

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2022  
OR

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

FOR THE TRANSITION PERIOD FROM TO  
COMMISSION FILE NUMBER 001-36485



**ARDELYX, INC.**

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE  
(STATE OR OTHER JURISDICTION OF  
INCORPORATION OR ORGANIZATION)

26-1303944  
(I.R.S. EMPLOYER  
IDENTIFICATION NO.)

400 FIFTH AVE., SUITE 210, WALTHAM, MASSACHUSETTS 02451  
(ADDRESS OF PRINCIPAL EXECUTIVE OFFICES, INCLUDING ZIP CODE)  
(510) 745-1700  
(REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE)

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 \$0.0001 per share	ARDX	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 type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Small reporting company	<input checked="" 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.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

The aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2022, based on the last reported sales price of the Registrant's common stock on the Nasdaq Global Market of \$0.59 per share was \$89,227,062.

The number of shares of Registrant's Common Stock outstanding as of February 28, 2023, was 206,492,664.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the Registrant's Definitive Proxy Statement for its 2023 Annual Meeting of Stockholders, which will be filed with the Commission within 120 days of December 31, 2022, the close of the Registrant's 2022 fiscal year, are incorporated by reference into Part III of this Report.

## NOTE REGARDING FORWARD-LOOKING STATEMENTS

Unless the context requires otherwise, in this Annual Report on Form 10-K the terms “Ardelyx”, “we,” “us,” “our” and “the Company” refer to Ardelyx, Inc.

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “continue,” “could,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “potential,” “positioned,” “seek,” “should,” “target,” “will,” “would,” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our expectations regarding the timing of the resubmission of the new drug application (“NDA”) for XPHOZAH<sup>®</sup> (tenapanor) for the control of serum phosphorus in adult patients with chronic kidney disease patients (“CKD”) on dialysis to the U.S. Food and Drug Administration (“FDA”);
- our expectations regarding the development of a label for the commercialization of XPHOZAH and our belief regarding what indication may be included in such a label;
- our expectations regarding the potential for FDA approval for the NDA for XPHOZAH;
- our plans to address our operating cash flow requirements with our current cash and short-term investments, cash generated from the sales of IBSRELA<sup>®</sup>, and if approved, sales of XPHOZAH, the potential receipt of anticipated milestone payments from our collaboration partners, the potential receipt of anticipated payments from our Japanese collaboration partner under the second amendment to our License Agreement, with additional financing sources and through the implementation of cash preservation activities to reduce or defer discretionary spending;
- our plans with respect to RDX013 and RDX020;
- estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital; and
- other risks and uncertainties, including those under the caption “Risk Factors.”

We have based these forward-looking statements largely on management’s current expectations, estimates, forecasts and projections about our business and the industry in which we operate and management’s beliefs and assumptions, and these forward-looking statements are not guarantees of future performance or development and involve known and unknown risks, uncertainties and other factors that are in some cases beyond our control. Factors that could cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those more fully described in the “ITEM 1A. RISK FACTORS” section and elsewhere in this Annual Report on Form 10-K. Except as required by law, we assume no obligation to update any forward-looking statement publicly, or to revise any forward-looking statement to reflect events or developments occurring after the date of this Annual Report on Form 10-K, even if new information becomes available in the future. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in any such forward-looking statement.

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## SUMMARY OF PRINCIPAL RISKS ASSOCIATED WITH OUR BUSINESS

The principal risks and uncertainties affecting our business include the following:

- We have incurred significant losses since our inception and will incur losses in the future, which makes it difficult for us to assess our future viability; although our financial statements have been prepared on a going concern basis, our current level of cash, cash equivalents and short-term investments alone is not sufficient to meet our operating plans for the next twelve months, raising substantial doubt regarding our ability to continue as a going concern.
- We will require additional financing for the foreseeable future as we invest in the commercialization of IBSRELA, and prepare for and commercialize XPHOZAH in the U.S., if approved. The inability to access necessary capital when needed on acceptable terms, or at all, could force us to reduce our efforts to commercialize IBSRELA or, delay or limit the commercialization of XPHOZAH, if approved.
- We have generated limited revenue from product sales and may never be profitable.
- We are substantially dependent on the successful commercialization of IBSRELA, and there is no guarantee that we will achieve sufficient market acceptance for IBSRELA; secure adequate coverage and reimbursement for IBSRELA; or generate sufficient revenue from product sales of IBSRELA.
- We are pursuing regulatory approval for XPHOZAH. There can be no assurances that we will be successful in obtaining such regulatory approval.
- Even if we are successful in obtaining regulatory approval for XPHOZAH, there is no guarantee that we will achieve sufficient market acceptance for XPHOZAH; secure adequate coverage and reimbursement for XPHOZAH; or generate sufficient revenue from product sales of XPHOZAH.
- IBSRELA and/or, if approved and commercialized, XPHOZAH, may cause undesirable side effects or have other properties that could limit the commercial success of the product.
- Third-party payor coverage and reimbursement status of newly-commercialized products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for IBSRELA and, if approved, for XPHOZAH could limit our ability to market those products and decrease our ability to generate revenue.
- We rely completely on third parties to manufacture IBSRELA and XPHOZAH. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties or are otherwise unable to manufacture sufficient quantities to meet demand, our commercialization of IBSRELA and, if approved and commercialized, of XPHOZAH, and our future development efforts for tenapanor may be materially harmed.
- Our operating activities may be restricted as a result of covenants related to the indebtedness under our loan and security agreement and we may be required to repay the outstanding indebtedness in an event of default, which could have a materially adverse effect on our business.

The summary risk factors described above should be read together with the text of the full risk factors below in the section entitled “Risk Factors” and the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the U.S. Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not precisely known to us or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations, and future growth prospects.

### NOTE REGARDING TRADEMARKS

ARDELYX®, IBSRELA®, and XPHOZAH® are trademarks of Ardelyx. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

**ARDELYX, INC.**  
**FORM 10-K FOR THE FISCAL YEAR ENDED December 31, 2022**  
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## ITEM 1. BUSINESS

### Overview

We are a biopharmaceutical company founded with a mission to discover, develop and commercialize innovative, first-in-class medicines that meet significant unmet medical needs. We developed a unique and innovative platform that enabled the discovery of new biological mechanisms and pathways to develop potent, and efficacious therapies that minimize the side effects and drug-drug interactions frequently encountered with traditional, systemically absorbed medicines. The first molecule we discovered and developed was tenapanor, a targeted, first-in-class, oral, small molecule therapy. Tenapanor, branded as IBSRELA<sup>®</sup>, is approved in the U.S. for the treatment of adults with irritable bowel syndrome with constipation ("IBS-C"). Tenapanor is in development for the control of serum phosphorus in adult patients with chronic kidney disease ("CKD") on dialysis under the brand name XPHOZAH<sup>®</sup>. We also have a developmental stage asset, RDX013, for adult CKD and/or heart failure patients with hyperkalemia, or elevated serum potassium, and a discovery stage asset, RDX020, for adult CKD patients with metabolic acidosis, a serious electrolyte disorder.

Since commencing operations in October 2007, substantially all our efforts have been dedicated to our research and development ("R&D") activities, including developing tenapanor and developing our proprietary drug discovery and design platform. We realized our first product sales of IBSRELA (tenapanor) in March 2022. As of December 31, 2022, we had an accumulated deficit of \$780.1 million.

We expect to continue to incur substantial operating losses for the foreseeable future as we invest in the commercialization of IBSRELA, seek to gain approval in the U.S. for XPHOZAH (tenapanor); prepare for and commercialize XPHOZAH in the U.S., if approved; and incur manufacturing and development cost for tenapanor. To date, we have funded our operations from the sale and issuance of common stock and convertible preferred stock, funds from our collaboration partnerships, which includes license fees, milestones and product supply revenue, funds from our loan agreements with our lenders, as well as from sales of IBSRELA.

### Our Commercial Product

#### *IBSRELA for IBS-C*

Our unique discovery platform and deep understanding of the primary mechanism of sodium transport in the intestine resulted in our discovery and development of IBSRELA, a first-in-class, U.S. Food and Drug Administration ("FDA") approved, sodium hydrogen exchange 3 ("NHE3") inhibitor for the treatment of IBS-C in adults. IBSRELA acts locally in the gut and is minimally absorbed. IBS-C is a gastrointestinal ("GI") disorder characterized by both abdominal pain and altered bowel movements, and is estimated to affect 12 million people in the U.S. IBS-C is associated with significantly impaired quality of life, reduced productivity, and substantial economic burden.

We recognized our first sales of IBSRELA in the U.S. in March 2022. For our commercial launch of IBSRELA, we designed a market-responsive commercial strategy and built a commercial organization highly experienced in launching novel therapies into specialty areas. The dynamics of the IBS-C market reflected an established patient base, limited number of competitors all confined to a single mechanism of action, concentrated number of prescribers, and recognized unmet need. In addition, market research indicated a favorable response to the IBSRELA product profile as a novel mechanism therapy. These dynamics enabled a targeted promotional focus on patients currently being managed for IBS-C by the approximately 9,000 high-writing healthcare providers that account for 50% of IBS-C prescriptions. Central to the go to market strategy for IBSRELA is a highly experienced specialty sales force, many with existing relationships across their GI target base, full company engagement, and innovative peer-to-peer and digital initiatives.

We expect competition for IBSRELA will come largely from the three prescription products indicated for IBS-C: Linzess (linaclotide), Amitiza (lubiprostone) and Trulance (plecanatide). Generic lubiprostone is also available in the U.S. Additionally, over-the-counter products, not indicated for IBS-C, are commonly used to treat the constipation component of IBS-C, alone and in combination with the IBS-C-indicated prescription therapies.

We have established commercial agreements with Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. ("Fosun Pharma") in China and Knight Therapeutics, Inc. ("Knight") in Canada for IBSRELA for IBS-C. Knight is currently marketing IBSRELA in Canada.

## **Our Product Pipeline**

### ***Development Candidate XPHOZAH: A Potential New Approach for the Control of Serum Phosphorus in Adult Patients with CKD on Dialysis***

XPHOZAH (tenapanor) is a first-in-class medicine being developed for the control of serum phosphorus, or hyperphosphatemia, in adult patients with CKD on dialysis. XPHOZAH has a unique mechanism of action and acts locally in the gut to inhibit NHE3. This results in the tightening of the epithelial cell junctions, thereby significantly reducing paracellular uptake of phosphate, the primary pathway of phosphate absorption. It is estimated that there are more than 550,000 adult patients with CKD on dialysis in the U.S., and approximately 80% of those patients are being treated with phosphate lowering therapies. Seventy-seven percent of patients treated with phosphate binders to treat hyperphosphatemia were unable to consistently maintain phosphorous levels  $\leq 5.5$  mg/dL over a six-month period. If approved, XPHOZAH would be the first therapy for phosphate management that blocks phosphorus absorption at the primary site.

In June 2020, we submitted a new drug application ("NDA") to the FDA for XPHOZAH. The NDA was supported by three Phase 3 trials involving more than 1,200 adult patients that evaluated the use of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, with two trials evaluating tenapanor as monotherapy and one trial evaluating tenapanor as part of a dual mechanism approach with phosphate binders. All three Phase 3 trials met their primary and key secondary endpoints.

On July 28, 2021, we received a Complete Response Letter ("CRL") from the FDA's Division of Cardiology and Nephrology ("Division") regarding our NDA for XPHOZAH. In December 2021, we submitted a Formal Dispute Resolution Request ("FDRR") to the Office of Cardiology, Hematology, Endocrinology and Nephrology ("OCHEN"). At the request of the FDA's Office of New Drugs ("OND"), as part of our second level of appeal of the CRL, a Cardiovascular and Renal Drug Advisory Committee meeting was held on November 16, 2022 with the committee voting that the benefits of XPHOZAH outweigh its risks nine to four as a monotherapy and ten to two, with one abstention, in combination with phosphate binder therapy. In December 2022, the OND granted our appeal of the CRL for the NDA for XPHOZAH and directed the Division to work with us to develop an appropriate label for the commercialization of XPHOZAH. We believe that a label could reflect an indication for patients whose hyperphosphatemia is insufficiently managed on binder therapy. On February 13, 2023, we participated in a Type A meeting with the Division where we discussed the resubmission of the NDA, and the information to be contained in the resubmitted NDA. We currently expect to resubmit the NDA for XPHOZAH early in the second quarter of 2023. Within thirty (30) days of resubmitting the NDA, we expect to receive notification from the Division as to the classification of the resubmission (Class 1 or Class 2) at which point the expected timing for review will also be known (2-months for a Class 1 and 6-months for a Class 2) as well as a goal review date. We currently believe that the FDA will act upon the XPHOZAH NDA in the second half of 2023, and, if approved, we expect to launch XPHOZAH in the second half of 2023.

We have established commercial agreements with Kyowa Kirin, Co. Ltd. ("KKC") in Japan, Fosun Pharma in China and Knight in Canada for tenapanor for hyperphosphatemia. In October 2022, KKC submitted an NDA to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis.

### **Discovery and Developmental Assets**

We have a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia, or elevated serum potassium. Hyperkalemia is a common problem in patients with heart and kidney disease, particularly in patients taking customary blood pressure medications known as renin-angiotensin-aldosterone system ("RAAS") inhibitors. RDX013 is a novel mechanism agent designed to target the underlying biological mechanisms of potassium secretion to lower elevated potassium. We have completed a Phase 2 dose ranging clinical trial evaluating the safety and efficacy of RDX013 for the treatment of hyperkalemia in CKD patients who are not on dialysis. While the results of the study demonstrated an acceptable safety and tolerability profile for RDX013 and supported proof of concept in its ability to lower serum potassium levels, with statistically significant reductions compared to placebo after eight days of treatment, the study did not meet its primary endpoint of significantly reducing serum potassium levels compared to placebo after four weeks of treatment.

We have a discovery program targeting the inhibition of bicarbonate exchange inhibitor for the treatment of metabolic acidosis, a highly prevalent comorbidity in CKD patients that is strongly correlated with disease progression and adverse outcomes. We have identified lead compounds that are potent, selective and proprietary inhibitors of bicarbonate secretion.

We do not currently expect to meaningfully advance either of these two assets until such time as we have determined our available resources can support additional activities after prioritization of the commercialization of IBSRELA and, if approved, XPHOZAH.

## Our Commercial Strategy

We have developed a portfolio of novel products to address unmet medical needs across gastrointestinal and cardiorenal therapeutic areas and intend to commercialize our products in the U.S. We have established a high quality commercial organization highly experienced in bringing novel products to our customers, including patients, payors and healthcare providers. Our commercial capabilities, including marketing, access, patient services and sales are designed to support our commercialization of IBSRELA, and the commercialization of XPHOZAH, if approved. We have executed ex-U.S. collaborations with established industry leaders to efficiently bring XPHOZAH and IBSRELA to patients in specific territories outside of the U.S.

We continue to evaluate our strategy for the commercialization of IBSRELA and XPHOZAH in other ex-U.S. territories.

## Collaboration Partners

We have exclusive rights to tenapanor in the U.S. and we have established agreements with KKC in Japan, Fosun Pharma in China and Knight in Canada for the development and commercialization of tenapanor for certain indications in their respective territories.

In March 2018, we entered into an exclusive license agreement with Knight ("Knight Agreement") for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. In March 2021, Knight announced the commercial availability of IBSRELA in Canada, following its approval by Health Canada in April 2020. Under the terms of the Knight Agreement, Knight paid us a \$2.3 million non-refundable, one-time payment in March 2018. We may also be eligible to receive approximately CAD 22.2 million for development and commercialization milestones, or approximately \$16.3 million at the currency exchange rate on December 31, 2022, of which \$0.7 million has been received and recognized as revenue as of December 31, 2022. We are also eligible to receive royalties throughout the term of the agreement, and a transfer price for manufacturing services. The variable consideration related to the remaining development milestone payments has not been included in the transaction price as they were fully constrained at December 31, 2022.

In November 2017, we entered into an exclusive license agreement with KKC ("2017 KKC Agreement") for the development, commercialization and distribution of tenapanor in Japan for cardiorenal indications. Under the terms of the 2017 KKC Agreement, we received a \$30.0 million upfront payment from KKC, and we may be entitled to receive up to \$55.0 million in total development and regulatory milestones, of which \$20.0 million has been received and recognized as revenue as of December 31, 2022. We may also be eligible to receive approximately ¥8.5 billion for commercialization milestones, or approximately \$64.6 million at the currency exchange rate on December 31, 2022, as well as reimbursement of costs plus a reasonable overhead for the supply of product and royalties on net sales throughout the term of the agreement. As discussed in *Note 8. Deferred Royalty Obligation Related to the Sale of Future Royalties*, the future royalties and commercial milestone payments we may receive under the 2017 KKC Agreement will be remitted to HealthCare Royalty Partners IV, L.P. pursuant to a Royalty and Sales Milestone Interest Acquisition Agreement.

On April 11, 2022, we entered into a second amendment to the 2017 KKC Agreement ("2022 Amendment"). Under the terms of the 2022 Amendment, we and KKC agreed to a reduction in the royalty rate payable to us by KKC upon net sales of tenapanor in Japan. The royalty rate was reduced from the high teens to low double digits for a two-year period of time following the first commercial sale in Japan, and then to mid-single digits for the remainder of the royalty term. As discussed in *Note 8. Deferred Royalty Obligation Related to the Sale of Future Royalties*, the future royalties we may receive under the 2017 KKC Agreement will be remitted to HealthCare Royalty Partners IV, L.P. pursuant to a Royalty and Sales Milestone Interest Acquisition Agreement. As consideration for the reduction in the royalty rate, KKC agreed to pay us up to an additional \$40.0 million payable in two tranches, with the first payment received in the fourth quarter of 2022 following KKC's October 2022 filing with the Japanese Ministry of Health, Labour and Welfare of its application for marketing approval for tenapanor and the second payment due following KKC's receipt of regulatory approval to market tenapanor for hyperphosphatemia in Japan.

In October 2022, we announced that KKC submitted a NDA to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis, which resulted in payment to us from KKC for an aggregate of \$35.0 million for milestone payments and payments under the 2022 Amendment.

In December 2017, we entered into an exclusive license agreement with Fosun Pharma (“Fosun Agreement”) for the development and commercialization of tenapanor in China for both hyperphosphatemia and IBS-C. Under the terms of the Fosun Agreement, Fosun paid us a \$12.0 million upfront license fee. We may be entitled to receive development and commercialization milestones of up to \$110.0 million, of which \$3.0 million has been received and recognized as revenue as of December 31, 2022, as well as reimbursement of cost plus a reasonable overhead for the supply of product and tiered royalties on net sales ranging from the mid-teens to 20%.

### **Corporate Restructurings**

We implemented restructuring plans in August 2021 and October 2021 following the receipt of a CRL from the FDA relating to our NDA for XPHOZAH and following the conclusion of an End of Review Type A meeting with the FDA, respectively. Both restructuring plans were substantially completed in December 2021 and most of the cash payments related to the reduction in workforce were disbursed prior to December 31, 2021.

Impacted employees were eligible to receive severance benefits and additional Company funded COBRA premiums, contingent upon an impacted employee’s execution (and non-revocation) of a separation agreement, which included a general release of claims against us. In connection with restructuring, we incurred restructuring charges of \$6.2 million, which were recorded during the twelve months ended December 31, 2021, related to one-time employee termination benefits, including severance payments and other employee-related costs. We did not incur any significant contract termination costs pursuant to restructuring. Of these charges, \$2.7 million was recorded in research and development expenses and \$3.5 million was recorded in general and administrative expense in the accompanying statements of operations and comprehensive loss. We incurred no restructuring charges during the twelve months ended December 31, 2022. We reported remaining estimated liabilities for the restructuring costs of zero and \$0.5 million as accrued compensation and benefits in our Balance Sheet as of December 31, 2022 and 2021, respectively.

### **Corporate Financings**

In July 2020, we filed a Form S-3 registration statement, which became effective in August 2020 (“2020 Registration Statement”), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$100.0 million of our common stock that may be issued and sold, from time to time, under an Open Market Sales Agreement with Jefferies LLC, as sales agent, deemed to be “at-the-market offerings” (“2020 Open Market Sales Agreement”). Pursuant to the 2020 Open Market Sales Agreement, Jefferies, as sales agent, received a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2020 Open Market Sales Agreement. We sold a cumulative total of 23.3 million shares and received the full gross proceeds of \$100.0 million at a weighted average sales price of approximately \$4.30 per share under the 2020 Open Market Sales Agreement.

In August 2021, we filed an additional prospectus supplement under the 2020 Registration Statement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under an additional sales agreement we entered into with Jefferies (“2021 Open Market Sales Agreement”), pursuant to which we may, from time to time, sell up to \$150.0 million in shares of our common stock through Jefferies. We are not required to sell shares under the 2021 Open Market Sales Agreement. Pursuant to the 2021 Open Market Sales Agreement, Jefferies, as our sales agent, receives a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2021 Open Market Sales Agreement. As of December 31, 2022, we have sold 79.8 million shares and received gross proceeds of \$98.1 million at a weighted average sales price of approximately \$1.23 per share under the 2021 Open Market Sales Agreement. During the period January 1, 2023 to January 12, 2023, we received additional gross proceeds of \$20.0 million for the sale of an additional 7.7 million shares which were sold at a weighted average sales price of approximately \$2.60 per share under the 2021 Open Market Sales Agreement. There have been no other sales under the 2021 Open Market Sales Agreement after December 31, 2022.



In January 2023, we filed a Form S-3 registration statement, which became effective in January 2023 ("2023 Registration Statement"), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies LLC ("Jefferies"), deemed to be "at-the-market offerings" ("2023 Open Market Sales Agreement"). Pursuant to the 2023 Open Market Sales Agreement, Jefferies, as sales agent, may receive a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2023 Open Market Sales Agreement. There have been no sales of our common stock under the 2023 Open Market Sales Agreement.

As of December 31, 2022, we had cash, cash equivalents and short-term investments totaling \$123.9 million.

## **Intellectual Property**

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, manufacturing and process discoveries, and other know-how, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our intellectual property by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology and inventions that are important to the development and operation of our business. We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of our issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties. If third parties prepare and file patent applications in the U.S. that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office ("USPTO") to determine priority of invention, which would result in substantial costs to us even if the eventual outcome is favorable to us.

The term of individual patents depends upon the legal term of the patents in countries in which they are obtained. In most countries, including the U.S., the patent term is generally 20 years from the earliest date of filing a non-provisional patent application in the applicable country. In the U.S., a patent's term may, in certain cases, be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over a commonly owned patent or a patent naming a common inventor and having an earlier expiration date.

In addition, in the U.S., the Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of a U.S. patent as partial compensation for the patent term lost during the FDA regulatory review process occurring while the patent is in force. A patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to each regulatory review period may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar provisions are available in the European Union and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug.

We may rely, in some circumstances, on trade secrets to protect our technology. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaboration partners, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning the business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during the normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property.

### **Tenapanor Patents**

Our tenapanor patent portfolio is wholly owned by us. This portfolio includes five issued U.S. patents, three issued patents in each of Israel and Mexico, two issued patents in each of European Patent Organization, Japan, Korea, and Hong Kong and one issued patent in each of the following territories: Australia, Brazil, India, and China. These issued patents cover the composition and certain methods of using tenapanor and are predicted, without extension or adjustment, to expire in December 2029. However, the term of U.S. patent no. 8,541,448 was extended under the Hatch-Waxman Act to August 1, 2033. The portfolio further includes patents covering the use of tenapanor for controlling serum phosphorus that have been issued in the U.S., Europe, Japan, China, Australia, Gulf Co-op countries, Hong Kong, Israel, Korea, Macao, Mexico, New Zealand, Russia, South Africa and Taiwan and are pending in other countries. These patents are predicted, without extension or adjustment, to expire in April 2034.

Additional U.S. and international patent applications are pending covering additional methods of treatment with tenapanor, and composition of matter and methods of using compounds that we believe may be follow on compounds to tenapanor.

### **Other Program Patents**

We have patent applications pending in the U.S. and internationally that cover the compositions and methods of using compounds in our RDX013 program.

### **Manufacturing**

To date, we have relied upon third-party contract manufacturing organizations (“CMOs”) to manufacture both the active pharmaceutical ingredient and final drug product dosage forms of our potential drug candidates used as clinical trial material. We expect that we will continue to rely upon CMOs for the manufacture of commercial product for IBSRELA, our clinical trial materials and for our commercial product requirements for XPHOZAH, when and if regulatory approval is received. Our license agreements with Knight, and Fosun Pharma require us to supply final drug product dosage forms of tenapanor for their use in the development and commercialization of tenapanor in each of their respective territories. We are further obligated to supply active pharmaceutical ingredient to KKC to support their development and commercialization of tenapanor in Japan. We expect that we will use CMOs to satisfy our supply obligations to our collaboration partners.

