlier termination in accordance with the provisions of this Section 16, shall end on December 31, 2021. Unless terminated by one of the Parties with at least eleven (11) months’ prior written notice to the other Party before the end of the original or renewal term then in effect, this Agreement shall automatically renew for subsequent terms of one (1) year.

2. For the purpose of this Amendment No. 1, the defined terms used herein shall have the same meaning as those used in the Agreement, unless otherwise specified in this Amendment No. 1.
3. Except as provided for in this Amendment No. 1, all other terms and conditions of the Agreement shall remain in full force and effect.
4. The governing law and jurisdiction applicable to the Agreement shall apply to this Amendment No. 1.

*[Signature page follows]*



**IN WITNESS WHEREOF**, Vendor and Keryx hereto have caused this Amendment No. 1 to be executed by their duly authorized representatives as of the date first above written.

Signed on behalf of Siegfried Evionnaz SA    Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ Marianne Spane                      By: /s/ Michel Dahan

Name: Marianne Spane                      Name: Michel Dahan

Date: 21/12/2020                              Date: December 21, 2020

Signed on behalf of Siegfried Evionnaz SA

By: /s/ Luca Parlanti

Name: Luca Parlanti

Date: 21/12/2020

**AMENDMENT NO. 2 TO  
MASTER MANUFACTURING SERVICES AND SUPPLY AGREEMENT**

This Amendment No. 2 to Master Manufacturing Services and Supply Agreement (“Amendment No. 2”) is made effective and entered into on January 29, 2021 (the “Amendment Effective Date”) by and between **Siegfried Evionnaz SA**, with principal offices located at Route du Simplon 1, 36, 1902 Evionnaz, Switzerland (together with its Affiliates and subsidiaries “Vendor”); and **Keryx Biopharmaceuticals, Inc.**, with its offices at 245 First Street, Cambridge, Massachusetts, USA 02142 (“Keryx”).

WHEREAS, Vendor and Keryx entered into a Master Manufacturing Services and Supply Agreement dated December 20, 2017 (“Agreement”) under which Vendor manufactures Product for purchase by Keryx; and

WHEREAS, on December 12, 2018, Keryx merged with Akebia Therapeutics, Inc. (“Akebia”) and, pursuant to such merger, Akebia assumed all of Keryx’s rights and obligations under the Agreement. Keryx continues to operate as a wholly owned subsidiary of Akebia, and Akebia is an Affiliate of Keryx; and

WHEREAS, Vendor and Keryx wish to amend the Agreement as herein provided.

NOW THEREFORE, Vendor and Keryx hereto mutually agree as follows:

1. The text of Section 16.1 of the Agreement is be deleted and is hereby replaced by the following:

16.1 The term of this Agreement (the “Term”) shall commence as of the Agreement Date and, subject to earlier termination in accordance with the provisions of this Section 16, shall end on December 31, 2021. Unless terminated by one of the Parties on or before February 11, 2021 by providing prior written notice to the other Party, or, for any subsequent terms, with at least twelve (12) months prior written notice, this Agreement shall automatically renew for subsequent terms of one (1) year.

2. For the purpose of this Amendment No. 2, the defined terms used herein shall have the same meaning as those used in the Agreement, unless otherwise specified in this Amendment No. 2.
3. Except as provided for in this Amendment No. 2, all other terms and conditions of the Agreement shall remain in full force and effect.
4. The governing law and jurisdiction applicable to the Agreement shall apply to this Amendment No. 2.

*[Signature page follows]*

**IN WITNESS WHEREOF**, Vendor and Keryx hereto have caused this Amendment No. 2 to be executed by their duly authorized representatives as of the date first above written.