### **Government Regulation**

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling, and export and import of our product candidates.

In the U.S., the FDA regulates drug products under the Federal Food, Drug, and Cosmetic Act (“FFDCA”) and the FDA’s implementing regulations. If we fail to comply with applicable FDA or other requirements at any time during the drug development process, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA’s refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us. FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the U.S.

The process required by the FDA before a drug may be marketed in the U.S. generally involves:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies, some performed in accordance with the FDA’s current Good Laboratory Practice (“GLP”) regulations;
- submission to the FDA of an Investigational New Drug (“IND”) application which must become effective before human clinical trials in the U.S. may begin;
- approval by an independent institutional review board, (“IRB”) or ethics committee at each clinical trial site before each trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice ("GCP") regulations to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice ("cGMP") regulations;
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or commercial shipment of the drug.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. Nonclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of preclinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Additional preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises concerns or questions relating to the IND and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND.

An independent IRB or ethics committee for each medical center proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP requirements, including the requirements for informed consent.

All clinical research performed in the U.S. in support of an NDA must be submitted in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with GCP and if the FDA is able to validate the data from the study through an onsite inspection, if necessary. GCP includes review and approval by an independent ethics committee, such as an IRB, and obtaining and documenting the freely given informed consent of each subject before study initiation. If the applicant seeks approval of an NDA solely on the basis of foreign data, the FDA will only accept such data if they are applicable to the U.S. population and U.S. medical practice, the studies have been performed by clinical investigators of recognized competence, and the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or through other appropriate means.

### ***Clinical Trials***

The clinical investigation of a new drug is typically conducted in three or four phases, which may overlap or be combined, and generally proceed as follows.

- *Phase 1:* Clinical trials are initially conducted in a limited population of subjects to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.
- *Phase 2:* Clinical trials are generally conducted in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific targeted indications in patients with the disease or condition under study.

- *Phase 3:* Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as “pivotal” studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. Phase 3 clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites.
- *Phase 4:* In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor’s agreement to conduct additional clinical trials after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the drug. Such post approval trials are typically referred to as Phase 4 clinical trials.

Concurrent with clinical trials, companies usually complete additional nonclinical studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with GMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

The FDA, the IRB or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study.

We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

### ***New Drug Applications***

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use.

Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs for new molecular entities within ten months after the 60-day filing review period, or six months after the 60-day filing review period for priority review NDAs. For non-new molecular entities, the FDA has a goal of responding within ten months of receipt of standard review NDAs and six months of receipt for priority review NDAs. These timeframes are often extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities where the drug product and/or its API will be produced, if deemed necessary, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy (“REMS”) if it is determined that a REMS is necessary to ensure that the drug’s benefits outweigh its risks and a REMS to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization. The FDA has the authority to prevent or limit

further marketing of a drug based on the results of these post-market programs. Once the FDA approves an NDA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the drug reaches the market.

Drugs may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the drug, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA or NDA supplement, which may require the applicant to develop additional data or conduct additional preclinical studies and clinical trials.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our drug candidates for the proposed indication, the results may not be satisfactory to the FDA. Nonclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the drugs. After approval, certain changes to the approved drug, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval. Depending on the nature of the change proposed, an NDA supplement must be filed and approved before the change may be implemented.

### ***Other Regulatory Requirements***

Any drugs manufactured or distributed by us or our collaboration partners pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic announced and unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning or untitled letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may, among other things, halt our clinical trials, require us to recall a drug from distribution or withdraw approval of the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. A company can make only those claims relating to safety and efficacy that are in the final label or consistent with the final label. Failure to comply with these requirements can result in, among other things, adverse publicity, warning or untitled letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

### ***Hatch-Waxman Act***

Under the Price Competition and Patent Term Restoration Act, or Hatch-Waxman Act, Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A Section 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application ("ANDA"). An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product.

ANDAs are termed “abbreviated” because they are generally not required to include nonclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject’s bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant’s drug or a method of using the drug. 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 competitors in support of approval of an ANDA or 505(b)(2) NDA.

Upon submission of an ANDA or a 505(b)(2) NDA, an applicant must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

If the ANDA or 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must send notice of the Paragraph IV certification to the NDA holder and patent owners once the application 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. If the Paragraph IV certification is challenged by an NDA holder or the patent owner(s), the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the Paragraph IV certification, the expiration of the patent, when the infringement case concerning each such patent was favorably decided in the applicant’s favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a Paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor’s decision to initiate patent litigation.

The Hatch-Waxman Act establishes periods of regulatory exclusivity for certain approved drug products, during which the FDA cannot approve (or in some cases accept) an ANDA or 505(b)(2) application that relies on the branded reference drug. For example, the holder of an NDA, including a 505(b)(2) NDA, may obtain five years of exclusivity upon approval of a new drug containing a new chemical entity (“NCE”) that has not been previously approved by the FDA. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a Paragraph IV certification of patent invalidity or non-infringement.

The Hatch-Waxman Act also provides three years of marketing exclusivity to the holder of an NDA (including a 505(b)(2) NDA) for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. This three-year exclusivity period protects against FDA approval of ANDAs and 505(b)(2) NDAs for the specific condition of the new drug’s approval. As a general matter, the three-year exclusivity does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

### ***Fraud and Abuse Laws***

In the U.S. the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services (“CMS”) other divisions of the U.S. Department of Health and Human Services (e.g., the Office of Inspector General), the U.S. Department of Justice, state Attorneys General, and other state and local government agencies.

These laws include but are not limited to, the Anti-Kickback Statute, the federal False Claims Act, the federal Physician Payments Sunshine Act, and other state and federal laws and regulations.

The Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, or prescription of a particular drug, for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term remuneration has been interpreted broadly to include anything of value. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal False Claims Act prohibits anyone from knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to “cause” the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. Moreover, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. If the government were to allege that we were, or convict us of, violating these false claims laws, we could be subject to a substantial fine and may suffer a decline in our stock price. In addition, private individuals have the ability to bring actions under the federal False Claims Act.

The civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute, or the specific intent to violate it, to have committed a violation.

In addition to the laws described above, the Physician Payments Sunshine Act requires certain drug manufacturers to report payments and other transfer of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in significant civil monetary penalties, and additional penalties for knowing failures, for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Manufacturers must submit reports by the 90th day of each subsequent calendar year.

Many states have also adopted laws similar to the federal laws discussed above. Some of these state prohibitions apply to the referral of patients for healthcare services reimbursed by any insurer, not just federal healthcare programs such as Medicare and Medicaid. There has also been a recent trend of increased regulation of payments made to physicians and other healthcare providers. Certain states mandate implementation of compliance programs, impose restrictions on drug manufacturers' marketing practices and/or require the tracking and reporting of pricing and marketing information as well as gifts, compensation and other remuneration to physicians. Many of these laws contain ambiguities as to what is required to comply with such laws, which may affect our sales, marketing, and other promotional activities by imposing administrative and compliance burdens on us. In addition, given the lack of clarity with respect to these laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state and perhaps federal, authorities.

Violations of any of such laws or any other governmental regulations that apply may result in penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, reporting obligations and integrity oversight, exclusion from participation in federal and state healthcare programs and imprisonment.

### ***Third-Party Coverage and Reimbursement***

Sales of pharmaceutical products depend in significant part on the availability of coverage and adequate reimbursement by third-party payors, such as state and federal governments, including Medicare and Medicaid, and commercial managed care providers. In the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for our product candidates, if approved, will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our future sales, results of operations and financial condition. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

There is increased uncertainty related to insurance coverage and reimbursement for certain drugs, like XPHOZAH, which, if approved, will be marketed for the control of serum phosphorus in adult patients with CKD on dialysis. In January 2011, CMS implemented a new prospective payment system for dialysis treatment. Under the End Stage Renal Disease ("ESRD") prospective payment system, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home, including the cost of certain routine drugs. The inclusion of oral medications without injectable or intravenous equivalents in the bundled payment was initially delayed until January 1, 2014 and through several subsequent legislative actions was delayed until January 1, 2025. As a result, absent further legislation or regulation on this matter, beginning in 2025, oral ESRD-related drugs without injectable or intravenous equivalents may be included in the ESRD bundle and separate Medicare payment for these drugs will no longer be available, as is the case today under Medicare Part D. While it is too early to project the full impact that bundling may have on XPHOZAH and our business should XPHOZAH be brought into the bundle in 2025, or at any time, we may be unable to sell XPHOZAH, if approved, to dialysis providers on a profitable basis.

### ***Healthcare Reform***

In March 2010, Congress passed the Patient Protection and Affordable Care Act, a healthcare reform measure ("ACA"). The ACA was signed into law and substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the pharmaceutical industry.

The ACA contained a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, which have impacted existing government healthcare programs and have resulted in the development of new programs, including Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.



Additionally, the ACA:

- increased the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1% of the average manufacturer price;
- required collection of rebates for drugs paid by Medicaid managed care organizations;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded access to commercial health insurance coverage through new state-based health insurance marketplaces, or exchanges;
- required manufacturers to participate in a coverage gap discount program, under which they must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and
- imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs" to specified federal government programs.

Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace from February 15, 2021 through August 15, 2021. The executive order instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers, which went into effect on April 1, 2013, and, due to subsequent legislative amendments, will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Recently, there has also been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. Additionally, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing. These new laws and the regulations and policies implementing them, as well as other healthcare reform measures that may be adopted in the future, may have a material adverse effect on our industry generally and on our ability to successfully develop and commercialize our products.

## ***Government Price Reporting***

Medicaid is a joint federal and state program for low-income and disabled beneficiaries. Medicare is a federal program covering individuals age 65 and over as well as those with certain disabilities. As a condition of having federal funds being made available for our covered drugs under Medicaid, we have enrolled in the Medicaid Drug Rebate Program (“MDRP”), which requires us to pay a rebate to state Medicaid programs for each unit of our covered drugs dispensed to a Medicaid beneficiary and paid for by a state Medicaid program. Medicaid drug rebates are based on pricing data that we must report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services (“CMS”), the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the average manufacturer price (“AMP”) and the best price (“BP”) for each drug. If we become aware that our MDRP price reporting submission for a prior period was incorrect or has changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. Manufacturers who fail to provide information timely or are found to have knowingly submitted false information to the government may be subject to civil monetary penalties and other sanctions, including termination from the MDRP.

Federal law requires that a manufacturer that participates in the MDRP also participate in the Public Health Service’s 340B drug pricing program (“340B program”) in order for federal funds to be available for the manufacturer’s drugs under Medicaid and Medicare Part B. We participate in the 340B program, which is administered by the Health Resources and Services Administration (“HRSA”), and requires us to charge statutorily defined covered entities no more than the 340B “ceiling price” for our covered outpatient drugs used in an outpatient setting. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered outpatient drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. We must report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs.

In order to be eligible to have drug products paid for with federal funds under Medicaid and purchased by certain federal agencies and grantees, manufacturers must also participate in the U.S. Department of Veterans Affairs (“VA”) Federal Supply Schedule (“FSS”) pricing program. Under the VA/FSS program, manufacturers must report the Non-Federal Average Manufacturer Price (“Non-FAMP”) for their covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). Manufacturers must also pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. Manufacturers who fail to provide timely information or are found to have knowingly submitted false information may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for certain drugs, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information.

## ***Data Privacy and Security Laws***

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the U.S., numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. Further, certain foreign laws govern the privacy and security of personal data, including health-related data. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are

constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

### **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.

### **Impact of COVID-19**

The global COVID-19 pandemic has impacted the operational decisions of companies worldwide. We have undertaken measures to protect our employees, partners, collaborators, and vendors, some of which impact our operations. To date, we have been able to continue our operations with our workforce, most of whom have the ability to work in company-provided offices or remotely, and our pre-existing infrastructure that supports secure access to our internal systems. For a discussion of risks of COVID-19 relating to our business, see “Part II: Other Information-Item 1A.- Risk Factors- Risks Related to Our Business- *The ongoing effects of the COVID-19 pandemic, or any other outbreak of epidemic diseases, or the perception of their effects, could have a material adverse effect on our business, financial condition, results of operations or cash flows.*” As of the date of issuance of this financial report, we are not aware of any specific event or circumstance that would require updates to our estimates and judgments or revisions to the carrying value of our assets or liabilities. These estimates may change as new events occur and additional information is obtained.

### **Human Capital**

The future success of our company depends on our ability to attract, retain, and further develop top talent. In preparation of our launch of IBSRELA in March 2022, we built an experienced commercial team and expanded our internal resources to support a commercial organization. Throughout this transition and expansion of our workforce, we have remained steadfastly committed to our core values, including our goal to develop and maintain an inclusive, diverse, and safe workplace with opportunities for our employees to grow and develop in their careers, supported by strong compensation and benefits.

At December 31, 2022, we had 133 full-time employees, 43 of whom were engaged directly in development and manufacturing, and 90 in marketing, sales and administrative activities. During 2022, our employee base increased by approximately 47, or 55%.

### **Inclusion and Diversity**

Our culture is supported by an unwavering commitment to inclusion and diversity. As of December 31, 2022, approximately 56% of our workforce was female; 43% of our executive leadership team was female and 20% of our employees in managerial roles were female. As of December 31, 2022, minorities represented approximately 38% of our workforce, and 17% of our employees in managerial roles were minorities. We strive to foster a culture where mutual respect, inclusive behavior, and dignity are core to our individual expectations.

We believe that our success will be significantly impacted by our ability to create and maintain a safe inclusive environment where everyone is empowered to do their best work—regardless of race, color, national origin, religion, sex, sexual orientation, gender identity and expression, age, or disability. We are united by our desire to serve our patients, and we are proud financial sponsors of the California Life Sciences Association Racial and Social Equity Initiative, a first step in a unified effort for the life sciences industry in California to do more for the under-served and under-represented, focusing on the most critical need to address the inequality for Black, Hispanic, Native American and Pacific Islander populations in California.

### **Core Values**

Fostering and maintaining a strong, healthy culture is a key strategic focus. Our core values reflect who we are and the way our employees interact with one another, our partners and our stockholders. We are dedicated to our core values, recognizing that this dedication will foster an environment where we will be able to realize our vision of advancing patient care. We are Passionate, aware that with integrity and determination, we make a difference for patients. We are Fearless, aware that by challenging convention, we truly innovate. We are Dedicated, aware that working tirelessly together, we are greater than the sum of our parts. We are Inclusive, aware that with respect, grace and humor, we are family. We encourage our employees to live out our core values and to discuss our core values with potential candidates looking to join our team. We believe that this is an important step in helping our culture stay strong and unique.

### **Health, Safety, and Wellness**

The health, safety, and wellness of our employees is a priority in which we have always invested, and will continue to do so. These investments and the prioritization of employee health, safety, and wellness took on particular significance in light of COVID-19. In response to the COVID-19 pandemic, we implemented significant changes that we determined were in the best interest of our employees, as well as the communities in which we operate, in compliance with government regulations. This included having the vast majority of our employees work from home. We have reopened our facilities and employees have returned to our facilities in the manner in which they are comfortable. We will continue to adopt and align our policies to focus on the health, safety and wellness of our employees, and the needs of our business.

### **Compensation and Benefits**

We recognize that we operate within an industry where there is significant competition for top talent, and we endeavor to provide not only a strong healthy culture, but also important compensation and benefits programs to help meet the needs of our employees. In addition to base compensation, these programs, include annual bonuses, stock awards, an Employee Stock Purchase Plan, 401(k), healthcare and insurance benefits, health savings (funded by the Company) and flexible spending accounts, family leave, family care resources, and flexible work schedules, among many others.

Ensuring fair and equitable pay is integral to our commitment to our employees. Our executive team and Board of Directors strongly support this commitment. We conduct pay equity reviews annually to help us understand whether our compensation structure is appropriate and to identify what improvements can be made.

### **Corporate Information**

We were founded in October 2007 as a Delaware corporation under the name Nteryx. We changed our name to Ardelyx, Inc. in June 2008. We operate in one business segment, which is the development and commercialization of biopharmaceutical products. Our principal executive offices are located at 400 Fifth Avenue, Suite 210, Waltham, Massachusetts 02415, and our telephone number is (510) 745-1700. Our website address is [www.ardelyx.com](http://www.ardelyx.com).

We file electronically with the Securities and Exchange Commission (“SEC”) our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended. We make available on our website at [www.ardelyx.com](http://www.ardelyx.com), free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is [www.sec.gov](http://www.sec.gov).

### **ITEM 1A. RISK FACTORS**

*Our business involves significant risks, some of which are described below. You should carefully consider these risks, as well as other information in this Annual Report on Form 10-K, including our financial statements and the notes thereto and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations, cash flows, the trading price of our common stock and our growth prospects. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.*

#### **Risks Related to our Financial Condition and Capital Requirements**

***We have incurred significant losses since our inception and will incur losses in the future, which makes it difficult for us to assess our future viability; although our financial statements have been prepared on a going concern basis, our current level of cash and short-term investments alone is not sufficient to meet our operating plans for the next twelve months, raising substantial doubt regarding our ability to continue as a going concern.***

In March 2022, we commenced the commercialization of our first product, IBSRELA<sup>®</sup> (tenapanor) for the treatment of irritable bowel syndrome with constipation (“IBS-C”) in adult patients and have generated limited revenue from product sales to date.

We are not profitable and have incurred losses in each year since our inception in October 2007, and we do not know whether or when we will become profitable. We continue to incur significant commercialization, development and other expenses related to our ongoing operations. As of December 31, 2022, we had an accumulated deficit of \$780.1 million.

We expect to continue to incur substantial operating losses for the foreseeable future as we commercialize IBSRELA, seek to gain approval for XPHOZAH® (tenapanor) for the control of serum phosphorus in adult patients with chronic kidney disease (“CKD”) on dialysis; prepare for, and commercialize XPHOZAH, if approved; incur manufacturing and development cost for tenapanor; and incur manufacturing and development costs for tenapanor. .

Ernst & Young LLP, our independent registered public accounting firm for the fiscal year ended December 31, 2022, has included an explanatory paragraph in their opinion that accompanies our audited financial statements as of the year ended December 31, 2022, indicating our current liquidity position raises substantial doubt about our ability to continue as a going concern. We plan to address our operating cash flow requirements with our current cash and short-term investments, cash generated from the sales of IBSRELA, and if approved, cash generated from the sales of XPHOZAH, our potential receipt of anticipated milestone payments from our collaboration partners, our potential receipt of anticipated payments from our collaboration partner, Kyowa Kirin, Co., Ltd. (“KKC”) in connection with the transaction entered into with KKC in April 2022 (“2022 KKC Amendment”) which amended our License Agreement entered into with KKC in 2017; with additional financing sources and through the implementation of cash preservation activities to reduce or defer discretionary spending.

There are no assurances that our efforts to meet our operating cash flow requirements will be successful. If our current cash and short-term investments as well as our plans to meet our operating cash flow requirements are not sufficient to fund necessary expenditures and meet our obligations for at least the next twelve months, our liquidity, financial condition and business prospects will be materially affected.

Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders’ equity and working capital. Further, 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.

***Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.***

We have substantial net operating loss and tax credit carryforwards for Federal and California income tax purposes. Such net operating losses and tax credits carryforwards may be reduced as a result of certain intercompany restructuring transactions. In addition, the future utilization of such net operating loss and tax credit carryforwards and credits will be subject to limitations, pursuant to Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the “Code”). In general, if a corporation undergoes an “ownership change,” generally defined as a cumulative change of more than 50 percentage points (by value) in its equity ownership by certain stockholders over a three-year period, the corporation’s ability to use its pre-change net operating loss (“NOL”) carryforwards and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. We have experienced ownership changes in the past and may experience additional ownership changes in the future, as a result of subsequent changes in our stock ownership, some of which are outside our control. Accordingly, we may not be able to utilize a material portion of our NOL carryforwards, even if we achieve profitability

***We will require additional financing for the foreseeable future as we invest in the commercialization of IBSRELA, and prepare for and commercialize XPHOZAH in the U.S., if approved. The inability to access necessary capital when needed on acceptable terms, or at all, could force us to reduce our efforts to commercialize IBSRELA or delay or limit the commercialization of XPHOZAH, if approved.***

Since our inception, most of our resources have been dedicated to our research and development activities, including developing tenapanor. We believe that we will continue to expend substantial resources for the foreseeable future, including, costs associated with our efforts to commercialize IBSRELA, which we began selling in the U.S. in March 2022; costs associated with our efforts to pursue approval for our NDA for XPHOZAH; conducting pediatric clinical trials for IBSRELA and XPHOZAH, if approved; and manufacturing for IBSRELA and, if approved XPHOZAH. Our future funding requirements will depend on many factors, including, but not limited to:

- the extent to which we are able to generate product revenue from sales of IBSRELA;
- whether we are successful in securing approval for our NDA for XPHOZAH, and the time and cost associated with securing such approval;
- the availability of adequate third-party reimbursement for IBSRELA and, if approved, the sales price and the availability of adequate third-party reimbursement for XPHOZAH;

- the manufacturing, selling and marketing costs associated with IBSRELA and, if approved, XPHOZAH;
- our ability to maintain our existing collaboration partnerships and to establish additional collaboration partnerships, in-license/out-license, joint ventures or other similar arrangements and the financial terms of such agreements;
- the timing, receipt and amount of any milestones that may be received from our collaboration partners in connection with tenapanor, if any
- the timing, receipt, and amount of revenue, if any, that may be received from KKC in connection with the 2022 KKC Amendment;
- the timing, receipt, and amount of royalties we may receive as a result of sales of tenapanor by our collaboration partners in China and Canada, if any;
- the cash requirements for the discovery and/or development of other potential product candidates, including RDX013 and RDX020;
- the time and cost necessary to respond to technological and market developments;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into with SLR Investment Corp. in February 2022.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to limit or reduce our commercialization of IBSRELA, or delay or limit the commercialization of XPHOZAH, if approved, or delay or limit additional clinical trials for tenapanor. Additionally, our inability to access capital on a timely basis and on terms that are acceptable to us may force us to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the commercialization of IBSRELA or XPHOZAH, if approved, through the use of alternative structures.

***We have generated limited revenue from product sales and may never be profitable.***

We began selling IBSRELA in the U.S. in March 2022, and have generated limited revenue from product sales to date. We have no other products approved for sale. We are preparing to resubmit our NDA for XPHOZAH following the U.S. Food and Drug Administration’s (“FDA”) Center for Drug Evaluation and Research, Office of New Drugs (“OND”) decision to grant our appeal of the Complete Response Letter (“CRL”) for the NDA for XPHOZAH.

There can be no assurances that our NDA for XPHOZAH will be approved by the FDA. There can be no assurances that we will be successful in increasing the amount of product revenue from sales of IBSRELA. There can be no assurances that we will generate sufficient product revenue from sales of IBSRELA and, if approved, XPHOZAH, to cover our expenses. Our ability to generate product revenue from sales or pursuant to milestone or royalty payments depends heavily on many factors, including but not limited to:

- our ability to successfully commercialize IBSRELA;
- obtaining market acceptance of IBSRELA as a viable treatment option for IBS-C;
- our ability to obtain and sustain an adequate level of coverage and reimbursement for IBSRELA by third-party payors;
- whether we are successful in our efforts to secure approval for our NDA for XPHOZAH;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide an adequate (in amount and quality) supply of product to support the market demand for IBSRELA and, if approved, XPHOZAH;
- addressing any competing technological and market developments;

- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how, and our ability to develop, manufacture and commercialize our product candidates and products without infringing intellectual property rights of others; and
- attracting, hiring, and retaining qualified personnel.

With respect to our commercialization of IBSRELA, and if we are successful in obtaining regulatory approval to market XPHOZAH, our revenue will be dependent, in part, upon the size of the markets in the U.S. and the label for which approval is granted, accepted price for the product, and the ability to get reimbursement at any price. While there is significant uncertainty related to the insurance coverage and reimbursement of newly approved products in general in the U.S., there is additional uncertainty related to insurance coverage and reimbursement for drugs, like XPHOZAH, which, if approved, will be marketed for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication. If we are successful in obtaining regulatory approval to market XPHOZAH for such indication, our ability to generate and sustain future revenues from sales of XPHOZAH, may be dependent upon whether and when XPHOZAH, along with other oral end stage renal disease (“ESRD”)-related drugs without an injectable or intravenous equivalent, are bundled into the ESRD prospective payment system, and the manner in which such introduction into the ESRD prospective payment system may occur. See “Third-party payor coverage and reimbursement status of newly approved products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for IBSRELA and, if approved, XPHOZAH could limit our ability to market those products and decrease our ability to generate revenue” below. Additionally, if the number of adult patients for IBSRELA or, if approved XPHOZAH, is not as significant as we estimate, the indication approved by regulatory authorities for XPHOZAH is narrower than we expect, coverage and reimbursement for either IBSRELA or XPHOZAH, if approved, are not available in the manner and to the extent we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from the sale of IBSRELA or XPHOZAH, if approved. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to generate adequate revenue from product sales would likely depress our market value and could impair our ability to raise capital, expand our business, discover or develop other product candidates or continue our operations. A decline in the value of our common stock could cause our stockholders to lose all or part of their investment.

### **Principal Risks Related to Our Business**

***We are substantially dependent on the successful commercialization of IBSRELA, and there is no guarantee that we will achieve sufficient market acceptance for IBSRELA, secure adequate coverage and reimbursement for IBSRELA, or generate sufficient revenue from product sales of IBSRELA.***

We began selling IBSRELA in the U.S. in March 2022. The overall commercial success of IBSRELA will depend on a number of factors, including the following:

- the ability of the third-party manufacturers we contract with to provide an adequate (in amount and quality) supply of product to support the market demand for IBSRELA;
- our ability to obtain and sustain an adequate level of coverage and reimbursement for IBSRELA by third-party payors;
- the effectiveness of IBSRELA as a treatment for adult patients with IBS-C;
- the size of the treatable patient population;
- the effectiveness of our sales, market access and marketing efforts;
- whether physicians view IBSRELA as a safe and effective treatment for adult patients with IBS-C, which will impact the adoption of IBSRELA by physicians for the treatment of IBS-C;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of IBSRELA compared to alternative and competing treatments;
- the prevalence and severity of adverse side effects of IBSRELA;
- our potential involvement in lawsuits in connection with enforcing intellectual property rights in and to IBSRELA;

- our potential involvement in third-party interference, opposition, derivation or similar proceedings with respect to our patent rights directed to IBSRELA, and avoiding other challenges to our patent rights and patent infringement claims; and
- a continued acceptable safety and tolerability profile of IBSRELA following approval.

The amount of potential revenue we may achieve from the commercialization of IBSRELA is subject to these and other factors, and may be unpredictable from quarter-to-quarter. If the number of patients in the market for IBSRELA or the price that the market can bear is not as significant as we estimate, or if we are not able to secure adequate physician and patient acceptance of IBSRELA or adequate coverage and reimbursement for IBSRELA, we may not generate sufficient revenue from sales of IBSRELA. Any failure of IBSRELA to achieve market acceptance, sufficient third-party coverage or reimbursement, or commercial success would adversely affect our results of operations.

***We are pursuing regulatory approval for XPHOZAH. There can be no assurances that we will be successful in obtaining such regulatory approval.***

We are pursuing regulatory approval for XPHOZAH. To date, we have invested a significant amount of our efforts and financial resources in the research and development of XPHOZAH. On July 28, 2021, we received a CRL from the FDA's Division of Cardiology and Nephrology ("Division") regarding our NDA for XPHOZAH. According to the CRL, the Division determined that the magnitude of the treatment effect observed in our Phase 3 clinical trials was small and of unclear clinical significance. Following an End-of-Review Type A meeting ("End of Review Meeting") in October 2021, with the Division, we submitted a Formal Dispute Resolution Request ("FDRR") in December 2021. The FDRR was focused on demonstrating that the data submitted in the NDA supported the clinical significance of the treatment effect of tenapanor in the control of serum phosphorus in adult patients with CKD on dialysis. On February 4, 2022, we received an Appeal Denied Letter ("ADL") from the Office of Cardiology, Hematology, Endocrinology and Nephrology ("OCHEN"). On February 18, 2022, we submitted an appeal of the ADL to the OND. In April 2022, we received an interim response from the OND requesting additional input from the Cardiovascular and Renal Drug Advisory Committee ("CRDAC"). A CRDAC meeting was held in November 2022 with the Committee voting that the benefits of XPHOZAH outweigh its risks nine to four as a monotherapy and ten to two, with one abstention, in combination with phosphate binder therapy. In December 2022, the OND granted our appeal of the CRL for the NDA for XPHOZAH and directed the Division to work with us to develop an appropriate label for the commercialization of XPHOZAH. We believe that a label could reflect an indication for patients whose hyperphosphatemia is insufficiently managed on binder therapy. On February 13, 2023, we participated in a Type A meeting with the Division where we discussed the resubmission of the NDA, and the information to be contained in the resubmitted NDA. We currently expect to resubmit the NDA for XPHOZAH early in the second quarter of 2023. Within 30 days of resubmitting the NDA, we expect to receive notification from the Division as to the classification of the resubmission (Class 1 or Class 2) at which point the expected timing for review will also be known (2-months for a Class 1 and 6-months for a Class 2) as well as a goal review date. We currently that the FDA will act upon the XPHOZAH NDA in the second half of 2023, and that, if approved, we will launch XPHOZAH in the second half of 2023. There can be no assurances that the granting of our appeal to the CRL and resubmission of our NDA will result in approval of our NDA for XPHOZAH. Even if we are successful in obtaining approval for the NDA, the delay in obtaining such approval may result in delay in the regulatory process for our partners, which could have a material adverse effect on our business and results of operations.

***Even if we are successful in obtaining regulatory approval for XPHOZAH, there is no guarantee that we will achieve sufficient market acceptance for XPHOZAH, secure adequate coverage and reimbursement for XPHOZAH or generate sufficient revenue from product sales of XPHOZAH.***

We may not be successful in obtaining FDA approval for XPHOZAH, and if we are able to obtain approval, there is no guarantee that we will achieve sufficient market acceptance for XPHOZAH, secure adequate coverage and reimbursement for XPHOZAH or generate sufficient revenue from product sales of XPHOZAH. If we are successful in obtaining approval for XPHOZAH, the commercial success of XPHOZAH will depend on a number of factors, including the following:

- the ability of the third-party manufacturers we contract with to provide an adequate (in amount and quality) supply of product to support the market demand for both IBSRELA and XPHOZAH;
- whether or not the content and breadth of the label approved by the FDA for XPHOZAH may materially and adversely impact our ability to commercialize the product for the approved indication;



- whether or when XPHOZAH, along with other oral ESRD-related drugs without an injectable or intravenous equivalent, are bundled into the ESRD prospective payment system, and the manner in which such introduction into the ESRD prospective payment system may occur;
- the prevalence and severity of adverse side effects of XPHOZAH;
- acceptance of XPHOZAH as safe, effective and well-tolerated by patients and the medical community, and, the extent to which the issuance of a CRL by the FDA has impacted the potential acceptance of XPHOZAH as safe, effective and well-tolerated;
- our ability to manage the commercialization of IBSRELA and XPHOZAH and the complex pricing and reimbursement negotiations that may arise with marketing products containing the same active ingredient at different doses for separate indications;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of XPHOZAH compared to alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for XPHOZAH by third-party payors;
- our potential involvement in lawsuits in connection with enforcing intellectual property rights in and to XPHOZAH;
- our potential involvement in third-party interference, opposition, derivation or similar proceedings with respect to our patent rights, and avoiding other challenges to our patent rights and patent infringement claims; and
- a continued acceptable safety and tolerability profile of XPHOZAH following approval.

***IBSRELA and/or, if approved and commercialized, XPHOZAH, may cause undesirable side effects or have other properties that could limit the commercial success of the product.***

Undesirable side effects caused by IBSRELA and/or, if approved, XPHOZAH could cause us or regulatory authorities to interrupt, delay or halt the commercialization of the product. Despite our receipt of marketing approval for IBSRELA and the completion of our Phase 3 clinical program for XPHOZAH, the prevalence and/or severity of side effects caused by IBSRELA and/or, if approved and commercialized, XPHOZAH could result in a number of potentially significant negative consequences could occur, including:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we or a collaboration partner may be required to recall the product;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a Risk Evaluation and Mitigation Strategy (“REMS”) which could require creation of a Medication Guide or patient package insert outlining the risks of such side effects for distribution to patients, a communication plan to educate healthcare providers of the drugs’ risks, as well as other elements to assure safe use of the product, such as a patient registry and training and certification of prescribers;
- we or a collaboration partner may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of new labeling statements, such as a “black box” warning or a contraindication;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us, or a collaboration partner, from achieving or maintaining market acceptance of IBSRELA and/or, if approved, XPHOZAH, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

***As a company, we have limited experience in the marketing, sale and distribution of pharmaceutical products; and there are significant risks in building and managing a commercial organization.***

As a company, we have limited experience in building and managing a commercial organization, or in the marketing, sale and distribution of pharmaceutical products. There can be no assurances that we will be successful in our efforts to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, comply with regulatory requirements applicable to the marketing and sale of drug products and effectively manage a geographically dispersed sales and marketing team.

If we fail or are delayed in the development of our internal sales, marketing and distribution capabilities, the commercialization of IBSRELA, and if approved, XPHOZAH could be adversely impacted.

***Third-party payor coverage and reimbursement status of newly commercialized products are uncertain. Failure to obtain or maintain adequate coverage and reimbursement for IBSRELA and, if approved, XPHOZAH could limit our ability to market those products and decrease our ability to generate revenue.***

The pricing, coverage and reimbursement of IBSRELA and XPHOZAH, if approved, must be adequate to support a commercial infrastructure. The availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford treatments. Sales of IBSRELA and, if approved and commercialized, XPHOZAH, will depend substantially, both domestically and abroad, on the extent to which the costs of the product will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors. If coverage and reimbursement are not available, or are available only to limited levels, we, or our collaboration partners, may not be able to successfully commercialize IBSRELA, or XPHOZAH, if approved. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U.S., the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services (“CMS”), an agency within the United States Department of Health and Human Services responsible for administering the Medicare program, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the coverage reimbursement policies established by CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for products such as ours.

There is increased uncertainty related to insurance coverage and reimbursement for drugs, like XPHOZAH, which, if approved, may be marketed for the control of serum phosphorus in adult patients with CKD on dialysis or for another other related indication. In January 2011, CMS implemented a new prospective payment system for dialysis treatment. Under the ESRD prospective payment system, CMS generally makes a single bundled payment to the dialysis facility for each dialysis treatment that covers all items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home, including the cost of certain routine drugs. The inclusion of oral medications without injectable or intravenous equivalents in the bundled payment was initially delayed until January 1, 2014, and through several subsequent legislative actions was delayed until January 1, 2025. As a result, absent further legislation or regulation on this matter, beginning in 2025, oral ESRD-related drugs without injectable or intravenous equivalents may be included in the ESRD bundle and separate Medicare payment for these drugs will no longer be available, as is the case today under Medicare Part D. While it is too early to project the full impact that bundling may have on sales of XPHOZAH, if approved and commercialized, and on our business should XPHOZAH be brought into the bundle in 2025, or at any time, we may be unable to sell XPHOZAH, if approved, to dialysis providers on a profitable basis.

Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, Japan, China and other countries has and will continue to put pressure on the pricing and usage of IBSRELA and XPHOZAH, even if regulatory approval is received in such countries. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the U.S., the reimbursement for our products may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, these caps may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of IBSRELA, and if approved and commercialized, XPHOZAH, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

***We rely completely on third parties to manufacture IBSRELA and XPHOZAH. If they are unable to comply with applicable regulatory requirements, unable to source sufficient raw materials, experience manufacturing or distribution difficulties or are otherwise unable to manufacture sufficient quantities to meet demand, our commercialization of IBSRELA and, if approved and commercialized, XPHOZAH and our development efforts for tenapanor may be materially harmed.***

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture IBSRELA or XPHOZAH on a commercial scale, or to manufacture our drug supplies for use in the conduct of our nonclinical and clinical studies. The facilities used by our contract manufacturers to manufacture our drug supply are subject to inspection by the FDA. Our ability to control the manufacturing process of our product candidates is limited to the contractual requirements and obligations we impose on our contract manufacturer. Although they are contractually required to do so, we are completely dependent on our contract manufacturing partners for compliance with the regulatory requirements, known as current Good Manufacturing Practice requirements (“cGMPs”), for manufacture of both active drug substances and finished drug products.

The manufacture of pharmaceutical products requires significant expertise and capital investment. Manufacturers of pharmaceutical products often encounter difficulties in commercial production. These problems may include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, and shortages of qualified personnel, as well as compliance with federal, state and foreign regulations and the challenges associated with complex supply chain management. Even if our contract manufacturers do not experience problems and commercial manufacturing is achieved, their maximum or available manufacturing capacities may be insufficient to meet commercial demand. Finding alternative manufacturers or adding additional manufacturers requires a significant amount of time and involves significant expense. New manufacturers would need to develop and implement the necessary production techniques and processes, which along with their facilities, would need to be inspected and approved by the regulatory authorities in each applicable territory. In addition, the raw materials necessary to make API for our products are acquired from a limited number of sources. Any delay or disruption in the availability of these raw materials could result in production disruptions, delays or higher costs with consequent adverse effects on us.

If our contract manufacturers fail to adhere to applicable GMP or other regulatory requirements, experience delays or disruptions in the availability of raw materials or experience manufacturing or distribution problems, we may suffer significant consequences, including the inability to meet our product requirements for our clinical development programs, and if tenapanor is commercialized for any indication, such events could result in product seizures or recalls, loss of product approval, fines and sanctions, reputational damage, shipment delays, inventory shortages, inventory write-offs and other product-related charges and increased manufacturing costs. As a result, or if maximum or available manufacturing capacities are insufficient to meet demand, our development or our commercialization efforts for IBSRELA and/or, if approved, XPHOZAH may be materially harmed.

***Our operating activities may be restricted as a result of covenants related to the indebtedness under our loan and security agreement and we may be required to repay the outstanding indebtedness in an event of default, which could have a materially adverse effect on our business.***

On February 23, 2022, we entered into a loan and security agreement with SLR Investment Corp. (“Lender”) pursuant to which the Lender agreed to provide us with a loan facility for up to \$50.0 million with a maturity date of March 1, 2027, and on August 1, 2022 and February 9, 2023, we entered into amendments to the loan and security agreement (collectively, the “2022 Loan Agreement.”). The loan was funded in the amount of \$27.5 million on February 23, 2022 and the remaining \$22.5 million may be funded by December 20, 2023 upon the satisfaction of both (i) receipt from the FDA of approval of the NDA for XPHOZAH on or prior to November 30, 2023 and (ii) our achievement of certain product revenue milestone targets described in the 2022 Loan Agreement. Until we have repaid all funded indebtedness, the loan and security agreement subjects us to various customary covenants, including requirements as to financial reporting and insurance and restrictions on our ability to dispose of our business or property, to change our line of business, to liquidate or dissolve, to enter into any change in control transaction, to merge or consolidate with any other entity or to acquire all or substantially all the capital stock or property of another entity, to incur additional indebtedness, to incur liens on our property, to pay any dividends or other distributions on capital stock other than dividends payable solely in capital stock, to redeem capital stock, to enter into licensing agreements, to

engage in transactions with affiliates, and to encumber our intellectual property. Our business may be adversely affected by these restrictions on our ability to operate our business.

We are permitted to make interest only payments on the loan facility through March 2024, with principal repayments commencing on April 1, 2024, however, this interest only period will be extended to March 2025 with principal repayments delayed to April 1, 2025 if (i) we secure approval from the FDA for our NDA for XPHOZAH by November 30, 2023 or (ii) we achieve certain product revenue targets described in the 2022 Loan Agreement for the year ended December 31, 2023. In addition, we may be required to repay the outstanding indebtedness under the loan facility if an event of default occurs under the loan and security agreement. An event of default will occur if, among other things, we fail to make payments under the loan and security agreement; we breach any of our covenants under the loan and security agreement, subject to specified cure periods with respect to certain breaches; the Lender determines that a material adverse change has occurred; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit the Lender to accelerate the maturity of such indebtedness or that could have a material adverse change on us. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In this case, we may be required to limit or reduce our activities necessary to commercialize IBSRELA and/or, if approved, XPHOZAH, or delay or limit clinical trials for tenapanor or other product candidates. The Lender could also exercise its rights as collateral agent to take possession of and to dispose of the collateral securing the term loans, which collateral includes substantially all of our property (excluding intellectual property, which is subject to a negative pledge). Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events.

### **Additional Risks Related to Our Business and Industry**

#### ***Clinical drug development involves a lengthy and expensive process with an uncertain outcome.***

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. For example, while the results of our Phase 2 clinical trial evaluating RDX013 for the treatment of hyperkalemia demonstrated an acceptable safety and tolerability profile for RDX013 and supported proof of concept in its ability to lower serum potassium levels, with statistically significant reductions compared to placebo after eight days of treatment, the study did not meet its primary endpoint of significantly reducing serum potassium levels compared to placebo after four weeks of treatment. We currently expect that the next step for the program will be to evaluate a new formulation that potentially enhances subject compliance and the efficacy of RDX013 in an additional Phase 2 clinical study at such time as we have determined that our available resources support conducting such an additional clinical study. There can be no assurances that any additional clinical study that we determine to conduct with RDX013 will be successful.

Additionally, if we conduct additional clinical trials with RDX013 or any other product candidates, we could encounter delays in our future development if any clinical trials are suspended or terminated by us, by the IRBs of the institutions in which the trial is being conducted, or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

In addition, identifying and qualifying patients to participate in any clinical trials is critical to the success of the clinical trials. The timing of any future clinical trials, including any additional RDX013 clinical trial that we may determine to conduct, will depend, in part, on the speed at which we can recruit patients to participate in testing our product candidates. 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, 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, or our inclusion and exclusion criteria for our clinical trials may present challenges in identifying acceptable patients. As a result, the timeline for recruiting patients and conducting clinical trials may be delayed. These delays could result in increased costs, delays in advancing our development of the program, or termination of the clinical studies altogether. Any of these occurrences may significantly harm our business, financial condition and prospects.

***We will rely on third parties to conduct all of our nonclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for additional products or commercialize our product candidates.***

We do not have the ability to independently conduct nonclinical studies or clinical trials. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as Contract Research Organizations (“CROs”), to conduct clinical trials on our product candidates. The third parties with whom we contract for execution of the clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely, and will continue to rely, on these third parties to conduct our nonclinical studies and our clinical trials, we remain responsible for ensuring that each of our studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third parties does not relieve us of our regulatory responsibilities. We, and these third parties are required to comply with current GLPs for nonclinical studies, and good clinical practices (“GCPs”) for clinical studies. GLPs and GCPs are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area (“EEA”) and comparable foreign regulatory authorities for all of our products in nonclinical and clinical development, respectively. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the European Medicines Agency (“EMA”), or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which could add additional costs and could delay the regulatory approval process.

***We face substantial competition, and our competitors may discover, develop or commercialize products faster or more successfully than us.***

The biotechnology and pharmaceutical industries are highly competitive, and we face significant competition from companies in the biotechnology, pharmaceutical and other related markets that are researching and marketing products designed to address diseases that we are currently developing products to treat.

We are aware of three prescription products marketed for certain patients with IBS-C, including Linzess (linaclotide), Amitiza (lubiprostone) and Trulance (plecanatide). Generic lubiprostone is also available in the U.S.

XPHOZAH, if approved will compete with phosphate binders. The various types of phosphate binders commercialized in the U.S. include the following: Calcium acetate (several prescription brands including PhosLo and Phoslyra); Lanthanum carbonate (Fosrenol); Sevelamer hydrochloride (Renagel); Sevelamer carbonate (Renvela); Sucroferric oxyhydroxide (Velphoro); and Ferric citrate (Auryxia). All of the listed phosphate binders are available as generics in the U.S., with the exception of Velphoro and Auryxia. Additionally, over-the-counter calcium carbonate, such as Tums and Caltrate, is also used to bind phosphorus.

In addition to the currently available phosphate binders, we are aware of at least four other binders in development, including fermagate (Alpharen), an iron-based binder in Phase 3 being developed by Opko Health, Inc., PT20, an iron-based binder in Phase 3 being developed by Shield Therapeutics, AP-301 in Phase 2 being developed by Alebund Pharmaceutical (Hong Kong) Limited, and lanthanum dioxycarbonate (Renazorb), which has demonstrated pharmacodynamic bioequivalence to Fosrenol. Renazorb is being developed by Unicycive Therapeutics, which has announced its plans to file an NDA via the 505(b)(2) pathway in mid-2023. Additionally, Chugai and Alebund are developing EOS789, an inhibitor of phosphate transporters NaPi-2b, PiT-1, and PiT-2, thus far studied in a phase 1 clinical trial.

It is possible that our competitors' drugs may be less expensive and more effective than our product candidates, or may render our product candidates obsolete. It is also possible that our competitors will commercialize competing drugs or treatments before we or our collaboration partners can launch any products developed from our product candidates. We also may face increased competition in the future as new companies enter into our target markets.

Many of our competitors have materially greater name recognition and financial, manufacturing, marketing, research and drug development resources than we do. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Large pharmaceutical companies in particular have extensive expertise in preclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies, and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaboration partnerships or licensing relationships with our competitors.

***We may experience difficulties in managing our current activities and growth given our level of managerial, operational, financial and other resources.***

While we have continued to work to optimize our management composition, personnel and systems to support our current activities for future growth, these resources may not be adequate for this purpose. Our need to effectively execute our business strategy requires that we:

- manage any commercialization activities in which we may engage effectively;
- manage our clinical trials effectively;
- manage our internal development efforts effectively while carrying out our contractual obligations to licensors, contractors, collaborators, government agencies and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- retain and motivate our remaining employees and potentially identify, recruit, and integrate additional employees.

If we are unable to maintain or expand our managerial, operational, financial and other resources to the extent required to manage our development and commercialization activities, our business will be materially adversely affected.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and our commercial launch of IBSRELA and will face further risk following the commercial launch of XPHOZAH in the second half of 2023, if approved. For example, we may be sued if any product we develop 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, negligence, strict liability, and a 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 our product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for the product;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize or co-promote IBSRELA and/or, if approved, XPHOZAH.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products we develop. 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 deductibles, and we may be subject to a product liability claim for which we have no coverage. We will 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, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

***If we fail to attract, retain and motivate our executives, senior management and key personnel, our business will suffer.***

Recruiting and retaining qualified scientific, clinical, medical, manufacturing, and sales and marketing personnel is critical to our success. We are highly dependent on our executives, senior management and certain other key employees. The loss of the services of our executives, senior management or other key employees could impede the achievement of our development and commercial objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executives, senior management 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, gain marketing approval of and commercialize products. We may be unable to hire, train or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel, particularly in our geographic regions. 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.

***Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.***

The global data protection landscape is rapidly evolving, and we are or may become subject to numerous state, federal and foreign laws, requirements and regulations governing the collection, use, disclosure, retention, and security of personal data, such as information that we may collect in connection with clinical trials in the U.S. and abroad. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, and we cannot yet determine the impact future laws, regulations, standards, or perception of their requirements may have on our business. This evolution may create uncertainty in our business; affect our ability to operate in certain jurisdictions, or to collect, store, transfer use and share personal information; necessitate the acceptance of more onerous obligations in our contracts; result in liability; or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing our processing of personal information could result in negative publicity, government investigations and enforcement actions, claims by third parties and damage to our reputation, any of which could have a material adverse effect on our operations, financial performance and business.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the U.S., the Health Insurance Portability and Accountability Act of 1996, as amended, and regulations promulgated thereunder (collectively "HIPAA") imposes, among other things, certain standards relating to the privacy, security, transmission, and breach reporting of individually identifiable health information. We may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPAA.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act ("CCPA") went into effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risk associated with data breach litigation. Further, the California Privacy Rights Act ("CPRA") generally went into effect on January 1, 2023 and significantly amends the CCPA. It imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may also be required. Similar laws have passed in

Virginia, Connecticut, Utah and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the U.S. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Furthermore, the Federal Trade Commission (“FTC”) and many state Attorneys General continue to enforce federal and state consumer protection laws against companies for online collection, use, dissemination and security practices that appear to be unfair or deceptive. For example, according to the FTC, failing to take appropriate steps to keep consumers’ personal information secure can constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act. The FTC expects a company’s data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities.