Signed on behalf of Siegfried Evionnaz SA    Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ Luca Parlanti                      By: /s/ Michel Dahan

Name: Luca Parlanti                      Name: Michel Dahan

Date: 29/01/2021                      Date: January 29, 2021

Signed on behalf of Siegfried Evionnaz SA

By: /s/ Marianne Spane

Name: Marianne Spane

Date: 29/01/2021

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

**AMENDMENT NO. 3 TO  
MASTER MANUFACTURING SERVICES AND SUPPLY AGREEMENT**

This Amendment No. 3 to Master Manufacturing Services and Supply Agreement (“Amendment No. 3”) is made effective and entered into on February 11, 2021 (the “Amendment Effective Date”) by and between **Siegfried Evionnaz SA**, with principal offices located at Route du Simplon 1, 36, 1902 Evionnaz, Switzerland (together with its Affiliates and subsidiaries “Vendor”); and **Keryx Biopharmaceuticals, Inc.**, with its offices at 245 First Street, Cambridge, Massachusetts, USA 02142 (“Keryx”).

WHEREAS, Vendor and Keryx entered into a Master Manufacturing Services and Supply Agreement dated December 20, 2017, as amended (“Agreement”) under which Vendor manufactures Product for purchase by Keryx; and

WHEREAS, on December 12, 2018, Keryx merged with Akebia Therapeutics, Inc. (“Akebia”) and, pursuant to such merger, Akebia assumed all of Keryx’s rights and obligations under the Agreement. Keryx continues to operate as a wholly owned subsidiary of Akebia, and Akebia is an Affiliate of Keryx; and

WHEREAS, the Parties wish to amend the Agreement as herein provided;

NOW THEREFORE, the Parties hereto mutually agree as follows:

1. For the purpose of this Amendment No. 3, the defined terms used herein shall have the same meanings as those used in the Agreement, unless otherwise specified in this Amendment No. 3.
2. Effective as of the Amendment Effective Date, section 3.5 of the Agreement shall be deleted and replaced by the following:

3.5 Keryx will have the obligation to purchase minimum annual quantities of the Product at the Product Price as set forth in **Attachment B** during the Term of the Agreement (the “Minimum Annual Purchase Obligation”). The [\*\*] Minimum Annual Purchase Obligation [\*\*] and the Product Price are set forth in **Attachment B**. In the event that Vendor is [\*\*] for the delivery of Product pursuant to a binding Order for a given calendar year during the Term [\*\*], Vendor shall provide a regular [\*\*] updated production schedule (“Updated Schedule”) [\*\*] *provided that* Vendor may not provide an Updated Schedule for a given calendar year [\*\*] (an “Order Extension”).

3. Effective as of the Amendment Effective Date, section 3.10 of the Agreement shall be deleted and replaced by the following:

3.10 Vendor shall [\*\*] Keryx for Product upon Vendor Product Release (as defined in Section 6.1.3). Transfer from Vendor to Keryx of title and risk of loss for Product shall occur [\*\*]. Vendor shall procure and maintain, as set forth under Section 12 of this Agreement, at its sole cost and expense, general liability insurance coverage against partial or complete loss of the [\*\*], covering claims that may arise until such time the Invoiced Product is delivered to Keryx. Delivery of [\*\*], following receipt by Siegfried of a completed authorization to deliver form from Keryx in accordance with Section 6.1.3

below. Keryx assumes all responsibilities and liability arising out of the transport, storage, handling and use of the Product after delivery by Vendor to Keryx.

4. Effective as of the Amendment Effective Date, section 6.1.3 of the Agreement shall be deleted and replaced by the following:

6.1.3 For each Batch, Vendor will release Product against the Specifications and make available to Keryx a complete and accurate copy of the Batch records, containing all of the documentation and information set forth in **Attachment F** (collectively, the “Batch Documentation”) for such Batch (“Vendor Product Release”). Keryx will respond promptly to Vendor (no later than [\*\*]) after notice of Vendor Product Release and will provide Vendor with either (i) an authorization to deliver form or (ii) notification of rejection for non-compliance with the Specifications. If Keryx has determined that the Batch does not comply with the Specifications, the Parties shall proceed according to Sections 6.1.23 and 6.1.24 herein. Upon reasonable request, Vendor will also deliver to Keryx all Manufacturing Records, and other supporting documentation in the possession or under the control of Vendor relating to the manufacture of each Batch of Product (or any intermediate or component of Product).