We are also or may become subject to rapidly evolving data protection laws, rules and regulations in foreign jurisdictions. For example, in Europe, the European Union General Data Protection Regulation (“GDPR”) went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the European Economic Area (“EEA”). Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U.S.; in July 2020, the Court of Justice of the EU (“CJEU”) limited how organizations could lawfully transfer personal data from the EU/EEA to the U.S. by invalidating the Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses. In March 2022, the U.S. and EU announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU-U.S. Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European court and regulatory decisions subsequent to the CJEU decision of July 2020 have taken a restrictive approach to international data transfers. Relatedly, following the United Kingdom’s withdrawal from the EEA and the European Union, and the expiry of the transition period, companies have had to comply with both the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, CROs, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

***We and our collaborators, CROs and other contractors and consultants depend on information technology systems, and any failure of these systems could harm our business. Security breaches, loss of data, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.***

We and our collaborators, CROs, and other contractors and consultants collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we and our collaborators, CROs and other contractors and consultants collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we and our collaborators, CROs and other contractors and consultants do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures designed to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information.



Our information technology systems and infrastructure, and those of our current and any future collaborators, CROs, contractors and consultants and other third parties on which we rely, are vulnerable to attack, damage and interruption from computer viruses, malware (e.g., ransomware), natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, phishing attacks and other social engineering schemes, attachments to emails, human error, fraud, denial or degradation of service attacks, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. We may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. We do not believe that we have experienced any significant system failure, accident or security breach to date, but if such an event were to occur and cause interruptions in our operations, it could result in a material disruption to our business. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal and state privacy and security laws, if applicable. Moreover, if a computer security breach affects our systems or those of our collaborators, CROs or other contractors, or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition.

***If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors' views of us and could have a material adverse effect on the price of our common stock.***

Our failure to implement and maintain effective internal controls over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements and cause us to fail to meet our reporting obligations. If we cannot in the future favorably assess the effectiveness of our internal controls over financial reporting, investor confidence in the reliability of our financial reports may be adversely affected, which could have a material adverse effect on the trading price of our common stock.

***We have formed in the past, and may form in the future, collaboration partnerships, joint ventures and/or licensing arrangements, and we may not realize the benefits of such collaborations.***

We have current collaboration partnerships for the commercialization of tenapanor in certain foreign countries, and we may form additional collaboration partnerships, create joint ventures or enter into additional licensing arrangements with third parties in the U.S. and abroad that we believe will complement or augment our existing business. In particular, we have formed collaboration partnerships with KKC for commercialization of tenapanor for hyperphosphatemia in Japan; with Fosun Pharma for commercialization of tenapanor for hyperphosphatemia and IBS-C in China and related territories; and in Canada with Knight for commercialization of tenapanor for IBS-C and hyperphosphatemia. We face significant competition in seeking appropriate collaboration partners, and the process to identify an appropriate partner and negotiate appropriate terms is time-consuming and complex. Any delays in identifying suitable additional collaboration partners and entering into agreements to develop our product candidates could also delay the commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. There is no guarantee that our current collaboration partnerships or any such arrangements we enter into in the future will be successful, or that any collaboration partner will commit sufficient resources to the development, regulatory approval, and commercialization effort for such products, or that such alliances will result in us achieving revenues that justify such transactions. We received a CRL from the FDA regarding our NDA for XPHOZAH.

Following the OND's decision to grant our appeal of the CRL, we are preparing to resubmit our NDA for XPHOZAH. There can be no assurances that the granting of our appeal of the CRL and resubmission of our NDA will result in approval of our NDA for XPHOZAH. Even if we are successful in obtaining approval for the NDA, the delay in obtaining such approval may result in delay in the regulatory process for our partners, which could have a material adverse effect on our business and results of operations.

***The ongoing effects of the COVID-19 pandemic, or any other outbreak of epidemic diseases, or the perception of their effects, could have a material adverse effect on our business, financial condition, results of operations or cash flows.***

Outbreaks of epidemic, pandemic, or contagious diseases, such as the current novel coronavirus ("COVID-19") pandemic or, historically, the Ebola virus, Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome or the H1N1 virus, could disrupt our business. Economic and health conditions related to the COVID-19 pandemic in the U.S. and across most of the globe remain uncertain and continue to evolve. The continuing effects of the coronavirus pandemic may result in delays in the manufacture of tenapanor, or in the delivery of key intermediates or raw materials required to manufacture tenapanor or delays in clinical development activities by us, or our collaboration partners. Such effects could also materially and negatively impact our ability to successfully commercialize IBSRELA and/or, if approved, XPHOZAH, or the ability of our collaboration partners to successfully commercialize such products, if approved for marketing and sale by the foreign regulatory authorities, including our ability, and that of our collaboration partners to educate physicians and patients about the benefits, administration and use of the product.

- Although we have reopened our offices and invited our personnel to return to the office, we continue to permit our personnel to work remotely, which could negatively impact productivity, or disrupt, delay, or otherwise adversely impact our business. In addition, this could increase our cyber-security risk, create data accessibility concerns, and make us more susceptible to communication disruptions, any of which could adversely impact our business operations or delay necessary interactions with local and federal regulators, ethics committees, manufacturing sites, research or clinical trial sites and important agencies and contractors.
- The FDA and comparable foreign regulatory agencies may continue to experience operational interruptions or delays, which may impact timelines for regulatory submission, trial initiation and regulatory approval.

The full effects of the COVID-19 remain unknown. The extent to which the outbreak may continue to impact our business, including, our commercialization and manufacturing will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as access to physician offices for our commercial and medical teams, business closures or supply chain or business disruptions.

***We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.***

We may consider strategic transactions, such as acquisitions of companies, asset purchases, and/or in-licensing of products, product candidates or technologies. In addition, if we are unable to access capital on a timely basis and on terms that are acceptable to us, we may be forced to further restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the commercialization of IBSRELA, our continued efforts to seek approval for our NDA for XPHOZAH and/or the development of discovery and developmental assets through the use of alternative structures. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, spin outs, collaboration partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- up-front, milestone and royalty payments, equity investments and financial support of new research and development candidates including increase of personnel, all of which may be substantial;
- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities;

- higher-than-expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and could have a material adverse effect on our business, results of operations, financial condition and prospects.

***Our CMOs manufacture tenapanor API outside of the U.S., and we may seek and obtain approval to commercialize IBSRELA and XPHOZAH outside of the U.S., and as a result a variety of risks associated with international operations could materially adversely affect our business.***

We or our collaboration partners may decide to seek marketing approval for IBSRELA or XPHOZAH outside the U.S. Additionally, we have contractual agreements with CMOs involving the manufacture of tenapanor API outside of the U.S., and may otherwise engage in business outside of the U.S., including entering into additional contractual agreements with third parties. We are subject to additional risks related to entering these international business markets and relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs;
- 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;
- foreign taxes, including withholding of payroll taxes;
- 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 U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

***Our business involves the use of hazardous materials and we and third-parties with whom we contract must comply with environmental laws and regulations, which can be expensive and restrict how we do business.***

We and manufacturers and suppliers with whom we may contract are subject to laws and regulations governing the use, manufacture, storage, handling, and disposal of hazardous materials, including the components of our tenapanor and our product candidates. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, and business operations, and could result in environmental damage requiring costly clean-up and resulting in liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. We cannot guarantee that the safety procedures utilized by third-party manufacturers and suppliers with whom we may contract will comply with the standards prescribed by laws and regulations or will eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage.

***We may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.***

We currently occupy a leased facility located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our leased facilities, including our California facility, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

#### **Risks Related to Government Regulation**

***Despite having received regulatory approval for IBSRELA, and even if we receive regulatory approval for XPHOZAH, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, IBSRELA and, if approved, XPHOZAH could be subject to other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.***

Even if a drug is approved by the FDA or foreign regulatory authorities, the manufacturing processes, labeling, packaging, distribution, pharmacovigilance, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP regulations for any clinical trials that we conduct post-approval. As such, we and our third-party CMOs will be subject to continual review and periodic inspections to assess compliance with regulatory requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Regulatory authorities may also impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance.

We will also be required to report certain adverse reactions and production problems, if any, to the FDA, and to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote our products for indications or uses for which they do not have FDA approval.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- warning or untitled letters or fines;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- injunctions or the imposition of civil or criminal penalties;
- suspension or revocation of existing regulatory approvals;
- suspension of any of our ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications submitted by us;
- restrictions on our or our CMOs' operations; or
- product seizure or detention, or refusal to permit the import or export of products.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize IBSRELA and, if approved, XPHOZAH. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

In addition, the FDA's policies may change, and additional government regulations may be enacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad.

***Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, or otherwise review and process regulatory submissions in a timely manner, which could negatively impact our business.***

The ability of the FDA to review and process regulatory submissions can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

***We and our CMOs are subject to significant regulation with respect to manufacturing IBSRELA and XPHOZAH. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.***

All entities involved in the preparation of product for commercial sale, or product candidates for clinical trials, including our existing contract manufacturers are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP regulations. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our products or product candidates that may not be detectable in final product testing. We or our CMOs must supply all necessary

documentation in support of an NDA or comparable regulatory filing on a timely basis and must adhere to cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the manufacture of our product or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the CMOs, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent suspension of production or closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA or other applicable regulatory authority can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product, withdrawal of an approval, or suspension of production. As a result, our business, financial condition, and results of operations may be materially harmed.

Additionally, if supply from one approved manufacturer is interrupted, an alternative manufacturer would need to be qualified through an NDA, a supplemental NDA or equivalent foreign regulatory filing, which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause us to incur higher costs and could cause the delay or termination of clinical studies, regulatory submissions, required approvals, or commercialization of our product candidates. Furthermore, if our suppliers fail to meet contractual requirements and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed, or we could lose potential revenue.

***If we fail to comply or are found to have failed to comply with FDA and other regulations related to the promotion of our products for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.***

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. With respect to the commercialization of IBSRELA and/or, if approved, XPHOZAH we will be restricted from marketing the product outside of its approved labeling, also referred to as off-label promotion. However, physicians may nevertheless prescribe an approved product to their patients in a manner that is inconsistent with the approved label, which is an off-label use. We have implemented compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations regarding off-label promotion. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our product candidates for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the FTC and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government

alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as “whistleblower suits,” are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

***IBSRELA and/or, if approved, XPHOZAH may cause or contribute to adverse medical events that we are required to report to regulatory agencies and if we fail to do so we could be subject to sanctions that would materially harm our business.***

We are required to report certain information about adverse medical events if our products may have caused or contributed to those adverse events. The timing of our obligation to report is triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory agency could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

***Our employees, independent contractors, principal investigators, CROs, collaboration partners, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.***

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, collaboration partners, 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 any of the following: FDA regulations, including those laws that require the reporting of true, complete and accurate financial and other information to the FDA; manufacturing standards; or federal and state healthcare fraud and abuse laws and regulations. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These activities also include the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other 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 comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

***Failure to obtain regulatory approvals in foreign jurisdictions would prevent us from marketing our products internationally.***

In order to market any product in the EEA (which is composed of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, separate regulatory approvals are required. In the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization (“MA”). Before the MA is granted, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for regulatory approvals or to do so on a timely basis, and even if we do file, we may not receive necessary approvals to commercialize our products in any market.

***We and our collaboration partners are subject to healthcare laws, regulation and enforcement; our failure or the failure of any such collaboration partners to comply with these laws could have a material adverse effect on our results of operations and financial conditions.***

We and our collaboration partners are subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. The laws that may affect our ability to operate as a commercial organization include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the false claims statutes;
- the federal Civil Monetary Penalties law, which prohibits, among other things, offering or transferring remuneration to a federal healthcare beneficiary that a person knows or should know is likely to influence the beneficiary's decision to order or receive items or services reimbursable by the government from a particular provider or supplier;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation;
- the federal physician sunshine requirements under the ACA, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to CMS information related to payments and other transfers of value to physicians, (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and teaching hospitals, and ownership and investment interests held by physicians (as defined by the statute) and their immediate family members;
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers;
- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources;
- state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or pricing information and marketing expenditures; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.



Because of the breadth of these laws 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. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to market our products and adversely impact our financial results.

***Legislative or regulatory healthcare reforms in the U.S. may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates and to produce, market and distribute our products after clearance or approval is obtained.***

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the regulatory clearance or approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recall, replacement, or discontinuance of one or more of our products; and
- additional record keeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products would harm our business, financial condition and results of operations.

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the U.S., the ACA was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. The ACA, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. These new laws, among other things, included aggregate reductions of Medicare payments to providers that will remain in effect through 2032, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022, unless additional action is taken by Congress, additional specific reductions in Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, beginning January 1, 2024.

Recently, there has also been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. On August 16, 2022, the Inflation Reduction Act of 2022 (the “IRA”) was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023), and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated. Additionally, individual states have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing.

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 any drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a 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 our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs in the U.S., we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, results of operations and financial condition.***

With the commercial launch of IBSRELA, we participate in the Medicaid Drug Rebate Program (“MDRP”) and other federal and state government pricing programs in the U.S., and we may participate in additional government pricing programs in the future. These programs generally require manufacturers to pay rebates or otherwise provide discounts to government payors in connection with drugs that are dispensed to beneficiaries of these programs. Medicaid drug rebates are based on pricing data that we will be obligated to report on a monthly and quarterly basis to the U.S. Centers for Medicare & Medicaid Services (“CMS”), the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the average manufacturer price (“AMP”) and the best price (“BP”) for each drug. If we become aware that our MDRP price reporting submission for a prior period was incorrect or has changed as a result of recalculation of the pricing data, we must resubmit the corrected data for up to three years after those data originally were due. In addition, there is increased focus by the Office of Inspector General within the U.S. Department of Health and Human Services on the methodologies used by manufacturers to calculate AMP, and BP, to assess manufacturer compliance with MDRP reporting requirements. If we fail to provide information timely or are found to have knowingly submitted false information to the government, we may be subject to civil monetary penalties and other sanctions, including termination from the MDRP, which would result in payment not being available for our covered drugs under Medicaid. Failure to make necessary disclosures and/or to identify overpayments could result in allegations against us under the Federal False Claims Act and other laws and regulations.

Federal law requires that a manufacturer that participates in the MDRP also participate in the Public Health Service’s 340B drug pricing program (“340B program”) in order for federal funds to be available for the manufacturer’s drugs under Medicaid. We participate in the 340B program, which is administered by the Health Resources and Services Administration (“HRSA”), and requires us to charge statutorily defined covered entities no more than the 340B “ceiling price” for our covered drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the AMP and rebate amount for the covered drug as calculated under the MDRP. In general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. We are obligated to report 340B ceiling prices to HRSA on a quarterly basis, and HRSA publishes them to 340B covered entities. HRSA has finalized regulations regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities for 340B-eligible drugs. HRSA has also finalized an administrative dispute resolution process through which 340B covered entities may pursue claims against participating manufacturers for overcharges, and through which manufacturers may pursue claims against 340B covered entities for engaging in unlawful diversion or duplicate discounting of 340B drugs.

In order to be eligible to have drug products paid for with federal funds under Medicaid and purchased by certain federal agencies and grantees, we also participate in the U.S. Department of Veterans Affairs (“VA”) Federal Supply Schedule (“FSS”) pricing program. Under the VA/FSS program, we are obligated to report the Non-Federal Average Manufacturer Price (“Non-FAMP”) for our covered drugs to the VA and charge certain federal agencies no more than the Federal Ceiling Price, which is calculated based on Non-FAMP using a statutory formula. These four agencies are the VA, the U.S. Department of Defense, the U.S. Coast Guard, and the U.S. Public Health Service (including the Indian Health Service). We are also required to pay rebates on products purchased by military personnel and dependents through the TRICARE retail pharmacy program. If we fail to provide timely information or are found to have knowingly submitted false information, we may be subject to civil monetary penalties.

Individual states continue to consider and have enacted legislation to limit the growth of healthcare costs, including the cost of prescription drugs and combination products. A number of states have either implemented or are considering implementation of drug price transparency legislation that may prevent or limit our ability to take price increases at certain rates or frequencies. Requirements under such laws include advance notice of planned price increases, reporting price increase amounts and factors considered in taking such increases, wholesale acquisition cost information disclosure to prescribers, purchasers, and state agencies, and new product notice and reporting. Such legislation could limit the price or payment for IBSRELA and, if approved and launched, XPHOZAH, and a number of states are authorized to impose civil monetary penalties or pursue other enforcement mechanisms against manufacturers who fail to comply with drug price transparency requirements, including the untimely, inaccurate, or incomplete reporting of drug pricing information. If we are found to have violated state law requirements, we may become subject to penalties or other enforcement mechanisms, which could have a material adverse effect on our business.

Pricing and rebate calculations are complex, vary among products and programs, and are often subject to interpretation by us, governmental or regulatory agencies, and the courts. The terms, scope and complexity of these government pricing programs change frequently, as do interpretations of applicable requirements for pricing and rebate calculations. Responding to current and future changes may increase our costs and the complexity of compliance will be time consuming. Any required refunds to the U.S. government or responding to a government investigation or enforcement action would be expensive and time consuming and could have a material adverse effect on our business, results of operations and financial condition. Price recalculations under the MDRP also may affect the ceiling price at which we are required to offer products under the 340B program. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. In the event that CMS were to terminate our Medicaid rebate agreement, no federal payments would be available under Medicaid or Medicare for IBSRELA or, if approved and launched, XPHOZAH. We cannot offer any assurances that our submissions will not be found to be incomplete or incorrect.

## **Risks Related to Intellectual Property**

### ***Our success will depend on our ability to obtain, maintain and protect our intellectual property rights***

Our success and ability to compete depend in part on our ability to obtain, maintain and enforce issued patents, trademarks and other intellectual property rights and proprietary technology in the U.S. and elsewhere. If we cannot adequately obtain, maintain and enforce our intellectual property rights and proprietary technology, competitors may be able to use our technologies or the goodwill we have acquired in the marketplace and erode or negate any competitive advantage we may have and our ability to compete, which could harm our business and ability to achieve profitability and/or cause us to incur significant expenses.

We rely on a combination of contractual provisions, confidentiality procedures and patent, trademark, copyright, trade secret and other intellectual property laws to protect the proprietary aspects of our products, product candidates, brands, technologies, trade secrets, know-how and data. These legal measures afford only limited protection, and competitors or others may gain access to or use our intellectual property rights and proprietary information. Our success will depend, in part, on preserving our trade secrets, maintaining the security of our data and know-how and obtaining, maintaining and enforcing other intellectual property rights. We may not be able to obtain, maintain and/or enforce our intellectual property or other proprietary rights necessary to our business or in a form that provides us with a competitive advantage.

Failure to obtain, maintain and/or enforce intellectual property rights necessary to our business and failure to protect, monitor and control the use of our intellectual property rights could negatively impact our ability to compete and cause us to incur significant expenses. The intellectual property laws and other statutory and contractual arrangements in the U.S. and other jurisdictions we depend upon may not provide sufficient protection in the future to prevent the infringement, use, violation, or misappropriation of our patents, trademarks, data, technology, and other intellectual property rights and products by others; and may not provide an adequate remedy if our intellectual property rights are infringed, misappropriated, or otherwise violated by others.

We rely in part on our portfolio of issued and pending patent applications in the U.S. and other countries to protect our intellectual property and competitive position. However, it is also possible that we may fail to identify patentable aspects of inventions made in the course of our development, manufacture and commercialization activities before it is too late to obtain patent protection on them. If we fail to timely file for patent protection in any jurisdiction, we may be precluded from doing so at a later date. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, suppliers, consultants, advisors, and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in any of our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Moreover, should we become a licensee of a third party's patents or patent applications, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted, maintained and/or enforced in a manner consistent with the best interests of our business. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent positions of companies, including our patent position, may involve complex legal and factual questions that have been the subject of much litigation in recent years, and, therefore, the scope of any patent claims that we have or may obtain cannot be predicted with certainty. Accordingly, we cannot provide any assurances about which of our patent applications will issue, the breadth of any resulting patent, whether any of the issued patents will be found to be infringed, invalid or unenforceable or will be threatened or challenged by third parties, that any of our issued patents have, or that any of our currently pending or future patent applications that mature into issued patents will include, claims with a scope sufficient to protect our products and services. Our pending and future patent applications may not result in the issuance of patents or, if issued, may not issue in a form that will be advantageous to us. The coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing, manufacturing and commercializing a product or technologies in a non-infringing manner that would be competitive with one or more of our products or technologies, or otherwise provide us with any competitive advantage. Furthermore, any successful challenge to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for our commercial success. Further, there can be no assurance that we will have adequate resources to enforce our patents.

Patents have a limited lifespan. In the U.S., the natural expiration of a utility patent is generally 20 years from the earliest effective non-provisional filing date. Though an issued patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products or services. Patents, if issued, may be challenged, deemed unenforceable, invalidated, narrowed or circumvented. Proceedings challenging our patents or patent applications could result in either loss of the patent, or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. Any successful challenge to our patents and patent applications could deprive us of exclusive rights necessary for our commercial success. In addition, defending such challenges in such proceedings may be costly. Thus, any patents that we may own may not provide the anticipated level of, or any, protection against competitors. Furthermore, an adverse decision may result in a third party receiving a patent right sought by us, which in turn could affect our ability to develop, manufacture or commercialize our products or technologies.

Some of our patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products, services and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- Any of our patents, or any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our products or product candidates;
- Any of our pending patent applications will issue as patents;
- We were the first to make the inventions covered by each of our patents and pending patent applications;
- We were the first to file patent applications for these inventions;
- Others will not develop, manufacture and/or commercialize similar or alternative products or technologies that do not infringe our patents;
- Any of our challenged patents will be found to ultimately be valid and enforceable;
- Any patents issued to us will provide a basis for an exclusive market for our commercially viable products or technologies will provide us with any competitive advantages or will not be challenged by third parties;
- We will develop additional proprietary technologies or products that are separately patentable; or
- Our commercial activities or products will not infringe upon the patents of others.

***We may become subject to third-party claims alleging infringement, misappropriation or violation of such third parties' patents or other intellectual property rights and/or third-party claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development, manufacture or commercialization of our products or product candidates.***

Our commercial success depends, in part, on our ability to develop, manufacture or commercialize our products and product candidates without infringing, misappropriating or otherwise violating the intellectual property rights of third parties. There have been many lawsuits and other proceedings asserting infringement or misappropriation of patents and other intellectual property rights in the pharmaceutical and biotechnology industries, and companies in the industry have used intellectual property litigation to gain a competitive advantage. While we take steps to ensure that we do not infringe upon, misappropriate or otherwise violate the intellectual property rights of others, there can be no assurances that we will not be subject to claims alleging that the manufacture, use or sale of IBSRELA or XPHOZAH or of any other product candidates infringes existing or future third-party patents, or that such claims, if any, will not be successful. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of IBSRELA or XPHOZAH or other product candidates. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of IBSRELA or XPHOZAH or our other product candidates.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights. These proceedings could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third party's patents. We may be required to indemnify future collaboration partners against such claims. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us, we could be forced to stop or delay development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we may choose to seek, or be required to seek, a license from the third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, we may be unable to maintain such licenses and the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms, or unable to maintain such licenses when granted. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

We also could be ordered to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third party's patents or other intellectual property right. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third party patents are valid and enforceable, and infringed by the use of our products and/or technologies, which could have a negative impact on the commercial success of our current and any future products or technologies. If we were to challenge the validity of any such third party U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. We will have similar burdens to overcome in foreign courts in order to successfully challenge a third party claim of patent infringement. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

In addition to infringement claims against us, third parties may also raise similar claims before administrative bodies in the U.S. or abroad. Such mechanisms include reexamination, post grant review, inter parties review, derivation or opposition proceedings before the United States Patent and Trademark Office ("USPTO") or other jurisdictional body relating to our intellectual property rights or the intellectual property rights of others. If third parties prepare and file patent applications in the U.S. that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the USPTO to determine which party is entitled to a patent on the disputed invention. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to our products and technology. Since patent applications are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Such administrative proceedings could result in revocation of or amendment to our patents in such a way that they no longer cover our products or product candidates. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity and/or unenforceability, we may lose at least part, and perhaps all, of the patent protection on our products or technologies. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations, and prospects.

***If our intellectual property related to IBSRELA, XPHOZAH, RDX013 or any future product candidates is not adequate or if we are not able to successfully enforce our intellectual property rights, the commercial value of IBSRELA, if approved, XPHOZAH, or other product candidates may be adversely affected and we may not be able to compete effectively in our market.***

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the U.S. or in foreign countries. Additionally, our research and development efforts may result in product candidates for which patent protection is limited or not available. Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time before one year after that person is served an infringement complaint based on the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the U.S., Europe and other jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third party may develop a competitive product that provides therapeutic benefits similar to one or more of our product candidates but has a sufficiently different composition to fall outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to IBSRELA, XPHOZAH, RDX013 or any future product candidates is successfully challenged, then our ability to commercialize such product could be negatively affected, and we may face unexpected competition that could have a material adverse impact on our business. Further, we have reported that we have completed the data analysis from our Phase 2 clinical trial evaluating the safety and efficacy of RDX013 for the treatment of hyperkalemia, and that we currently expect that the next steps for the RDX013 program will be to evaluate a new formulation that potentially enhances subject compliance and the efficacy of RDX013 in an additional Phase 2 clinical study. We currently expect to delay further development of RDX013 until such time as we have determined that our available resources support conducting such additional formulation work and an additional clinical study. As a result of this delay in our development program for RDX013, the period of time during which we or our collaboration partners could market RDX013 under patent protection would be reduced.

Even where laws provide protection, costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. If we or one of our collaboration partners were to initiate legal proceedings against a third party to enforce a patent covering a product or product candidate, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability against our intellectual property related to a product or a product candidate, we would lose at least part, and perhaps all, of the patent protection on such product or product candidate. Such a loss of patent protection would have a material adverse impact on our business. Moreover, our competitors could counterclaim that we infringe their intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

We also rely on trade secret protection and confidentiality agreements to protect proprietary know-how that may not be patentable, processes for which patents may be difficult to obtain and/or enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology, to assign their inventions to us, and endeavor to execute confidentiality agreements with all such parties, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements will not be breached by such consultants, advisors or third parties, or by our former employees. The breach of such agreements by individuals or entities who were actively involved in the discovery and design of our products or potential drug candidates, or in the development of our discovery and design platform could require us to pursue legal action to protect our trade secrets and confidential information, which would be expensive, and the outcome of which would be unpredictable. If we are not successful in prohibiting the continued breach of such agreements, our business could be negatively impacted. We cannot guarantee that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

***Although we have obtained patent term extension in the U.S. under the Hatch-Waxman Act, extending the term of marketing exclusivity for tenapanor, if we do not obtain patent term extension in foreign countries under similar legislation, our business may be materially harmed.***

Following the approval by the FDA for our NDA to market tenapanor for IBS-C, we obtained patent term restoration under the Hatch-Waxman Act until August 1, 2033 for U.S. patent no. 8,541,448 covering our approved product or the use thereof. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Despite seeking patent term extension for tenapanor, we may not be granted patent term extension in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

If we are unable to obtain patent term extension or restoration in any particular foreign country, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product in such foreign country will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

***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.***

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. Noncompliance with these requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the U.S. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties.

Europe's planned Unified Patent Court may, in particular, present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. In 2012, the European Patent Package ("EU Patent Package") regulations were passed with the goal of providing a single pan-European Unitary Patent and a new European Unified Patent Court ("UPC"), for litigation involving European patents. Implementation of the EU Patent Package will likely occur in the first half of 2023. Under the UPC, all European patents, including those issued prior to ratification of the European Patent Package, will by default automatically fall under the jurisdiction of the UPC. The UPC will provide our competitors with a new forum to centrally revoke our European patents, and allow for the possibility of a competitor to obtain pan-European injunctions. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by the UPC. Under the EU Patent Package as currently proposed, we will have the right to opt our patents out of the UPC over the first seven years of the court's existence, but doing so may preclude us from realizing the benefits of the new unified court.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the U.S. and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

***We may be subject to claims that we or our employees have misappropriated the intellectual property, including know-how or trade secrets, of a third party, or claiming ownership of what we regard as our own intellectual property.***

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors do not use the intellectual property and other proprietary information or know-how or trade secrets of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may be subject to claims that we or these employees, consultants and contractors have used or disclosed such intellectual property, including know-how, trade secrets or other proprietary information. In addition, an employee, advisor or consultant who performs work for us may have obligations to a third party that are in conflict with their obligations to us, and as a result such third party may claim an ownership interest in the intellectual property arising out of work performed for us. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.



In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

## **Risks Related to Our Common Stock**

***Our stock price may be volatile and our stockholders may not be able to resell shares of our common stock at or above the price they paid.***

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this “Risk Factors” section and others such as:

- the success or lack of success with regards to our commercialization of IBSRELA;
- announcements of regulatory decisions regarding our NDA seeking marketing approval for XPHOZAH;
- the success or lack of success with regards to our commercial launch of XPHOZAH, if approved;
- results of regulatory inspections of our facilities or those of our CMOs, or specific label restrictions or patient populations for XPHOZAH’s use, if approved, or changes or delays in the regulatory review process;
- results of regulatory inspections of our facilities or those of our CMOs, or specific label restrictions or patient populations for XPHOZAH’s use, if approved, or changes or delays in the regulatory review process;
- announcements regarding whether XPHOZAH, if approved, alone or with other oral only medications, will be included in the ESRD prospective payment system, and the time and manner in which such transition is achieved;
- announcements relating to our current or future collaboration partnerships;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our product label, our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to our approved products or our product candidates;
- the success of our testing and clinical trials;
- failure to meet any of our projected timelines or goals with regard to the commercialization of IBSRELA, the commercial launch of XPHOZAH, if approved, or the clinical development and commercialization of any of our product candidates;
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- the success of our efforts to obtain adequate intellectual property protection for our product candidates;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;

- FDA or other U.S. or foreign regulatory actions affecting us or our industry or other healthcare reform measures in the U.S.;
- changes in financial estimates or recommendations by securities analysts;
- trading volume of our common stock;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- sales of debt securities and sales or licensing of assets;
- general economic and market conditions and overall fluctuations in the U.S. equity markets; and
- the loss of any of our key scientific or management personnel.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

***If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.***

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

## **General Risk Factors**

***We incur significant costs as a result of operating as a public company, and our management will devote substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm our business.***

We incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended (“Exchange Act”) and regulations regarding corporate governance practices. The listing requirements of The Nasdaq Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors’ and officers’ insurance, on acceptable terms.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002 (“Section 404”) and the related rules of the Securities and Exchange Commission (“SEC”) which generally require, among other things, our management to report on the effectiveness of our internal control over financial reporting, subject to certain exceptions applicable to non-accelerated filers. Our compliance with Section 404 requires that we incur substantial expense and expend significant management efforts.

During the course of our review and testing of our internal controls, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Market or other adverse consequences that would materially harm our business.

***We may be adversely affected by the global economic environment.***

Our ability to attract and retain collaboration partners or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the U.S., presidential elections, other political influences and inflationary pressures. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets, including the current inflationary environment and rising interest rates. For example, the 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. We cannot anticipate all the ways in which the global economic climate and global financial market conditions could adversely impact our business in the future.

We are exposed to risks associated with reduced profitability and the potential financial instability of our collaboration partners or customers, many of which may be adversely affected by volatile conditions in the financial markets. For example, unemployment and underemployment, and the resultant loss of insurance, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, our collaboration partners or customers may experience reductions in revenues, profitability and/or cash flow that could lead them to reduce their support of our programs or financing activities. If collaboration partners or customers are not successful in generating sufficient revenue or are precluded from securing financing, they may not be able to pay, or may delay payment of, accounts receivable that are owed to us. In addition, volatility in the financial markets could cause significant fluctuations in the interest rate and currency markets. We currently do not hedge for these risks. The foregoing events, in turn, could adversely affect our financial condition and liquidity. In addition, if economic challenges in the U.S. result in widespread and prolonged unemployment, either regionally or on a national basis, or if certain provisions of the Patient Protection and ACA, as amended by the Health Care and Education Reconciliation Act, collectively known as the ACA, are repealed, a substantial number of people may become uninsured or underinsured. To the extent economic challenges result in fewer individuals pursuing or being able to afford our product candidates once commercialized, our business, results of operations, financial condition and cash flows could be adversely affected.

***Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.***

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least two-thirds of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;

- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

***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 amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such a 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.
- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnities, except with respect to proceedings authorized by our board of directors or brought to enforce a right 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.

- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

***We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.***

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Additionally, the terms of our loan and security agreements could restrict our ability to pay dividends. Therefore, our stockholders are not likely to receive any dividends on our common stock for the foreseeable future. Since we do not intend to pay dividends, our stockholders' ability to receive a return on their investment will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

***The continuing impact of "Brexit" may have a negative effect on our business.***

Following a national referendum and subsequent legislation the United Kingdom formally withdrew from the European Union, commonly referred to as "Brexit" and ratified a trade and cooperation agreement governing its future relationship with the European Union. Among other things, the agreement became effective in 2021, addresses trade, economic arrangements, law enforcement, judicial cooperation and governance. Because the agreement merely sets forth a framework that in many respects requires complex additional bilateral negotiations between the United Kingdom and the European Union significant uncertainty remains about how the precise terms of the relationship between the parties will differ from the terms before withdrawal.

We cannot yet predict the full implications of Brexit, including whether it will increase our operational costs or otherwise have a negative effect on our business, financial condition or results of operations, which could reduce the price of our common stock.

#### **ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

#### **ITEM 2. PROPERTIES**

Our headquarters is currently located in Waltham, Massachusetts and consists of 12,864 square feet of leased office space under a lease agreement that expires in June 2026. In addition, we lease 72,500 square feet of office and laboratory space in Fremont, California under a lease agreement that expires in March 2025 and 4,768 square feet of office space in Milwaukee, Wisconsin under a lease agreement that expires in February 2026. Prior to October 2021, our headquarters were co-located in Fremont, California and Waltham, Massachusetts.

#### **ITEM 3. LEGAL PROCEEDINGS**

On July 30 and August 12, 2021, two putative securities class action lawsuits were commenced in the U.S. District Court for the Northern District of California naming as defendants Ardelyx and two current officers captioned *Strezsak v. Ardelyx, Inc., et al.*, Case No. 4:21-cv-05868-HSG, and *Siegel v. Ardelyx, Inc., et al.*, Case No. 5:21-cv-06228-HSG (together, the "Securities Class Actions"). The complaints allege that the defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 thereunder, by making false and misleading statements and omissions of material fact related to tenapanor. The plaintiffs seek to represent all persons who purchased or otherwise acquired Ardelyx securities between August 6, 2020, and July 19, 2021. The plaintiffs seek damages and interest, and an award of costs, including attorneys' fees. On July 19, 2022, the court consolidated the two putative class actions and appointed a lead plaintiff and lead counsel. The lead plaintiff filed an amended complaint on September 29, 2022. Defendants filed a motion to dismiss the amended complaint on December 2, 2022. In January and February 2023, in lieu of filing a response to defendant's motion to dismiss, plaintiffs filed a motion seeking leave to further amend their complaint and defendants filed an opposition to the motion for leave to further amend the complaint. A hearing on the motion for leave to further amend the complaint is scheduled for mid-May 2023. We believe the plaintiff's claims are without merit and we have not recorded any accrual for a contingent liability associated with these legal proceedings.

On December 7, 2021 and March 29, 2022, two verified shareholders derivative lawsuits were filed in the U.S. District Court for the Northern District of California purportedly on behalf of Ardelyx against certain of Ardelyx's executive officers and members of our board of directors, captioned Go v. Raab, et al., Case No. 4:21-cv-09455-HSG, and Morris v. Raab, et al., Case No. 4:22-cv-01988-JSC. The complaints allege that the defendants violated Section 14(a) of the Securities Exchange Act of 1934, as amended, breaches of fiduciary duties, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets for personally making and/or causing Ardelyx to make materially false and misleading statements regarding the Company's business, operations and prospects. The complaint seeks contribution under Sections 10(b) and 21D of the Securities Exchange Act of 1934, as amended, from two executive officers. On January 19, and April 27, 2022, the court granted the parties' stipulation to stay the Go and Morris actions, respectively, until resolution of the anticipated motion(s) to dismiss in the Securities Class Actions. On October 25, 2022, the parties filed a stipulation to consolidate and stay the Go and Morris actions, and on October 27, 2022, the court consolidated the Go and Morris action and stayed the consolidated action pending resolution of the anticipated motion(s) to dismiss in the Securities Class Action. We believe the plaintiff's claims are without merit and we have not recorded any accrual for a contingent liability associated with these legal proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. As of December 31, 2022, there is no litigation pending that would reasonably be expected to have a material adverse effect on our results of operations and financial condition, and no contingent liabilities were accrued as of December 31, 2022.

**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

#### Common Stock

On June 19, 2014, our common stock commenced trading on The Nasdaq Global Market under the symbol "ARDX". Prior to that date, there was no public trading market for our common stock. As of December 31, 2022, there were 27 holders of record of our common stock.

#### Dividends

We have never declared or paid cash dividends on our capital stock. We currently intend to retain any future earnings to finance the growth and development of our business.

#### Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item regarding executive compensation will be incorporated by reference to the information set forth in the sections titled "Executive Compensation" in our Proxy Statement.

#### Recent Sales of Unregistered Securities

None.

#### Use of Proceeds

Not applicable.

#### Issuer Purchases of Equity Securities

Not applicable.

### ITEM 6. [RESERVED]

### ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our financial statements and related notes included elsewhere in this report. This discussion and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this report entitled "Risk Factors." These forward-looking statements speak only as of the date hereof. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason. Unless the context requires otherwise, the terms "Ardelyx", "Company", "we", "us", and "our" refer to Ardelyx, Inc.*

#### OVERVIEW

We are a biopharmaceutical company founded with a mission to discover, develop and commercialize innovative first-in-class medicines that meet significant unmet medical needs. We developed a unique and innovative platform that enabled the discovery of new biological mechanisms and pathways to develop potent, and efficacious therapies that minimize the side effects and drug-drug interactions frequently encountered with traditional, systemically absorbed medicines. The first molecule we discovered and developed was tenapanor, a targeted, first-in-class, oral, small molecule therapy. Tenapanor, branded as IBSRELA, is approved in the U.S. for the treatment of adults with irritable bowel syndrome with constipation ("IBS-C"). Tenapanor is in development for the control of serum phosphorus, or hyperphosphatemia, in adult patients with chronic kidney disease ("CKD") on dialysis under the brand name XPHOZAH. We also have a development stage asset, RDX013 for adult patients with CKD and/or heart failure with hyperkalemia, or elevated serum potassium, and a discovery stage asset, RDX020, for adult patients with metabolic acidosis, a serious electrolyte disorder, in patients with CKD.

Since commencing operations in October 2007, substantially all our efforts have been dedicated to our research and development (“R&D”) activities, including developing tenapanor and developing our proprietary drug discovery and design platform. We realized our first product sales of IBSRELA<sup>®</sup> (tenapanor) in March 2022. As of December 31, 2022, we had an accumulated deficit of \$780.1 million.

We expect to continue to incur substantial operating losses for the foreseeable future as we invest in the commercialization of IBSRELA, seek to gain approval in the U.S. for XPHOZAH<sup>®</sup> (tenapanor); prepare for and commercialize XPHOZAH in the U.S., if approved; and incur manufacturing and development cost for tenapanor. To date, we have funded our operations from the sale and issuance of common stock and convertible preferred stock, funds from our collaboration partnerships, which includes license fees, milestones and product supply revenue, funds from our loan agreements with our lenders, as well as from sales of IBSRELA.

## **OUR COMMERCIAL PRODUCT**

### ***IBSRELA for IBS-C***

Our unique discovery platform and deep understanding of the primary mechanism of sodium transport in the intestine resulted in our discovery and development of IBSRELA, a first-in-class, U.S. Food and Drug Administration (“FDA”) approved, sodium hydrogen exchange 3 (“NHE3”) inhibitor for the treatment of IBS-C in adults. IBSRELA acts locally in the gut and is minimally absorbed. IBS-C is a gastrointestinal (“GI”) disorder characterized by both abdominal pain and altered bowel movements, and is estimated to affect 12 million people in the U.S. IBS-C is associated with significantly impaired quality of life, reduced productivity, and substantial economic burden.

We recognized our first sales of IBSRELA in the U.S. in March 2022. For our commercial launch of IBSRELA, we designed a market-responsive commercial strategy and built a commercial organization highly experienced in launching novel therapies into specialty areas. The dynamics of the IBS-C market reflect an established patient base, limited number of competitors all confined to a single mechanism of action, concentrated number of prescribers, and recognized unmet need. In addition, market research indicated a favorable response to the IBSRELA product profile as a novel mechanism therapy. These dynamics enabled a targeted promotional focus on patients currently being managed for IBS-C by the approximately 9,000 high-writing healthcare providers that account for 50% of IBS-C prescriptions. Central to the go to market strategy for IBSRELA is a highly experienced specialty sales force, many with existing relationships across their GI target base, full company engagement, and innovative peer-to-peer and digital initiatives.

We expect competition for IBSRELA will come largely from the three prescription products indicated for IBS-C: Linzess (linaclotide), Amitiza (lubiprostone) and Trulance (plecanatide). Generic lubiprostone is also available in the U.S. Additionally, over-the-counter products, not indicated for IBS-C are commonly used to treat the constipation component of IBS-C, alone and in combination with the IBS-C-indicated prescription therapies.

We have established commercial agreements with Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. (“Fosun Pharma”) in China and Knight Therapeutics, Inc. (“Knight”) in Canada for IBSRELA for IBS-C. Knight is currently marketing IBSRELA in Canada.

## **OUR PRODUCT PIPELINE**

### ***Development Candidate XPHOZAH: A Potential New Approach for the Control of Serum Phosphorus in Adult Patients with CKD on Dialysis***

XPHOZAH (tenapanor) is a first-in-class medicine being developed for the control of serum phosphorus, or hyperphosphatemia, in adult patients with CKD on dialysis. XPHOZAH has a unique mechanism of action and acts locally in the gut to inhibit NHE3. This results in the tightening of the epithelial cell junctions, thereby significantly reducing paracellular uptake of phosphate, the primary pathway of phosphate absorption. It is estimated that there are more than 550,000 adult patients with CKD on dialysis in the U.S. and approximately 80% of those patients are being treated with phosphate lowering therapies. Seventy-seven percent of patients treated with phosphate binders to treat hyperphosphatemia were unable to consistently maintain phosphorous levels  $\leq 5.5$  mg/dL over a six-month period. If approved, XPHOZAH would be the first therapy for phosphate management that blocks phosphorus absorption at the primary site of uptake. It is not a phosphate binder.



In June 2020, we submitted a new drug application ("NDA") to the FDA for XPHOZAH. The NDA was supported by three Phase 3 trials involving more than 1,200 adult patients that evaluated the use of tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, with two trials evaluating tenapanor as monotherapy and one trial evaluating tenapanor as part of a dual mechanism approach with phosphate binders. All three Phase 3 trials met their primary and key secondary endpoints.

On July 28, 2021, we received a Complete Response Letter ("CRL") from the FDA's Division of Cardiology and Nephrology ("the Division") regarding our NDA for XPHOZAH. In December 2021 we submitted a Formal Dispute Resolution Request ("FDRR") to the Office of Cardiology, Hematology, Endocrinology and Nephrology ("OCHEN"). At the request of the FDA's Office of New Drugs ("OND"), as part of our second level of appeal of the CRL, a Cardiovascular and Renal Drug Advisory Committee meeting was held on November 16, 2022 with the committee voting that the benefits of XPHOZAH outweigh its risks nine to four as a monotherapy and ten to two, with one abstention, in combination with phosphate binder therapy. In December 2022, the OND granted our appeal to the CRL for the NDA for XPHOZAH and directed the Division to work with us to develop an appropriate label for the commercialization of XPHOZAH. We believe that a label could reflect an indication for patients whose hyperphosphatemia is insufficiently managed on binder therapy. On February 13, 2023, we participated in a Type A meeting with the Division where we discussed the resubmission of the NDA, and the information to be contained in the resubmitted NDA. We currently expect to resubmit the NDA for XPHOZAH early in the second quarter of 2023. Within thirty (30) days of resubmitting the NDA, we expect to receive notification from the Division as to the classification of the resubmission (Class 1 or Class 2) at which point the expected timing for review will also be known (2-months for a Class 1 and 6-months for a Class 2) as well as a goal review date. We currently that the FDA will act upon the XPHOZAH NDA in the second half of 2023, and that, if approved, we will launch XPHOZAH in the second half of 2023.

We have established commercial agreements with Kyowa Kirin, Co. Ltd. ("KKC") in Japan, Fosun Pharma in China and Knight in Canada for tenapanor for hyperphosphatemia. In October 2022, KKC submitted an NDA to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis.

### **Discovery and Developmental Assets**

We have a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia, or elevated serum potassium. Hyperkalemia is a common problem in patients with heart and kidney disease, particularly in patients taking customary blood pressure medications known as renin-angiotensin-aldosterone system ("RAAS") inhibitors. RDX013 is a novel mechanism agent designed to target the underlying biological mechanisms of potassium secretion to lower elevated potassium. We have completed a Phase 2 dose ranging clinical trial evaluating the safety and efficacy of RDX013 for the treatment of hyperkalemia in CKD patients who are not on dialysis. While the results of the study demonstrated an acceptable safety and tolerability profile for RDX013 and supported proof of concept in its ability to lower serum potassium levels, with statistically significant reductions compared to placebo after eight days of treatment, the study did not meet its primary endpoint of significantly reducing serum potassium levels compared to placebo after four weeks of treatment.

We have a discovery program targeting the inhibition of bicarbonate exchange inhibitor for the treatment of metabolic acidosis, a highly prevalent comorbidity in CKD patients that is strongly correlated with disease progression and adverse outcomes. We have identified lead compounds that are potent, selective and proprietary inhibitors of bicarbonate secretion.

We do not currently expect to meaningfully advance either of these two assets until such time as we have determined our available resources can support additional activities after prioritization of the commercialization of IBSRELA and, if approved, XPHOZAH.

## FINANCIAL OPERATIONS OVERVIEW

### *Revenue*

Our revenue to date has been generated primarily through license, research and development collaborative agreements with various collaboration partners. We realized our first commercial product sales of IBSRELA beginning in March 2022. In the future, we may generate revenue from a combination of our own product sales and payments in connection with our current or future collaborative partnerships, including license fees, other upfront payments, milestone payments, royalties and payments for drug product and/or drug substance. We expect that any revenue we generate will fluctuate in future periods as a result of, among other factors: the extent to which we are successful in our commercialization of IBSRELA; whether we are able to gain approval from the FDA for our NDA for XPHOZAH; our ability to obtain and sustain an adequate level of coverage and reimbursement for IBSRELA by third-party payors; whether and the extent to which we are successful in our commercialization of XPHOZAH, if approved; the timing and progress of goods and services provided pursuant to our current or future collaborative partnerships; our or our collaborators' achievement of clinical, regulatory or commercialization milestones, to the extent achieved; the timing and amount of any payments to us relating to the aforementioned milestones; addressing any competing technological and market developments; maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how, and our ability to develop, manufacture and commercialize our product candidates and products without infringing intellectual property rights of others; attracting, hiring, and retaining qualified personnel; and the extent to which tenapanor is approved and successfully commercialized by a collaboration partner. If our current collaboration partners or any future collaboration partners fail to obtain regulatory approval for tenapanor, our ability to generate future revenue from our collaborative arrangements, and our results of operations and financial position, would be materially and adversely affected. Our past revenue performance is not necessarily indicative of results to be expected in future periods.

### *Cost of Revenue*

Cost of revenue consists of the cost of commercial goods sold to our Customers and international partners under product supply agreements, as well as royalty expense based on sales of tenapanor. We capitalize inventory costs associated with the production of our products after regulatory approval or when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Otherwise, such costs are expensed as research and development. A portion of the costs of IBSRELA units recognized as revenue during the twelve months ended December 31, 2022 were expensed prior to the fourth quarter of 2021, at which time our intent to commercialize IBSRELA was established and we commenced preparation for the commercial launch of IBSRELA. We believe our cost of revenue for the year ended December 31, 2022 would have been \$1.9 million higher if we had not previously expensed certain material and production costs with respect to the units sold. As of December 31, 2022, we had approximately \$28.0 million of inventory on hand that was previously expensed as research and development expense and will not be reported as cost of revenue sold in future periods when sales of IBSRELA are recognized as revenue.

Cost of revenue includes payments due to AstraZeneca AB ("AstraZeneca"), which under the terms of a termination agreement entered into in 2015 ("AZ Termination Agreement") is entitled to (i) future royalties at a rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from our collaboration partners in connection with the development and commercialization of tenapanor or certain other NHE3 inhibitors. We have agreed to pay AstraZeneca up to a maximum of \$75.0 million in the aggregate for (i) and (ii). We recognize these expenses as cost of revenue when we recognize the corresponding revenue that gives rise to payments due to AstraZeneca. To date, we have recognized an aggregate of \$15.3 million as cost of revenue under the AZ Termination Agreement. See details in *Note 7, Collaboration and Licensing Agreements*, under AstraZeneca, in the notes to our financial statements, included in Part II, Item 8, of this Annual Report on Form 10-K.