If Vendor has provided the requisite documentation specified in this Section 6.1.3 and Keryx [\*\*], the Batch shall be deemed authorized to deliver by Keryx, provided that Keryx still retains its rights of rejection as specified in Section 6.1.22. Any scope changes to the release requirements or quality requirements and associated impact(s), including impacts to costs, will be reviewed and assessed prior to implementation, and in all cases subject to the prior written approval of Keryx.

5. Effective as of the Amendment Effective Date, the text of Section 16.1 shall be deleted and replaced by the following:

a. **Term.**

16.1.1 The term of this Agreement (the “Term”) shall commence as of the Agreement Date and, subject to earlier termination in accordance with the provisions of this Section 16, shall end on December 31, 2022 unless otherwise agreed by the Parties. Notwithstanding the foregoing, Keryx may elect to extend the Term through December 31, 2023 with written notice sent at least twelve (12) months prior to the expiry of the Term, in accordance with Section 22 herein. In the event of such an election by Keryx, Keryx’s Minimum Annual Purchase Obligation for 2023 set forth in **Attachment B** shall apply. For the avoidance of doubt, expiration of the Term in accordance with this Section 16.1.1 shall not relieve Keryx of its responsibilities to pay any undisputed invoices issued by Vendor for Product or other Services performed in accordance with Section 3 of the Agreement.

16.1.2 In the event there is an Order Extension in accordance with Section 3.5 and the Term would have otherwise expired in accordance with Section 16.1.1, subject to Sections 16.2-16.5, the Term shall be automatically extended for the period of the Order Extension (an “Automatic Term Extension”), *provided that* an Automatic Term Extension whereby the Term extends into calendar year 2023 shall not obligate Keryx to exercise its right to extend the Term through December 31, 2023 in accordance with Section 16.1.1, nor shall it obligate Keryx to purchase the Minimum Annual Purchase Obligation for 2023 set forth in **Attachment B**.

6. Effective as of the Amendment Effective Date, a new Section 16.8 is hereby added to the Agreement as follows:

16.8 **Removal of [\*\*] Manufacturing Facility.**

16.8.1 Notwithstanding any other term in the Agreement, including the Minimum Annual Purchase Obligation detailed in **Attachment B**, as of [\*\*] (as such date may be extended in accordance with Section 16.8.2, the “[\*\*] Removal Date”), the [\*\*] Manufacturing Facility will be removed as a Manufacturing Facility under this Agreement. Removal of the [\*\*] Manufacturing Facility pursuant to this Section 16.8.1 shall, as of the [\*\*] Removal Date, eliminate Keryx’s Minimum Annual Purchase Obligation, Keryx’s Forecasting obligations, Vendor’s Operational Capacity obligations and other obligations of Vendor under this Agreement associated with the [\*\*] Manufacturing Facility (except (i) Vendor’s obligation to maintain any Product on stability studies and (ii) any obligations that are arising out of provisions deemed to survive the expiration or termination of this Agreement as set forth under Section 16.7 of this Agreement), and shall render the [\*\*] Manufacturing Facility as [\*\*] under this Agreement. For the avoidance of doubt, the foregoing removal of the [\*\*] Manufacturing Facility as a Manufacturing Facility under this Agreement shall not relieve Keryx of its responsibilities to pay any undisputed invoices issued by Vendor for Product or other Services performed, in accordance with Section 3 of the Agreement.

16.8.2 In the event there is an Order Extension in accordance with Section 3.5 with respect to Product to be delivered under Keryx’s [\*\*] for the [\*\*] Manufacturing Facility, the [\*\*] Removal Date shall be automatically extended for the period of the Order Extension.

7. Effective as of the Amendment Effective Date, **Attachment A** (Expansion Services and Operational Capacity) of the Agreement is hereby deleted in its entirety and replaced with the text of Exhibit 1 hereto.
8. Effective as of the Amendment Effective Date, the text of **Attachment B** (Product Price) of the Agreement is hereby deleted in its entirety and replaced with the text of Exhibit 2 hereto.
9. Effective January 23, 2020, **Attachment D** (Specifications) of the Agreement is hereby deleted in its entirety and replaced with the text of Exhibit 3 hereto.
10. Effective as of the Amendment Effective Date, **Attachment F** (Batch Documentation) is hereby added to the Agreement with the text of Exhibit 4 hereto.
11. From and after this Amendment Effective Date, all references in the Agreement to “this Agreement,” “hereof,” “herein,” and similar words or phrases shall mean and refer to the Agreement as amended by this Amendment No. 3.
12. Except as provided for in this Amendment No. 3, all other terms and conditions of the Agreement shall remain in full force and effect.
13. The governing law and jurisdiction applicable to the Agreement shall apply to this Amendment No. 3.