### ***Research and Development***

Pursuant to the October 2021 restructuring plan, we eliminated our internal research organization and we do not currently expect to meaningfully advance our discovery efforts with respect to our discovery and developmental assets until such time as we have determined our available resources can support additional activities after prioritization of the commercialization of IBSRELA and, if approved, XPHOZAH. We recognize all research and development expenses as they are incurred to support the discovery, research, development and manufacturing of our product candidates. Research and development expenses include, but are not limited to, the following:

- external research and development expenses incurred under agreements with consultants, third-party contract research organizations (“CROs”) and investigative sites where a substantial portion of our clinical studies are conducted, and with contract manufacturing organizations where our clinical supplies are produced;
- expenses associated with supplies and materials consumed in connection with our research operations;
- expenses associated with producing XPHOZAH prior to FDA approval;
- expenses associated with producing discovery and developmental assets prior to FDA approval;
- other costs associated with research, clinical development and regulatory activities;
- employee-related expenses, which include salaries, bonuses, benefits, travel and stock-based compensation; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense, information technology expense and other supplies.

### ***Selling, General and Administrative***

Selling, general and administrative expenses relate to sales and marketing, finance, human resources, legal and other administrative activities, including information technology investments. Selling, general and administrative expenses consist primarily of personnel costs, outside professional services, marketing, advertising and legal expenses, facilities costs not otherwise allocated to research and development and other general and administrative costs.

### ***Interest Expense***

Interest expense represents the interest paid on our loan payable.

### ***Non-cash interest expense related to the sale of future royalties***

Non-cash interest expense related to the sale of future royalties represents the imputed interest expense on our deferred royalty obligation related to the sale of future royalties using the effective interest method. As further described in *Note 8. Deferred Royalty Obligation Related to the Sale of Future Royalties*, in June 2022, we and HealthCare Royalty Partners IV, L.P. (“HCR”) entered into a Royalty and Sales Milestone Interest Acquisition Agreement (“HCR Agreement”). Under the terms of the HCR Agreement, HCR agreed to pay us up to \$20.0 million in exchange for the royalty payments and commercial milestone payments (collectively the “Royalty Interest Payments”) that we may receive under our 2017 License Agreement with KKC based upon KKC's net sales of tenapanor in Japan for hyperphosphatemia. As part of the HCR Agreement, we received a \$10.0 million upfront payment from HCR in June 2022 and recorded it as a deferred royalty obligation on our balance sheet. Non-cash interest expense will be recognized over the life of the HCR Agreement using the effective interest method based on the imputed interest rate derived from estimated amounts and timing of future royalty payments to be received from KKC.

### ***Other Income, net***

Other income, net consists of interest income earned on our cash and cash equivalents and available-for-sale investments, the periodic revaluation of the exit fee related to our loan, gains on sales of property and equipment, and currency exchange gains and losses.

### ***Provision for Income Taxes***

Our provision for income taxes includes current and deferred tax, including foreign withholding taxes paid on payments received from certain collaboration partners. Deferred income taxes reflect the 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. Our deferred tax assets continue to be fully offset by a valuation allowance, including deferred tax assets related to our net operating loss carryforwards, which may be subject to annual limitations as a result of ownership changes that may have occurred or could occur in the future.

### **CRITICAL ACCOUNTING POLICIES AND ESTIMATES**

A detailed discussion of our significant accounting policies can be found in *Note 2, Summary of Significant Accounting Policies*, in the notes to our financial statements, included in Part II, Item 8, of this Annual Report on Form 10-K. Critical accounting policies are those that require significant judgment and/or estimates by management at the time that financial statements are prepared such that materially different results might have been reported if other assumptions had been made. These estimates form the basis for making judgments about the carrying values of assets and liabilities. We base our estimates and judgments on experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ materially from these estimates.

We consider certain accounting policies related to revenue recognition, accrued research and development expenses and stock-based compensation to be critical policies to understanding the judgments and estimates applied in our reported financial results.

### ***Product Sales, Net***

We account for our commercial product sales, net in accordance with Topic 606— *Revenue from Contracts with Customers*. We received approval from the FDA in September 2019 to market IBSRELA in the U.S. We began selling IBSRELA in the U.S. in March 2022. We distribute IBSRELA principally through major wholesalers, specialty pharmacies and group purchasing organizations ("GPOs") (collectively, our "Customers"). Our Customers subsequently sell IBSRELA to pharmacies and patients. Separately, we enter into arrangements with third parties that provide for government-mandated rebates, chargebacks and discounts. Revenue from product sales is recognized when our performance obligations are satisfied, which is when Customers obtain control of our product and occurs upon delivery.

### ***Reserves for Variable Consideration***

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration which may be settled in the form of off-invoice discounts, chargebacks, or rebates. Variable consideration includes discounts to customers and government programs, wholesaler fees, group purchasing organization administrative fees, patient copay assistance, and estimated product returns. These estimates are based on the amounts earned or to be claimed for related sales and are classified as reductions of gross accounts receivable if settlement is expected to occur through a reduction in the amounts paid by our Customers or a current liability if settlement is expected to occur through a payment from us. Where appropriate, these estimates are based on factors such as industry data and forecasted customer buying and payment patterns, our experience, current contractual and statutory requirements, specific known market events and trends. These reductions to gross sales reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. Variable consideration is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we adjust these estimates, which would affect product revenue and earnings in the period such variances become known. As we gain more experience, estimates will be more heavily based on the expected utilization from historical data we have accumulated since the IBSRELA product launch.

Rebates: Rebates include wholesaler fees, GPO fees, as well as mandated discounts under the Medicaid Drug Rebate Program ("Medicaid") and the Medicare Coverage Gap Program ("Medicare"). Estimates for rebates are recorded in the same period the related gross revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the balance sheets. We estimate our Medicaid and Medicare rebates based upon the estimated payor mix, and statutory discount rates. Our estimates for payor mix are guided by payor information received from specialty pharmacies, expected utilization for wholesaler sales to pharmacies, and available industry payor information.

**Chargebacks:** Chargebacks are discounts that occur when certain contracted purchasers purchase directly from our wholesalers at a discounted price. The wholesaler, in turn, charges back the difference between the price initially paid to us by the wholesaler and the discounted price paid to the wholesaler by the contracted purchaser. Amounts for estimated chargebacks are established in the same period that the related gross revenue is recognized, resulting in a reduction of product revenue and accounts receivable. The accrual for wholesaler chargebacks is estimated based on known chargeback rates, known sales to wholesalers, and estimated utilization by types of contracted purchasers.

**Discounts and Fees:** Our payment terms are generally 30 to 60 days. Wholesalers, GPOs and specialty pharmacies are offered various forms of consideration, including off-invoice discounts which may be paid to GPOs and specialty pharmacies. Wholesalers and GPOs may also receive prompt pay discounts for payment within a specified period. We expect discounts to be earned when offered and therefore, we deduct the full amount of these discounts from product sales when revenue is recognized, resulting in a reduction of product revenue and accounts receivable.

**Other Reserves:** Patients who have commercial insurance may receive copay assistance when product is dispensed by pharmacies to patients. We estimate the amount of copay assistance provided to eligible patients based on the terms of the program and redemption information provided by third-party claims processing organizations and are recorded in accounts payable and accrued expenses and other current liabilities on the balance sheets. Other reserves include estimated product returns which are recorded in the same period the related gross revenue is recognized, resulting in a reduction of product revenue as well as accounts receivable. We estimate our product returns reserve based upon our experience, and specific known market events and trends.

### ***Collaboration Revenue Recognition***

We generate collaboration revenue primarily from research and collaboration and license agreements with customers. Goods and services in the agreements may include the grant of licenses for the use of our technology, the provision of services associated with the research and development of product candidates, manufacturing services, and participation in joint steering committees. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; research, development, regulatory and commercial milestone payments; reimbursement of research and development services; option payments; reimbursement of certain costs; payments for manufacturing supply services; and future royalties on net sales of licensed products.

When two or more contracts are entered into with the same customer at or near the same time, we evaluate the contracts to determine whether the contracts should be accounted for as a single arrangement. Contracts are combined and accounted for as a single arrangement if one or more of the following criteria are met: (i) the contracts are negotiated as a package with a single commercial objective; (ii) the amount of consideration to be paid in one contract depends on the price or performance of the other contract; or (iii) the goods or services promised in the contracts (or some goods or services promised in each of the contracts) are a single performance obligation.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, management performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including any constraints on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for contracts with customers, we develop assumptions that require judgment to determine whether promised goods and services represent distinct performance obligations and the standalone selling price for each performance obligation identified in the contract. This evaluation is subjective and requires us to make judgments about the promised goods and services and whether those goods and services are separable from other aspects of the contract. Further, determining the standalone selling price for performance obligations requires significant judgment, and when an observable price of a promised good or service is not readily available, we consider relevant assumptions to estimate the standalone selling price, including, as applicable, market conditions, development timelines, probabilities of technical and regulatory success, reimbursement rates for personnel costs, forecasted revenues, potential limitations to the selling price of the product and discount rates.

We apply judgment in determining whether a combined performance obligation is satisfied at a point in time or over time, and, if over time, concluding upon the appropriate method of measuring progress to be applied for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, as estimates related to the measure of progress change, related revenue recognition is adjusted accordingly. Changes in our estimated measure of progress are accounted for prospectively as a change in accounting estimate. We recognize collaboration revenue by measuring the progress toward complete satisfaction of the performance obligation using an input measure. In order to recognize revenue over the research and development period, we measure actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. Revenues are recognized as the program costs are incurred. We will re-evaluate the estimate of expected costs to satisfy the performance obligation each reporting period and make adjustments for any significant changes. Amounts received prior to satisfying the revenue recognition criteria are recorded as contract liabilities in our balance sheets. If the related performance obligation is expected to be satisfied within the next twelve months, this will be classified in current liabilities. Amounts recognized as revenue prior to receipt are recorded as contract assets in our balance sheets. If we expect to have an unconditional right to receive the consideration in the next twelve months, this will be classified in current assets. A net contract asset or liability is presented for each contract with a customer.

*Milestone Payments:* At the inception of each arrangement that includes research and development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Milestone payments that are not within the control of us or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraints, 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 earnings in the period of adjustment.

*Manufacturing supply services:* Arrangements that include a promise for the future supply of drug substance or drug product for either clinical development or commercial supply at the customer'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 customer exercises these options, any payments are recorded in product supply revenue when the customer obtains control of the goods, which is upon delivery.

*Royalties:* For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and where the license is deemed to be the predominant item to which the royalties relate, we recognize revenue 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). To date, royalty revenue resulting from licensing arrangements has not been material.

*Licenses of intellectual property:* If a license granted to a customer to use our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from consideration allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we apply 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, to conclude upon the appropriate method of measuring progress for purposes of recognizing revenue related to consideration allocated to the performance obligation.

*Options:* Customer options, such as options granted to allow a licensee to choose to research, develop and commercialize licensed compounds are evaluated at contract inception in order to determine whether those options provide a material right (i. e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the standalone selling price, and revenue is recognized when or as the future goods or services are transferred or when the option expires. Customer options that are not material rights do not give rise to a separate performance obligation, and as such, the additional consideration that would result from a customer exercising an option in the future is not included in the transaction price for the current contract. Instead, the option is deemed a marketing offer, and additional option fee payments are recognized or being recognized as revenue when the licensee exercises the option. The exercise of an option that does not represent a material right is treated as a separate contract for accounting purposes.

*Contract modifications:* Contract modifications, defined as changes in the scope or price (or both) of a contract that are approved by the parties to the contract, such as a contract amendment, exist when the parties to a contract approve a modification that either creates new or changes existing enforceable rights and obligations of the parties to the contract. Depending on facts and circumstances, we account for a contract modification as one of the following: (i) a separate contract; (ii) a termination of the existing contract and a creation of a new contract; or (iii) a combination of the preceding treatments. A contract modification is accounted for as a separate contract if the scope of the contract increases because of the addition of promised goods or services that are distinct and the price of the contract increases by an amount of consideration that reflects our standalone selling prices of the additional promised goods or services. When a contract modification is not considered a separate contract and the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification, we account for the contract modification as a termination of the existing contract and a creation of a new contract. When a contract modification is not considered a separate contract and the remaining goods or services are not distinct, we account for the contract modification as an add-on to the existing contract and as an adjustment to revenue on a cumulative catch-up basis.

We receive payments from our licensees as established in each contract. Upfront payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements. Where applicable, amounts are recorded as unbilled revenue when our right to consideration is unconditional. We do not assess whether a contract with a customer has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less.

### ***Inventory***

We capitalize inventory costs associated with the production of our products after regulatory approval or when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Otherwise, such costs are expensed as research and development. Prior to the regulatory approval of drug product candidates, we incurred expenses for the manufacture of drug product that could potentially be available to support the commercial launch of our products or could be sold to our international partners under product supply agreements. We began to capitalize inventory costs associated with IBSRELA during the fourth quarter of 2021, when our intent to commercialize IBSRELA was established and we commenced preparation for the commercial launch of IBSRELA, which was when it was determined that the inventory had a probable future economic benefit.

Inventory is stated at the lower of cost or estimated net realizable value with cost determined under the first-in first-out method. Inventory costs include the cost of materials, third-party contract manufacturing, third-party packaging services, freight, labor costs for personnel involved in the manufacturing process, and indirect overhead costs. We primarily use actual costs to determine the cost basis for inventory. The determination of whether inventory costs will be realizable requires management review of the expiration dates of IBSRELA compared to our forecasted sales. If actual market conditions are less favorable than projected by management, write-downs of inventory may be required, which would be recorded as cost of revenue in the statement of operations and comprehensive loss. As of December 31, 2022, we have not recorded any write-offs for excess and obsolete inventory. The portion of inventory that represents product that is not expected to be sold or used within the next 12 months is classified as non-current on our balance sheets.

### ***Accrued Research and Development Expenses***

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with our service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors related to product manufacturing, development and distribution of clinical supplies; and

- vendors in connection with preclinical development activities.

We record expenses related to clinical studies and manufacturing development activities based on our estimates of the services received and efforts expended pursuant to contracts with our CROs and manufacturing vendors that conduct and manage these activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which each component of a service will be performed, and estimate, with vendor input if appropriate, the resulting level of completion of each component of the service, with such estimates often involving drivers that provide a surrogate measurement of completion such as number of enrolled subjects and/or number of sites activated in the calculation of clinical trial fee accruals. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrued or prepaid expense balance accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period.

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

We estimate the fair value of stock options and Employee Stock Purchase Plan ("ESPP") shares using the Black-Scholes valuation model. The Black-Scholes model requires the input of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

*Expected Term*—We have limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock-option grants. As such, the expected term is estimated using the simplified method whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option. Beginning in 2021, we estimate the expected term of our options based upon historical exercises and post-vesting termination behavior, which has not resulted in a material difference as compared to using the simplified method.

*Expected Volatility*—We use the historic volatility of our own stock over the retrospective period corresponding to the expected remaining term of the options, or the period since our shares were first quoted on The Nasdaq Global Market, if that is shorter, to compute our expected stock price volatility.

*Risk-Free Interest Rate*—The risk-free interest rate assumption is based on zero-coupon U.S. Treasury instruments on the date of grant with a maturity date consistent with the expected term of our stock option grants.

*Expected Dividend*— To date, we have not declared or paid any cash dividends and do not have any plans to do so in the future. Therefore, we use an expected dividend yield of zero.

As required, we review our valuation assumptions at each grant date and, as a result, we are likely to change our valuation assumptions used to value employee stock-based awards granted in future periods. Employee and director stock-based compensation costs are to be recognized over the vesting period of the award, and we have elected to use the straight-line attribution method. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. We estimate forfeitures based on historical experience.

Restricted stock units ("RSUs") are measured at the fair value of our common stock on the date of grant and expensed over the period of vesting using the straight-line attribution approach.

Performance-based RSUs ("PRSUs") are valued at grant-date fair market value. The vesting of the PRSUs is based on performance conditions. Performance conditions include: (i) a specific performance criteria and (ii) the employee's continuous employment by the company for a stated period of time in order to earn the right to the related PRSUs to vest. We recognize compensation cost with respect to the vesting of the PRSUs on a ratable basis over the requisite service period, upon the performance conditions being deemed probable of achievement.



## Restructuring

We recognize restructuring charges related to reorganization plans that have been committed to by management when liabilities have been incurred. In connection with these activities, we record restructuring charges at fair value for, (a) contractual employee termination benefits when obligations are associated to services already rendered, rights to such benefits have vested, and payment of benefits is probable and can be reasonably estimated, (b) one-time employee termination benefits when management has committed to a plan of termination, the plan identifies the employees and their expected termination dates, the details of termination benefits are complete, it is unlikely changes to the plan will be made or the plan will be withdrawn and communication to such employees has occurred, and (c) contract termination costs when a contract is terminated before the end of its term.

One-time employee termination benefits are recognized in their entirety when communication has occurred and future services are not required. If future services are required, the costs are recorded ratably over the remaining period of service. Contract termination costs to be incurred over the remaining contract term without economic benefit are recorded in their entirety when the contract is canceled.

## RESULTS OF OPERATIONS

### Comparison of the Years Ended December 31, 2022, 2021 and 2020

#### Revenue

Below is a summary of our total revenue (dollars in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
Product sales, net	\$ 15,600	\$ —	\$ —	\$ 15,600	(a)	\$ —	(a)
Product supply revenue	1,527	907	1,501	620	68.4 %	(594)	(39.6)%
Licensing revenue	35,031	5,013	706	30,018	598.8 %	4,307	610.1 %
Collaborative development revenue	—	4,177	5,364	(4,177)	(100.0)%	(1,187)	(22.1)%
<b>Total revenues</b>	<b>\$ 52,158</b>	<b>\$ 10,097</b>	<b>\$ 7,571</b>	<b>\$ 42,061</b>	<b>416.6 %</b>	<b>\$ 2,526</b>	<b>33.4 %</b>

(a) There were no product sales during the prior year period.

*Fiscal 2022 compared to 2021:* The increase to total revenues was primarily attributable to \$15.6 million of net product sales for IBSRELA to our Customers, as well as aggregate of \$35.0 million in milestone payments and payments under the second amendment to the 2017 KKC Agreement which we earned upon KKC's submission of a New Drug Application to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis. We also realized increased product supply revenue in connection with the 2017 KKC Agreement. Partially offsetting these increases was the full recognition of collaborative development revenue for upfront payments associated with the 2019 KKC Agreement through the end of 2021. There were no product sales during 2021 and 2020.

*Fiscal 2021 compared to 2020:* The increase to total revenues was primarily attributable to a \$5.0 million development milestone which we earned and recognized as licensing revenue during the twelve months ended December 31, 2021 upon the initiation by KKC of Phase 3 clinical studies in Japan to evaluate tenapanor for hyperphosphatemia. The increase was partially offset by lower collaborative development revenue and product supply revenue from KKC during the same period.

## Operating Expenses

Below is a summary of our operating expenses (dollars in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
Cost of revenue	\$ 4,117	\$ 1,000	\$ 145	\$ 3,117	311.7 %	\$ 855	589.7 %
Research and development	35,201	91,140	65,053	(55,939)	(61.4)%	26,087	40.1 %
Selling, general and administrative	76,599	72,303	33,153	4,296	5.9 %	39,150	118.1 %
Total operating expenses	\$ 115,917	\$ 164,443	\$ 98,351	\$ (48,526)	(29.5)%	\$ 66,092	67.2 %

## Cost of Revenue

*Fiscal 2022 compared to 2021:* The increase in cost of revenue was primarily attributable to payments due to AstraZeneca under the AZ Termination Agreement for IBSRELA product sales, net and for the milestone payment we received under the second amendment to the 2017 KKC Agreement, which we earned upon KKC's submission of a New Drug Application to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis. We also incurred \$0.5 million for the cost of product shipped for product sales of IBSRELA during the twelve months ended December 31, 2022.

*Fiscal 2021 compared to 2020:* The increase in cost of revenue was attributable to payment to AstraZeneca under the AZ Termination Agreement related to the development milestone we earned upon the initiation by KKC of Phase 3 clinical studies in Japan to evaluate tenapanor for hyperphosphatemia.

## Research and Development

Below is a summary of our research and development expenses (dollars in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
External R&D expenses	\$ 13,378	\$ 56,747	\$ 37,624	\$ (43,369)	(76.4)%	\$ 19,123	50.8 %
Employee-related expenses	15,065	27,268	20,911	(12,203)	(44.8)%	6,357	30.4 %
Facilities, equipment and depreciation expenses	3,097	5,803	5,738	(2,706)	(46.6)%	65	1.1 %
Other	3,661	1,322	780	2,339	176.9 %	542	69.5 %
Total research and development expenses	\$ 35,201	\$ 91,140	\$ 65,053	\$ (55,939)	(61.4)%	\$ 26,087	40.1 %

*Fiscal 2022 compared to 2021:* The decrease in our external R&D expenses was primarily the result of lower clinical study costs following the completion of the OPTIMIZE study, lower tenapanor manufacturing expense as we have begun to capitalize costs associated with the production of IBSRELA to inventory, and lower expenses for research following the elimination of our internal research organization in the fourth quarter of 2021. The decrease in our employee-related expenses for the twelve months ended December 31, 2022 is due to lower compensation and benefits expenses for our research and development workforce following restructuring actions in 2021. Similarly, the decrease in facilities, equipment and depreciation expenses is primarily due to a smaller proportion of such expenses being attributed to R&D following the restructuring in 2021. The increase in other expenses is primarily related to disease-related education grants during the twelve months ended December 31, 2022.

*Fiscal 2021 compared to 2020:* The increase in our external R&D expenses was the result of tenapanor manufacturing costs as well as clinical study costs from the advancement of our OPTIMIZE study which were partially offset by lower costs for the PHREEDOM clinical study. The increase in our employee-related expenses was related to compensation and benefits expenses for our research and development workforce. Employee-related expenses for twelve months ended December 31, 2021 include \$2.7 million of severance payments and other employee-related costs as discussed in *Note 14 - Restructuring* to the financial statements included elsewhere in this Annual Report.

### Selling, General and Administrative

*Fiscal 2022 compared to 2021:* The increase in selling, general and administrative expenses for the twelve months ended December 31, 2022 was primarily due to increased costs associated with the commercial launch of IBSRELA during 2022. The changes consisted of headcount and related personnel costs and external spending for disease awareness initiatives, commercial infrastructure and strategy. These increases were partially offset by a reduction in ongoing and one-time costs as a result of the restructuring action carried out during the third quarter of 2021.

*Fiscal 2021 compared to 2020:* The increase in general and administrative expenses was primarily due to increased costs associated with building and staffing our commercial infrastructure and teams as we prepared for a potential U.S. launch of XPHOZAH. The increase consisted of headcount and related personnel costs and an increase in external spending for disease awareness initiatives, commercial infrastructure and strategy. Selling, general and administrative expenses for the twelve months ended December 31, 2021 include \$3.5 million severance payments and other employee-related costs as discussed in *Note 14 - Restructuring* to the financial statements included elsewhere in this Annual Report.

### Interest Expense

Below is a summary of our interest expense (dollars in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
	Interest expense	\$ (3,400)	\$ (4,502)	\$ (5,099)	\$ 1,102	(24.5)%	\$ 597

*Fiscal 2022 compared to 2021:* The decrease in interest expense was due to lower principal outstanding on our loan payable in 2022 than in 2021 due to principal payments made on our 2018 Loan during the fourth quarter of 2021 through February 2022. In February 2022, we repaid the remaining outstanding principal balance of the 2018 Loan in the amount of \$25.0 million and entered into the new 2022 Loan in the amount of \$27.5 million which has an interest-only payment period through March 31, 2024.

*Fiscal 2021 compared to 2020:* The decrease in interest expense was primarily due to lower interest rates on our variable-rate term loan.

### Non-Cash Interest Expense Related to the Sale of Future Royalties

Below is a summary of our non-cash interest expense related to the sale of future royalties (dollars in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
	Non-cash interest expense related to the sale of future royalties	\$ (1,673)	\$ —	\$ —	\$ (1,673)	(a)	\$ —

(a) Percent change is not meaningful.

*Fiscal 2022 compared to 2021:* Non-cash interest expense related to the sale of future royalties reflects the recognized amortization of the deferred royalty obligation that we recorded following the receipt of the \$10.0 million upfront payment from HCR in June 2022.

### Other Income, net

Below is a summary of our other income (expense), net (dollars in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
Other income, net	\$ 1,633	\$ 687	\$ 1,568	\$ 946	137.7 %	\$ (881)	(56.2)%

*Fiscal 2022 compared to 2021:* The increase in other income, net was primarily due to sales of certain lab equipment and supplies for a net gain of \$1.5 million and increased investment income during the twelve months ended December 31, 2022. Partially offsetting these increases were fluctuations related to revaluation of our exit fees.

*Fiscal 2021 compared to 2020:* The changes in other income, net were primarily due to lower income earned on our investments, which was largely offset by the revaluation of our exit fee related to our term loan agreement following receipt of the FDA CRL on July 28, 2021.

### LIQUIDITY AND CAPITAL RESOURCES

Below is a summary of our cash, cash equivalents and short-term investments (in thousands):

	Year Ended December 31,		Change 2022 vs. 2021	
	2022	2021	\$	%
Cash and cash equivalents	\$ 96,140	\$ 72,428	\$ 23,712	32.7 %
Short-term investments	27,769	44,261	(16,492)	(37.3)%
Total liquid funds	\$ 123,909	\$ 116,689	\$ 7,220	6.2 %

As of December 31, 2022, we had cash and short-term investments of approximately \$123.9 million. We have incurred operating losses since inception in 2007 and our accumulated deficit as of December 31, 2022 is \$780.1 million. Our current level of cash and short-term investments alone is not sufficient to meet our plans for the next twelve months following the filing of these financial statements on March 2, 2023. These factors raise substantial doubt regarding our ability to continue as a going concern for a period of one year from the issuance of these financial statements. We plan to address our operating cash flow requirements with our current cash and short-term investments, cash generated from product sales of IBSRELA, and if approved, cash generated from sales of XPHOZAH, the potential receipt of anticipated milestone payments from our collaboration partners, the potential receipt of anticipated payments from KKC under the 2022 Amendment, with additional financing sources and through the implementation of cash preservation activities to reduce or defer discretionary spending.

There are no assurances that our efforts to meet our operating cash flow requirements will be successful. If our current cash and short-term investments as well as our plans to meet our operating cash flow requirements are not sufficient to fund necessary expenditures and meet our obligations for at least the next twelve months following the issuance of these financial statements, our liquidity, financial condition and business prospects will be materially affected. These financial statements have been prepared on a going concern basis and do not include any adjustments to the amounts and classification of assets and liabilities that may be necessary in the event that we can no longer continue as a going concern.

In July 2020, we filed a Form S-3 registration statement, which became effective in August 2020 ("2020 Registration Statement"), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$100.0 million of our common stock that may be issued and sold, from time to time, under an Open Market Sales Agreement with Jefferies LLC ("Jefferies"), as sales agent, deemed to be "at the market offerings" "2020 Open Market Sales Agreement"). Pursuant to the 2020 Open Market Sales Agreement, Jefferies received a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2020 Open Market Sales Agreement. As of December 31, 2021, we had sold 23.3 million shares and received the maximum gross proceeds of \$100.0 million pursuant to the 2020 Open Market Sales Agreement.

In August 2021, we filed an additional prospectus supplement under the 2020 Registration Statement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under an additional sales agreement we entered into with Jefferies ("2021 Open Market Sales Agreement"), pursuant to which we may, from time to time, sell up to \$150.0 million in shares of our common stock through Jefferies. We are not required to sell shares under the 2021 Open Market Sales Agreement. Pursuant to the 2021 Open Market Sales Agreement, Jefferies, as our sales agent, receives a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2021 Open Market Sales Agreement. As of December 31, 2022 we have sold 79.8 million shares and received gross proceeds of \$98.1 million at a weighted average sales price of approximately \$1.23 per share under the 2021 Open Market Sales Agreement. Subsequent to December 31, 2022, we received additional gross proceeds of \$20.0 million for the sale of an additional 7.7 million shares which were settled between January 1, 2023 to January 12, 2023 and were sold at a weighted average sales price of approximately \$2.60 per share under the 2021 Open Market Sales Agreement. There have been no other sales under the 2021 Open Market Sales Agreement after the January 12, 2023 settlement date.

In January 2023, we filed a Form S-3 registration statement, which became effective in January 2023 ("2023 Registration Statement"), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies, deemed to be "at-the-market offerings" ("2023 Open Market Sales Agreement"). Pursuant to the 2023 Open Market Sales Agreement, Jefferies, as sales agent, may receive a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2023 Open Market Sales Agreement. There have been no sales of our common stock under the 2023 Open Market Sales Agreement.

In February 2022, we entered into a loan and security agreement ("2022 Loan Agreement") with SLR Investment Corp ("SLR"). The 2022 Loan Agreement provides for a senior secured term loan facility, with \$27.5 million funded at closing and an additional \$22.5 million that we may borrow on or prior to July 25, 2023; provided that (i) we had received approval by the FDA for our NDA for XPHOZAH by December 31, 2022, and (ii) we have achieved certain product revenue milestone targets described in the 2022 Loan Agreement. In August 2022, we entered into an amendment to the 2022 Loan Agreement with SLR that extended the date by which we must receive approval by the FDA for our NDA for XPHOZAH in order to borrow the additional \$22.5 million from December 31, 2022 to March 31, 2023. In February 2023, we further amended the 2022 Loan Agreement ("2023 Amendment") such that, we may borrow the additional \$22.5 million under the 2022 Loan Agreement until December 20, 2023; provided that (i) we have received FDA approval for our NDA for XPHOZAH by November 30, 2023, or (ii) we have achieved certain product revenue milestone targets described in the 2023 Amendment.

The initial funding of \$27.5 million was used to repay the 2018 Loan and is funding our ongoing operations. We had \$25.0 million principal from the 2018 Loan outstanding as of the closing date. In connection with entering into the 2022 Loan Agreement, we entered into an agreement, whereby we agreed to pay an exit fee in the amount of 2% of the 2022 Loan funded ("2022 Exit Fee") upon (i) any change of control transaction or (ii) our achievement of net revenue from the sale of any products equal to or greater than \$100.0 million, measured on a six (6) months basis ("Revenue Milestone"), tested monthly at the end of each month. Notwithstanding the prepayment or termination of the 2022 Loan, the 2022 Exit Fee will expire on February 23, 2032. We concluded that the 2022 Exit Fee is a freestanding derivative which should be accounted for at fair value on a recurring basis. The estimated fair value of the 2022 Exit Fee is recorded as a derivative liability and included in accrued expenses and other current liabilities on the accompanying balance sheets.

In October 2022, we announced that our collaboration partner, KKC, submitted a New Drug Application to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis. In accordance with the terms of the 2022 Amendment, KKC paid an aggregate of \$35.0 million to us in milestone payments and payments associated with the 2022 Amendment during the quarter ended December 31, 2022.

Our primary sources of cash have been from the sale and issuance of common stock (in both public offerings and private placements), private placements of convertible preferred stock, funds from our collaboration partnerships, funds from our 2018 Loan Agreement and 2022 Loan Agreement, as well as from sales of IBSRELA.

Our primary uses of cash have been to fund operating expenses, primarily research and development expenditures, as well as pre-commercial and commercial expenses. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Our future funding requirements will depend on many factors, including, but not limited to:

- the extent to which we are able to generate product revenue from sales of IBSRELA;
- whether we are successful in securing approval for our NDA for XPHOZAH, and the time and cost associated with securing such approval;
- the availability of adequate third-party reimbursement for IBSRELA and, if approved, the sales price and the availability of adequate third-party reimbursement for XPHOZAH;
- The manufacturing, selling and marketing costs associated with IBSRELA and, if approved, XPHOZAH;
- our ability to maintain our existing collaboration partnerships and to establish additional collaboration partnerships, in-license/out-license, joint ventures or other similar arrangements and the financial terms of such agreements;
- the timing, receipt and amount of any milestones that may be received from our collaboration partners in connection with tenapanor, if any
- the timing, receipt, and amount of revenue, if any, that may be received by KKC in connection with the 2022 KKC Amendment;
- the timing, receipt, and amount of royalties we may receive as a result of sales of tenapanor by our collaboration partners in China and Canada, if any;
- the cash requirements for the discovery and/or development of other potential product candidates, including RDX013 and RDX020;
- the time and cost necessary to respond to technological and market developments;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into with SLR Investment Corp. in February 2022.

## CASH FLOW ACTIVITIES

The following table summarizes our cash flows for the periods indicated (in thousands):

	Year Ended December 31,			Change 2022 vs. 2021		Change 2021 vs. 2020	
	2022	2021	2020	\$	%	\$	%
Net cash used in operating activities	\$ (70,044)	\$ (152,551)	\$ (81,435)	\$ 82,507	(54.1)%	\$ (71,116)	87.3 %
Net cash provided by (used in) investing activities	18,415	50,948	(31,442)	(32,533)	(63.9)%	82,390	(262.0)%
Net cash provided by financing activities	75,341	82,999	22,776	(7,658)	(9.2)%	60,223	264.4 %
Net increase (decrease) in cash and cash equivalents	\$ 23,712	\$ (18,604)	\$ (90,101)	\$ 42,316	(227.5)%	\$ 71,497	(79.4)%

### ***Cash Flows from Operating Activities***

*Fiscal 2022 compared to 2021:* Net cash used in operating activities during the twelve months ended December 31, 2022 decreased by \$82.5 million primarily as a result of decreased spending on research and development expenses during the twelve months ended December 31, 2022 as compared to the twelve months ended December 31, 2021, as well net product sales of IBSRELA and \$35.0 million of milestone payments and payments under the second amendment to the 2017 KKC Agreement which we earned in 2022 upon KKC's submission of a New Drug Application to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis. Partially offsetting the net loss improvement were changes to our operating assets and liabilities related to expenditures for commercial manufacturing and inventory for the production of IBSRELA.

*Fiscal 2021 compared to 2020:* Net cash used in operating activities during the year ended December 31, 2021 increased by \$71.1 million as a result of our increased net loss for the period. The increased net loss was primarily driven by costs associated with building and staffing our commercial infrastructure and teams as we prepared for the anticipated U.S. launch of XPHOZAH. In addition to the increased net loss, cash flows related to our operating assets and liabilities increased in the amount of \$8.7 million.

### ***Cash Flows from Investing Activities***

*Fiscal 2022 compared to 2021:* Net cash provided by investing activities decreased by \$32.5 million due to lower investment balances and the timing of our investment maturities, which was partially offset by \$1.8 million proceeds from sale of laboratory equipment and supplies during the twelve months ended December 31, 2022.

*Fiscal 2021 compared to 2020:* Net cash provided by investing activities increased by \$82.4 million as our investment maturities increased to exceed the cost to purchase investments.

### ***Cash Flows from Financing Activities***

*Fiscal 2022 compared to 2021:* Net cash provided by financing activities decreased by \$7.7 million primarily due to \$29.5 million lower proceeds from issuance of common stock under at-the-market offerings and well as increased payments in the amount of \$13.6 million to repay the principal outstanding on the 2018 Loan. Partially offsetting these amounts were \$27.0 million net proceeds received from the 2022 Loan and \$9.6 million net proceeds from the sales of future royalties during the twelve months ended December 31, 2022

*Fiscal 2021 compared to 2020:* Net cash provided by financing activities increased by \$60.2 million due to net proceeds from issuance of our common stock pursuant to our at-the-market offerings, which were partially offset by principal repayments for our 2018 Loan.

### **SMALLER REPORTING COMPANY AND NON-ACCELERATED FILER STATUS**

On June 28, 2018, the SEC adopted amendments that raise the thresholds in the smaller reporting company ("SRC") definition, whereby we were determined to qualify as a SRC. On March 12, 2020, the SEC amended its rules to allow SRCs that have less than \$100.0 million in annual revenue and a public float of less than \$700.0 million to qualify as a non-accelerated filer. As a non-accelerated filer, we were not required to obtain an opinion of our independent auditors with respect to our internal controls over financial reporting as of December 31, 2020.

On June 30, 2022, our public float did not exceed \$700.0 million and we had less than \$100.0 million in annual revenue, thereby allowing us to qualify as a SRC and a non-accelerated filer as of December 31, 2022. We have determined to avail ourselves of most of the SRC scaled disclosure accommodations and we were not required to obtain an opinion of our independent auditors with respect to our internal controls over financial reporting for the period ended December 31, 2022.

## ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

### *Interest Rate Risk*

We are subject to market risks, including interest rate fluctuation exposure through our investments, in the ordinary course of our business. However, the goals of our investment policy are the preservation of capital, fulfillment of liquidity needs and fiduciary control of cash. To achieve our goal of maximizing income without assuming significant market risk, we maintain our excess cash and cash equivalents in money market funds and short-term debt securities. Because of the short-term maturities of our cash equivalents, we do not believe that a decrease in interest rates would have any material negative impact on the fair value of our cash equivalents.

As of December 31, 2022, we had cash, cash equivalents and short-term investments of \$123.9 million, which consist of bank deposits and money market funds, as well as high quality fixed income instruments including corporate bonds, commercial paper, U.S. treasury securities and U.S. government-sponsored agency bonds. The credit rating of our short-term investments must be rated A-1/P-1, or better by Standard and Poor's and Moody's Investors Service. Asset-backed securities must be rated AAA/Aaa. Money Market funds must be rated AAA/Aaa. Such interest-earning instruments carry a degree of interest rate risk. However, because our investments are high quality and short-term in duration, we believe that our exposure to interest rate risk is not significant and that a 10% movement in market interest rates would not have a significant impact on the total value of our portfolio, as noted above. We do not enter into investments for trading or speculative purposes.

We are subject to interest rate fluctuation exposure through our borrowings under the Loan Agreement and our investment in money market accounts which bear a variable interest rate. As of December 31, 2022, borrowings under the 2022 Loan bear interest at a floating per annum rate equal to 7.95% plus the greater of (i) one tenth percent (0.10%) and (ii) the one-month rate published by the Intercontinental Exchange Benchmark Administration Ltd ("ICE") or its successor. A hypothetical increase in one-month ICE of 100 basis points above the current one-month ICE rates would have increased our interest expense by approximately \$0.3 million for the year ended December 31, 2022. As of December 31, 2022 we had an aggregate principal amount of \$26.7 million outstanding pursuant to our 2022 Loan Agreement.

### *Foreign Currency Exchange Risk*

The majority of our transactions are denominated in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily Swiss francs and the euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities associated with a limited number of manufacturing activities.

We do not use derivative financial instruments for speculative trading purposes, nor do we hedge foreign currency exchange rate exposure in a manner that entirely offsets the earnings effects of changes in foreign currency exchange rates. The counterparties to our forward foreign currency exchange contracts are creditworthy commercial banks, which minimizes the risk of counterparty nonperformance.

As of December 31, 2022, we had no open forward foreign currency exchange contracts.



**ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**ARDELYX, INC.  
INDEX TO FINANCIAL STATEMENTS**

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## Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Ardelyx, Inc.

### Opinion on the Financial Statements

We have audited the accompanying balance sheets of Ardelyx, Inc. (“Company”) as of December 31, 2022 and 2021, the related statements of operations and comprehensive loss, stockholders’ equity, and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the “financial statements”). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

### The Company’s Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 2 to the financial statements, the Company has suffered recurring losses from operations and has stated that substantial doubt exists about the Company’s ability to continue as a going concern. Management’s evaluation of the events and conditions and management’s plans regarding these matters are also described in Note 2. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

### 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 Public Company Accounting Oversight Board (United States) (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. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

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 Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

**Estimates of Reserves for Variable Consideration**

*Description of the Matter*

As described in Note 2 to the financial statements, the Company recognizes revenues from product sales at the net sales price (transaction price), which includes estimates of variable consideration relating to off-invoice discounts, chargebacks or rebates, wholesaler fees, group purchasing organization administrative fees, patient copay assistance programs, and estimated product returns. These estimates are based on the amounts earned or to be claimed for related sales which may not be known at the point of sale. Government-mandated rebates under the Medicaid Drug Rebate Program ("Medicaid") and the Medicare Coverage Gap Program ("Medicare") are estimated based on estimated payor mix and statutory discount rates. Patient copay assistance program amounts are estimated based on terms of the program and redemption information provided by third-party claims processing organizations. Product returns are estimated based on the Company's experience and specific known market events and trends. The Company's total estimate of reserves for variable consideration was \$2.8 million as of December 31, 2022. During 2022, the Company recorded \$6.0 million in total reductions to gross commercial product sales as a result of reserves for variable consideration.

Auditing the Company's estimates of reserves for variable consideration relating to Medicaid and Medicare claims, patient copay assistance and product returns involved evaluation of management's subjective judgments regarding the reasonableness of various assumptions used. The Company has a limited history upon which to base such estimates, and changes in these estimated assumptions may have a material effect on the amount of reserves recorded for variable consideration.

*How We Addressed the Matter in Our Audit*

To test the Company's estimates of reserves for variable consideration relating to Medicaid and Medicare claims, patient copay assistance and product returns, our audit procedures included, among others, evaluating the methodologies and assumptions used and testing the accuracy and completeness of the underlying data used in the Company's analysis. We evaluated the assumptions used by management against third-party industry data and actual trends, evaluated the reasonableness of changes in estimated reserves during the year, and assessed the accuracy of the Company's estimates against actual results. We also performed sensitivity analyses to determine the effect of changes in management's assumptions on the amount of reserves recorded for variable consideration, where appropriate. Further, we evaluated the appropriateness of classification and disclosure of the Company's reserves for variable consideration in the financial statements.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2009.

San Mateo, California  
March 2, 2023

**ARDELYX, INC.**  
**BALANCE SHEETS**  
(in thousands, except share and per share amounts)

	December 31,	
	2022	2021
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 96,140	\$ 72,428
Short-term investments	27,769	44,261
Accounts receivable	7,733	502
Inventory	3,282	—
Prepaid commercial manufacturing	13,567	9,406
Prepaid expenses and other current assets	5,112	7,052
Total current assets	153,603	133,649
Property and equipment, net	1,223	2,362
Inventory, non-current	25,064	—
Right-of-use assets	9,295	12,752
Other assets	881	1,150
Total assets	\$ 190,066	\$ 149,913
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 10,859	\$ 4,277
Accrued compensation and benefits	7,548	5,422
Current portion of operating lease liability	3,894	3,492
Current portion of long-term debt	26,711	32,264
Deferred revenue	4,211	—
Accrued expenses and other current liabilities	12,380	7,366
Total current liabilities	65,603	52,821
Operating lease liability, net of current portion	5,855	9,748
Deferred revenue, non-current	9,025	4,727
Deferred royalty obligation related to the sale of future royalties	11,254	—
Total liabilities	91,737	67,296
Commitments and contingencies (Note 20)		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized; no shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively.	—	—
Common stock, \$0.0001 par value; 300,000,000 shares authorized; 198,575,016 and 130,182,535 shares issued and outstanding as of December 31, 2022 and December 31, 2021, respectively.	20	13
Additional paid-in capital	878,500	795,540
Accumulated deficit	(780,137)	(712,930)
Accumulated other comprehensive loss	(54)	(6)
Total stockholders' equity	98,329	82,617
Total liabilities and stockholders' equity	\$ 190,066	\$ 149,913

The accompanying notes are an integral part of these financial statements.

**ARDELYX, INC.**  
**STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**  
(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2022	2021	2020
<b>Revenues:</b>			
Product sales, net	\$ 15,600	\$ —	\$ —
Product supply revenue	1,527	907	1,501
Licensing revenue	35,031	5,013	706
Collaborative development revenue	—	4,177	5,364
Total revenues	<u>52,158</u>	<u>10,097</u>	<u>7,571</u>
<b>Operating expenses:</b>			
Cost of revenue	4,117	1,000	145
Research and development	35,201	91,140	65,053
Selling, general and administrative	76,599	72,303	33,153
Total operating expenses	<u>115,917</u>	<u>164,443</u>	<u>98,351</u>
Loss from operations	(63,759)	(154,346)	(90,780)
Interest expense	(3,400)	(4,502)	(5,099)
Non-cash interest expense related to the sale of future royalties	(1,673)	—	—
Other income, net	1,633	687	1,568
Loss before provision for income taxes	(67,199)	(158,161)	(94,311)
Provision for income taxes	8	4	2
Net loss	<u>\$ (67,207)</u>	<u>\$ (158,165)</u>	<u>\$ (94,313)</u>
Net loss per share of common stock - basic and diluted	<u>\$ (0.42)</u>	<u>\$ (1.52)</u>	<u>\$ (1.05)</u>
Shares used in computing net loss per share - basic and diluted	<u>158,690,083</u>	<u>104,205,645</u>	<u>89,582,138</u>
<b>Comprehensive loss:</b>			
Net loss	\$ (67,207)	\$ (158,165)	\$ (94,313)
Unrealized losses on available-for-sale securities	(48)	(2)	(24)
Comprehensive loss	<u>\$ (67,255)</u>	<u>\$ (158,167)</u>	<u>\$ (94,337)</u>

The accompanying notes are an integral part of these financial statements.

**ARDELYX, INC.**  
**STATEMENTS OF STOCKHOLDERS' EQUITY**  
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss) Income	Total Stockholders' Equity
	Shares	Amount				
<b>Balance as of December 31, 2019</b>	88,817,741	\$ 9	\$ 647,078	\$ (460,452)	\$ 20	\$ 186,655
Issuance of common stock under employee stock purchase plan	169,931	—	834	—	—	834
Issuance of common stock for services	42,403	—	310	—	—	310
Issuance of common stock upon exercise of options	445,942	—	1,020	—	—	1,020
Issuance of common stock upon vesting of restricted stock units	866,528	—	—	—	—	—
Stock-based compensation	—	—	10,583	—	—	10,583
Unrealized losses on available-for-sale securities	—	—	—	—	(24)	(24)
Issuance of common stock in at the market offering	3,257,430	—	21,047	—	—	21,047
Net loss	—	—	—	(94,313)	—	(94,313)
<b>Balance as of December 31, 2020</b>	93,599,975	\$ 9	\$ 680,872	\$ (554,765)	\$ (4)	\$ 126,112
Issuance of common stock under employee stock purchase plan	386,664	—	819	—	—	819
Issuance of common stock for services	25,989	—	190	—	—	190
Issuance of common stock upon exercise of options	331,310	—	584	—	—	584
Issuance of common stock upon vesting of restricted stock units	167,158	—	—	—	—	—
Taxes paid for net share settlement of equity awards	—	—	(106)	—	—	(106)
Issuance of common stock in at the market offering	35,671,439	4	101,142	—	—	101,146
Stock-based compensation	—	—	12,039	—	—	12,039
Unrealized losses on available-for-sale securities	—	—	—	—	(2)	(2)
Net loss	—	—	—	(158,165)	—	(158,165)
<b>Balance as of December 31, 2021</b>	130,182,535	\$ 13	\$ 795,540	\$ (712,930)	\$ (6)	\$ 82,617
Issuance of common stock under employee stock purchase plan	308,356	—	195	—	—	195
Issuance of common stock for services	711,675	—	390	—	—	390
Issuance of common stock upon exercise of options	14,080	—	7	—	—	7
Issuance of common stock upon vesting of restricted stock units	3,243,828	—	—	—	—	—
Issuance of common stock in at the market offering	64,114,542	7	71,618	—	—	71,625
Stock-based compensation	—	—	10,750	—	—	10,750
Unrealized losses on available-for-sale securities	—	—	—	—	(48)	(48)
Net loss	—	—	—	(67,207)	—	(67,207)
<b>Balance as of December 31, 2022</b>	198,575,016	\$ 20	\$ 878,500	\$ (780,137)	\$ (54)	\$ 98,329

The accompanying notes are an integral part of these financial statements.