*[Signature Page to Follow]*

**IN WITNESS WHEREOF**, the Parties hereto have caused this Amendment No. 3 to be executed by their duly authorized representatives as of the date first above written.

Signed on behalf of Siegfried Evionnaz SA      Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ Marianne Spane                      By: /s/ John Butler

Name: Marianne Spane                      Name: John Butler, Authorized Signatory,  
Chief Executive Officer, Akebia Therapeutics, Inc.

Date: 11-Feb-2021                              Date: February 11, 2021

EVP Global BD, Marketing and Sales

Signed on behalf of Siegfried Evionnaz SA      Signed on behalf of Keryx Biopharmaceuticals, Inc.

By: /s/ Luca Parlanti                              By: /s/ David Spellman

Name: Luca Parlanti                              Name: David Spellman, Authorized Signatory,  
Chief Financial Officer, Akebia Therapeutics, Inc.

Date: 11-Feb-2021                              Date: February 11, 2021

Head of Exclusive Sales DS

**EXHIBIT 2**

**ATTACHMENT B – PRODUCT PRICE AND MINIMUM ANNUAL PURCHASE OBLIGATION**

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## SUBSIDIARIES OF THE REGISTRANT

Name	Jurisdiction of Organization
Akebia Therapeutics Securities Corporation	Massachusetts
Akebia Europe Limited	Ireland
Keryx Biopharmaceuticals, Inc.	Delaware
ACCESS Oncology, Inc.	Delaware
AOI Pharma, Inc.	Delaware
AOI Pharmaceuticals, Inc.	Delaware
Online Collaborative Oncology Group, Inc.	Delaware
Accumin Diagnostics, Inc.	Delaware
Neryx Biopharmaceuticals, Inc.	Delaware
Keryx Biopharma UK Ltd.	United Kingdom

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the following Registration Statements:

- (1) Registration Statement (Form S-3 No. 333-223585) of Akebia Therapeutics, Inc.,
- (2) 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.,
- (3) 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.,
- (4) Registration Statement (Form S-8 No. 333-216475) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,
- (5) Registration Statement (Form S-8 No. 333-222728) pertaining to the 2014 Incentive Plan and the 2016 Inducement Award Program of Akebia Therapeutics, Inc.,
- (6) Registration Statement (Form S-4 No. 333-227622) of Akebia Therapeutics, Inc.,
- (7) 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.,
- (8) Registration Statement (Form S-8 No. 333-229366) pertaining to the 2014 Incentive Plan, the 2014 Employee Stock Purchase Plan, and the Inducement Grants (January 2018 – December 2018) of Akebia Therapeutics, Inc.,
- (9) Registration Statement (Form S-8 No. 333-233140) pertaining to the amended and restated 2014 Employee Stock Purchase Plan of Akebia Therapeutics, Inc.,
- (10) 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., and
- (11) 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.,

of our reports dated February 25, 2021, 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, 2020.

/s/ Ernst & Young LLP

Boston, Massachusetts  
February 25, 2021

**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: February 25, 2021

By: /s/ John P. Butler

John P. Butler  
President, Chief Executive Officer and Director  
(Principal Executive Officer)

**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: February 25, 2021

By: /s/ David A. Spellman

David A. Spellman  
Senior Vice President, Chief Financial Officer  
and Treasurer  
(Principal Financial Officer)

**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, 2020 (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: February 25, 2021

By: /s/ John P. Butler

John P. Butler  
President, Chief Executive Officer and Director  
(Principal Executive Officer)

Date: February 25, 2021

By: /s/ David A. Spellman

David A. Spellman  
Senior Vice President, Chief Financial Officer  
and Treasurer  
(Principal Financial Officer)