**ARDELYX, INC.**  
**STATEMENTS OF CASH FLOWS**  
(in thousands)

	2022	2021	2020
<b>Operating activities</b>			
Net loss	\$ (67,207)	\$ (158,165)	\$ (94,313)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization expense	1,144	2,807	2,541
Non-cash lease expense	3,457	3,085	2,147
Stock-based compensation	10,750	12,039	10,583
Change in derivative liabilities	583	(678)	407
Debt refinancing costs	102	—	—
Gain on sale of equipment	(1,260)	—	—
Non-cash interest expense	1,962	283	413
Changes in operating assets and liabilities:			
Unbilled revenue	—	—	750
Accounts receivable	(7,231)	(502)	—
Inventory	(28,346)	—	—
Prepaid commercial manufacturing	(4,161)	(9,406)	—
Prepaid expenses and other assets	2,299	502	(4,653)
Accounts payable	6,582	(1,349)	3,439
Accrued compensation and benefits	2,126	(250)	1,219
Operating lease liabilities	(3,491)	(2,853)	(2,604)
Accrued and other liabilities	4,138	1,386	(1,000)
Deferred revenue	8,509	550	(364)
Net cash used in operating activities	(70,044)	(152,551)	(81,435)
<b>Investing activities</b>			
Proceeds from maturities and redemptions of investments	67,000	125,550	119,734
Purchases of investments	(50,328)	(72,735)	(150,852)
Proceeds from sale of property and equipment	1,798	—	—
Purchases of property and equipment	(55)	(1,867)	(324)
Net cash provided by (used in) investing activities	18,415	50,948	(31,442)
<b>Financing activities</b>			
Proceeds from 2022 Loan, net of issuance costs	26,971	—	—
Payments for 2018 Loan, net of costs	(33,038)	(19,444)	(125)
Proceeds from the sale of future royalties, net of issuance costs	9,581	—	—
Proceeds from issuance of common stock in at the market offering, net of issuance costs	71,625	101,146	21,047
Proceeds from issuance of common stock under equity incentive and stock purchase plans	202	1,403	1,854
Payments for taxes related to net share settlement of equity awards	—	(106)	—
Net cash provided by financing activities	75,341	82,999	22,776
<b>Net increase (decrease) in cash and cash equivalents</b>	<b>23,712</b>	<b>(18,604)</b>	<b>(90,101)</b>
<b>Cash and cash equivalents at beginning of period</b>	<b>72,428</b>	<b>91,032</b>	<b>181,133</b>
<b>Cash and cash equivalents at end of period</b>	<b>\$ 96,140</b>	<b>\$ 72,428</b>	<b>\$ 91,032</b>
<b>Supplementary disclosure of cash flow information:</b>			
Cash paid for interest	\$ 2,901	\$ 3,469	\$ 4,200
Cash paid for income taxes	\$ 6	\$ 4	\$ 1
<b>Supplementary disclosure of non-cash activities:</b>			
Right-of-use assets obtained in exchange for lease obligations	\$ —	\$ 1,604	\$ 450
Issuance of common stock for services	\$ 390	\$ 190	\$ 310
Issuance of derivative in connection with issuance of loan payable	\$ 375	\$ —	\$ —

The accompanying notes are an integral part of these financial statements.

**ARDELYX, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

## **1. ORGANIZATION AND BASIS OF PRESENTATION**

Ardelyx, Inc. (“Company,” “we,” “us” or “our”) is a biopharmaceutical company founded with a mission to discover, develop and commercialize innovative first-in-class medicines that meet significant unmet medical needs. We developed a unique and innovative platform that enabled the discovery of new biological mechanisms and pathways to develop potent, and efficacious therapies that minimize the side effects and drug-drug interactions frequently encountered with traditional, systemically absorbed medicines. The first molecule we discovered and developed was tenapanor, a targeted, first-in-class, oral, small molecule therapy. Tenapanor, branded as IBSRELA, is approved in the U.S. for the treatment of adults with irritable bowel syndrome with constipation (“IBS-C”). Tenapanor is in development for the control of serum phosphorus in adult patients with chronic kidney disease (“CKD”) on dialysis under the brand name XPHOZAH. We also have a development stage asset, RDX013 for adult patients with CKD and/or heart failure with hyperkalemia, or elevated serum potassium, and a discovery phase asset, RDX020 for adult patients with metabolic acidosis, a serious electrolyte disorder, in patients with CKD.

We operate in one business segment, which is the development and commercialization of biopharmaceutical products.

## **2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

### ***Basis of Presentation***

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (“U.S. GAAP”).

### ***Use of Estimates***

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes thereto. On an ongoing basis, management evaluates its estimates, including those related to recognition of revenue, clinical trial accruals, contract manufacturing accruals, fair value of assets and liabilities, income taxes and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could materially differ from those estimates.

### ***Liquidity***

As of December 31, 2022, we had cash and short-term investments of approximately \$123.9 million. We have incurred operating losses since inception in 2007 and our accumulated deficit as of December 31, 2022 is \$780.1 million. Our current level of cash and short-term investments alone is not sufficient to meet our plans for the next twelve months following the issuance of these financial statements on March 2, 2023. These factors raise substantial doubt regarding our ability to continue as a going concern for a period of one year from the issuance of these financial statements. We plan to address our operating cash flow requirements with our current cash and short-term investments, cash generated from product sales of IBSRELA, and if approved, cash generated from sales of XPHOZAH, our potential receipt of anticipated milestones payments from our collaboration partners, our potential receipt of anticipated payments from our Japanese collaboration partner under the second amendment to our License Agreement, with additional financing sources and through the implementation of cash preservation activities to reduce or defer discretionary spending.

There are no assurances that our efforts to meet our operating cash flow requirements will be successful. If our current cash and short-term investments as well as our plans to meet our operating cash flow requirements are not sufficient to fund necessary expenditures and meet our obligations for at least the next twelve months following the issuance of these financial statements, our liquidity, financial condition and business prospects will be materially affected. These financial statements have been prepared on a going concern basis and do not include any adjustments to the amounts and classification of assets and liabilities that may be necessary in the event that we can no longer continue as a going concern.

### ***Cash and Cash Equivalents***

We consider all highly liquid investments purchased with an original maturity date of 90 days or less on the date of purchase to be cash equivalents.



### ***Short-Term Investments***

Short-term investments consist of debt securities classified as available-for-sale and have maturities greater than 90 days, but less than one year, from the date of acquisition. Short-term investments are carried at fair value based upon quoted market prices. Unrealized gains and losses on available-for-sale securities are included in accumulated other comprehensive loss on our balance sheets. The cost of available-for-sale securities sold is based on the specific-identification method.

### ***Concentration of Credit Risk***

Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash, cash equivalents, short-term investments and accounts receivable. We are exposed to credit risks in the event of default by the counterparties to the extent of the amount recorded in its balance sheet. Cash, cash equivalents and short-term investments are invested through banks and other financial institutions in the U.S.

### ***Foreign Currency***

We manage our foreign currency exposures with the use of foreign currency purchases. We primarily conduct business in U.S. dollars; however, a portion of our expense and capital activities are transacted in foreign currencies which are subject to exchange rate fluctuations that can affect cash or earnings. We have been in a loss position and therefore our primary objective is to conserve and manage cash. There are generally two methods by which we may manage the cash flow risk of foreign exchange fluctuations when a contract is signed (i) we can purchase the foreign funds, in full or in part, upon the execution of the contract, or (ii) we can obtain the right to purchase such funds, in full or in part, at the execution of the contract, i.e., obtain a forward contract from an appropriate bank, that can be exercised to obtain the currency of interest at a particular point in time. The derivative instruments that we may use to hedge the exposure shall generally not be designated as cash flow hedges, and as a result, changes in their fair value would be recorded in other income (expense), net, in our statements of operations and comprehensive loss. The fair values of forward foreign currency exchange contracts would be estimated using current exchange rates and interest rates and the current creditworthiness of the counterparties is taken into consideration.

### ***Property and Equipment***

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets, with ranges generally from three to five years. Leasehold improvements are amortized over the lesser of the estimated useful lives or the related remaining lease term.

### ***Impairment of Long-Lived Assets***

The carrying value of long-lived assets, including property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the asset may not be recoverable. An impairment loss is recognized when the total of estimated future undiscounted cash flows, expected to result from the use of the asset and its eventual disposition, are less than the asset's carrying amount. Impairment, if any, would be assessed using discounted cash flows or other appropriate measures of fair value. For the years ending December 31, 2022, 2021 and 2020 we have recognized no impairment losses.

### ***Income Taxes***

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

### ***Accounts Receivable***

Accounts receivable is reported net of allowances for returns, chargebacks and contractual off-invoice and prompt-pay discounts offered to our customers. Our estimate of the allowance for doubtful accounts is based on an evaluation of the aging of our receivables. Trade receivable balances are written off against the allowance when it is probable that the receivable will not be collected. To date, we have determined that an allowance for doubtful accounts is not required. As of December 31, 2022 our accounts receivable balance was comprised of \$0.7 million from our collaboration agreements and \$7.0 million from commercial customers. As of December 31, 2021 our accounts receivable balance was comprised of \$0.5 million from our collaborators.

## ***Inventory***

We capitalize inventory costs associated with the production of our products after regulatory approval or when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Otherwise, such costs are expensed as research and development. Prior to the regulatory approval of drug product candidates, we incurred expenses for the manufacture of drug product that could potentially be available to support the commercial launch of our products or could be sold to our international partners under product supply agreements. We began to capitalize inventory costs associated with IBSRELA during the fourth quarter of 2021, when our intent to commercialize IBSRELA was established and we commenced preparation for the commercial launch of IBSRELA, which was when it was determined that the inventory had a probable future economic benefit.

Inventory is stated at the lower of cost or estimated net realizable value with cost determined under the first-in first-out method. Inventory costs include the cost of materials, third-party contract manufacturing, third-party packaging services, freight, labor costs for personnel involved in the manufacturing process, and indirect overhead costs. We primarily use actual costs to determine the cost basis for inventory. The determination of whether inventory costs will be realizable requires management review of the expiration dates of IBSRELA compared to our forecasted sales. If actual market conditions are less favorable than projected by management, write-downs of inventory may be required, which would be recorded as cost of revenue in the statement of operations and comprehensive loss. As of December 31, 2022, we have not recorded any write-offs for excess and obsolete inventory. A portion of inventory that represents product that is not expected to be sold or used within the next 12 months is classified as non-current on our balance sheets.

## ***Product Sales, Net***

We account for our commercial product sales, net in accordance with Topic 606 - *Revenue from Contracts with Customers*. We received approval from the U.S. Food and Drug Administration ("FDA") in September 2019 to market IBSRELA in the U.S.. We began selling IBSRELA in the U.S. in March 2022. We distribute IBSRELA principally through major wholesalers, specialty pharmacies and group purchasing organizations ("GPOs") (collectively, our "Customers"). Our Customers subsequently sell IBSRELA to pharmacies and patients. Separately, we enter into arrangements with third parties that provide for government-mandated rebates, chargebacks and discounts. Revenue from product sales is recognized when our performance obligations are satisfied, which is when Customers obtain control of our product and occurs upon delivery.

## ***Reserves for Variable Consideration***

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration which may be settled in the form of off-invoice discounts, chargebacks, or rebates. Variable consideration includes discounts to customers and government programs, wholesaler fees, group purchasing organization administrative fees, patient copay assistance programs, and estimated product returns. These estimates are based on the amounts earned or to be claimed for related sales and are classified as reductions of gross accounts receivable if settlement is expected to occur through a reduction in the amounts paid by our customers or a current liability if settlement is expected to occur through a payment from us. Where appropriate, these estimates are based on factors such as industry data and forecasted customer buying and payment patterns, our experience, current contractual and statutory requirements, specific known market events and trends. These reductions to gross sales reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. Variable consideration is included in the transaction price only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, we adjust these estimates, which would affect product revenue and earnings in the period such variances become known. As we gain more experience, estimates will be more heavily based on the expected utilization from historical data we have accumulated since the IBSRELA product launch.

Rebates: Rebates include wholesaler fees, GPO fees, as well as mandated discounts under the Medicaid Drug Rebate Program ("Medicaid") and the Medicare Coverage Gap Program ("Medicare"). Estimates for rebates are recorded in the same period the related gross revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses on the balance sheets. We estimate our Medicaid and Medicare rebates based upon the estimated payor mix, and statutory discount rates. Our estimates for payor mix are guided by payor information received from specialty pharmacies, expected utilization for wholesaler sales to pharmacies, and available industry payor information.

**Chargebacks:** Chargebacks are discounts that occur when certain contracted purchasers purchase directly from our wholesalers at a discounted price. The wholesaler, in turn, charges back the difference between the price initially paid to us by the wholesaler and the discounted price paid to the wholesaler by the contracted purchaser. Amounts for estimated chargebacks are established in the same period that the related gross revenue is recognized, resulting in a reduction of product revenue and accounts receivable. The accrual for wholesaler chargebacks is estimated based on known chargeback rates, known sales to wholesalers, and estimated utilization by types of contracted purchasers.

**Discounts and Fees:** Our payment terms are generally 30 to 60 days. Wholesalers, GPOs and specialty pharmacies are offered various forms of consideration, including off-invoice discounts which may be paid to GPOs and specialty pharmacies. Wholesalers and GPOs may also receive prompt pay discounts for payment within a specified period. We expect discounts to be earned when offered and therefore, we deduct the full amount of these discounts from product sales when revenue is recognized, resulting in a reduction of product revenue and accounts receivable.

**Other Reserves:** Patients who have commercial insurance may receive copay assistance when product is dispensed by pharmacies to patients. We estimate the amount of copay assistance provided to eligible patients based on the terms of the program and redemption information provided by third-party claims processing organizations and are recorded in accounts payable and accrued expenses and other current liabilities on the balance sheets. Other reserves include estimated product returns which are recorded in the same period the related gross revenue is recognized, resulting in a reduction of product revenue as well as accounts receivable. We estimate our product returns reserve based upon our experience, and specific known market events and trends.

### ***Collaboration Revenue Recognition***

We generate collaboration revenue primarily from research and collaboration and license agreements with customers. Goods and services in the agreements may include the grant of licenses for the use of our technology, the provision of services associated with the research and development of product candidates, manufacturing services, and participation in joint steering committees. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; research, development, regulatory and commercial milestone payments; reimbursement of research and development services; option payments; reimbursement of certain costs; payments for manufacturing supply services; and future royalties on net sales of licensed products.

When two or more contracts are entered into with the same customer at or near the same time, we evaluate the contracts to determine whether the contracts should be accounted for as a single arrangement. Contracts are combined and accounted for as a single arrangement if one or more of the following criteria are met: (i) the contracts are negotiated as a package with a single commercial objective; (ii) the amount of consideration to be paid in one contract depends on the price or performance of the other contract; or (iii) the goods or services promised in the contracts (or some goods or services promised in each of the contracts) are a single performance obligation.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, management performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including any constraints on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for contracts with customers, we develop assumptions that require judgment to determine whether promised goods and services represent distinct performance obligations and the standalone selling price for each performance obligation identified in the contract. This evaluation is subjective and requires us to make judgments about the promised goods and services and whether those goods and services are separable from other aspects of the contract. Further, determining the standalone selling price for performance obligations requires significant judgment, and when an observable price of a promised good or service is not readily available, we consider relevant assumptions to estimate the standalone selling price, including, as applicable, market conditions, development timelines, probabilities of technical and regulatory success, reimbursement rates for personnel costs, forecasted revenues, potential limitations to the selling price of the product and discount rates.

We apply judgment in determining whether a combined performance obligation is satisfied at a point in time or over time, and, if over time, concluding upon the appropriate method of measuring progress to be applied for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, as estimates related to the measure of progress change, related revenue recognition is adjusted accordingly. Changes in our estimated measure of progress are accounted for prospectively as a change in accounting estimate. We recognize collaboration revenue by measuring the progress toward complete satisfaction of the performance obligation using an input measure. In order to recognize revenue over the research and

development period, we measure actual costs incurred to date compared to the overall total expected costs to satisfy the performance obligation. Revenues are recognized as the program costs are incurred. We will re-evaluate the estimate of expected costs to satisfy the performance obligation each reporting period and make adjustments for any significant changes.

Amounts received prior to satisfying the revenue recognition criteria are recorded as contract liabilities in our Balance Sheets. If the related performance obligation is expected to be satisfied within the next twelve months it will be classified in current liabilities. Amounts recognized as revenue prior to receipt are recorded as contract assets in our Balance Sheets. If we expect to have an unconditional right to receive the consideration in the next twelve months, it will be classified in current assets. A net contract asset or liability is presented for each contract with a customer.

*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 estimate the amount to be included in the transaction price using the most likely amount method. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Milestone payments that are not within our control or the control of the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative standalone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraints, 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 earnings 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 customer'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 customer exercises these options, any payments are recorded in product supply revenue when the customer obtains control of the goods, which is upon delivery.

*Royalties:* For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and where the license is deemed to be the predominant item to which the royalties relate, we recognize revenue 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). To date, royalty revenue resulting from licensing arrangements has not been material.

*Licenses of intellectual property:* If a license granted to a customer to use our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from consideration allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we apply 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, to conclude upon the appropriate method of measuring progress for purposes of recognizing revenue related to consideration allocated to the performance obligation.

*Options:* Customer options, such as options granted to allow a licensee to choose to research, develop and commercialize licensed compounds are evaluated at contract inception in order to determine whether those options provide a material right (i.e., an optional good or service offered for free or at a discount) to the customer. If the customer options represent a material right, the material right is treated as a separate performance obligation at the outset of the arrangement. We allocate the transaction price to material rights based on the standalone selling price, and revenue is recognized when or as the future goods or services are transferred or when the option expires. Customer options that are not material rights do not give rise to a separate performance obligation, and as such, the additional consideration that would result from a customer exercising an option in the future is not included in the transaction price for the current contract. Instead, the option is deemed a marketing offer, and additional option fee payments are recognized or being recognized as revenue when the licensee exercises the option. The exercise of an option that does not represent a material right is treated as a separate contract for accounting purposes.

*Contract modifications:* Contract modifications, defined as changes in the scope or price (or both) of a contract that are approved by the parties to the contract, such as a contract amendment, exist when the parties to a contract approve a modification that either creates new or changes existing enforceable rights and obligations of the parties to the contract. Depending on facts and circumstances, we account for a contract modification as one of the following: (i) a separate contract; (ii) a termination of the existing contract and a creation of a new contract; or (iii) a combination of the preceding treatments. A contract modification is accounted for as a separate contract if the scope of the contract increases because of the addition of promised goods or services that are distinct and the price of the contract increases by an amount of consideration that reflects

our standalone selling prices of the additional promised goods or services. When a contract modification is not considered a separate contract and the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification, we account for the contract modification as a termination of the existing contract and a creation of a new contract. When a contract modification is not considered a separate contract and the remaining goods or services are not distinct, we account for the contract modification as an add-on to the existing contract and as an adjustment to revenue on a cumulative catch-up basis.

We receive payments from our licensees as established in each contract. Upfront payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements. Where applicable, amounts are recorded as accounts receivable or unbilled revenue when our right to consideration is unconditional. We do not assess whether a contract with a customer has a significant financing component if the expectation at contract inception is such that the period between payment by the licensees and the transfer of the promised goods or services to the licensees will be one year or less.

### ***Cost of Revenue***

Cost of revenue consists of the cost of commercial goods sold to our Customers and international partners under product supply agreements as well as royalty expense based on sales of tenapanor. We capitalize inventory costs associated with the production of our products after regulatory approval or when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Otherwise, such costs are expensed as research and development. A portion of the costs of IBSRELA units recognized as revenue during the twelve months ended December 31, 2022 were expensed prior to the fourth quarter of 2021, at which time our intent to commercialize IBSRELA was established and we commenced preparation for the commercial launch of IBSRELA.

Cost of revenue includes payments due to AstraZeneca, which under the terms of a termination agreement entered into in 2015 ("AZ Termination Agreement") is entitled to (i) future royalties at a rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from our collaboration partners as a result of the development and commercialization of tenapanor or certain other NHE3 inhibitors. We have agreed to pay AstraZeneca up to a maximum of \$75.0 million in the aggregate for (i) and (ii). We recognize these expenses as cost of revenue when we recognize the corresponding revenue that gives rise to payments due to AstraZeneca. To date, we have recognized an aggregate of \$15.3 million as cost of revenue under the AZ Termination Agreement.

### ***Research and Development Costs***

Research and development costs are charged to expense as incurred and consisted of costs incurred to further our research and development activities and include salaries and related employee benefits, costs associated with clinical trials, costs related to pre-commercialization manufacturing activities such as manufacturing process validation activities and the manufacturing of clinical drug supply, nonclinical research and development activities, regulatory activities, research-related overhead expenses and fees paid to external service providers and contract research and manufacturing organizations that conduct certain research and development activities on our behalf.

### ***Accrued Research and Development Expenses***

We are required to estimate our accrued expenses at the end of each reporting period. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers submit invoices in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with our service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- contract research organizations ("CROs") in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors related to product manufacturing, development and distribution of clinical supplies; and
- vendors in connection with preclinical development activities.

We record expenses related to clinical studies and manufacturing development activities based on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs and manufacturing vendors that conduct and manage these activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrued or prepaid expense balance accordingly.

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

We recognize compensation expense for all stock-based payment awards made to employees, non-employees and directors based on estimated fair values. For employee and non-employee stock options, we determine the grant date fair value of the awards using the Black-Scholes option-pricing model and generally recognize the fair value as stock-based compensation expense on a straight-line basis over the vesting period of the respective awards. For restricted stock and performance-based restricted stock, to the extent they are probable, the compensation cost for these awards is based on the closing price of our common stock on the date of grant and recognized as compensation expense on a straight-line basis over the requisite service period. Stock-based compensation expense is based on the value of the portion of stock-based payment awards that is ultimately expected to vest. As such, our stock-based compensation is reduced for the estimated forfeitures at the date of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

### ***Derivatives and Hedging Activities***

We account for our derivative instruments as either assets or liabilities on the balance sheet and measure them at fair value. Derivatives are adjusted to fair value through other income (expense), net in the statements of operations and comprehensive loss.

### ***Non-cash Interest Expense on Deferred Royalty Obligation***

The net proceeds we receive from the sale of certain future royalties are recorded as deferred royalty obligation related to the sale of future royalties on our balance sheets. As we earn royalties and remit those royalties pursuant to the agreement, the balance of the deferred royalty obligation will be effectively repaid over the life of agreement and non-cash interest expense related to the sale of future royalties is recorded using the effective interest method. To determine the amortization of our deferred royalty obligation, we are required to estimate the total amount of future royalty payments we expect to earn. There are a number of factors that could materially affect the amount and timing of royalty payments, most of which are not within our control. We periodically assess the amount of royalty payments we expect to receive which are subject to the agreement and, to the extent that the amount or timing of such payments is materially different than our original estimates, we prospectively adjust the imputed interest rate and the related amortization of the deferred royalty obligation.

### ***Leases***

We determine if an arrangement is a lease at the inception of the arrangement. Operating leases are included in right-of-use assets, current portion of operating lease liability, and operating lease liability, net of current portion in our balance sheets. Right-of-use assets represent our right to use an underlying asset for the lease term and lease liabilities represent our obligation to make lease payments arising from the lease. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. The operating lease right-of-use assets also include any lease payments made and exclude lease incentives. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise any such options. Lease expense is recognized on a straight-line basis over the expected lease term. We have elected not to separate lease and non-lease components, such as common area maintenance charges, and instead it accounts for these as a single lease component.

### ***Restructuring***

We recognize restructuring charges related to reorganization plans that have been committed to by management when liabilities have been incurred. In connection with these activities, we record restructuring charges at fair value for, (a) contractual employee termination benefits when obligations are associated to services already rendered, rights to such benefits have vested, and payment of benefits is probable and can be reasonably estimated, (b) one-time employee termination benefits

when management has committed to a plan of termination, the plan identifies the employees and their expected termination dates, the details of termination benefits are complete, it is unlikely changes to the plan will be made or the plan will be withdrawn and communication to such employees has occurred, and (c) contract termination costs when a contract is terminated before the end of its term.

One-time employee termination benefits are recognized in their entirety when communication has occurred and future services are not required. If future services are required, the costs are recorded ratably over the remaining period of service. Contract termination costs to be incurred over the remaining contract term without economic benefit are recorded in their entirety when the contract is canceled.

### **Net Loss per Share**

Basic net loss per common share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period, without consideration of potential shares of common stock. Diluted net loss per common share in the periods presented is the same as basic net loss per common share, since the effects of potentially dilutive securities are antidilutive due to the net loss for all periods presented.

### **Recent Accounting Pronouncements**

#### **New Accounting Pronouncements - Recently Adopted**

We adopted Accounting Standards Update 2016-13, *Financial Instruments - Credit Losses: Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), as of December 1, 2021 under the modified retrospective approach. ASU 2016-13 requires an entity to measure and recognize expected credit losses for certain financial instruments, including trade receivables, as an allowance that reflects the entity's current estimate of credit losses expected to be incurred. For available-for-sale debt securities with unrealized credit losses, the standard requires allowances to be recorded through net income instead of directly reducing the amortized cost of the investment under the previous other-than-temporary impairment model. The adoption of this standard did not have a material impact on our financial statements or a significant impact on our internal controls.

#### **Recent Accounting Pronouncements Not Yet Adopted**

There were various accounting standards and interpretations issued recently, none of which are expected to have a material impact on our financial position, operations or cash flows.

### **3. CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS**

Securities classified as cash, cash equivalents and short-term investments as of December 31, 2022 and 2021 are summarized below (in thousands):

	<b>December 31, 2022</b>			
	<b>Amortized Cost</b>	<b>Gross Unrealized</b>		<b>Fair Value</b>
		<b>Gains</b>	<b>Losses</b>	
<b>Cash and cash equivalents:</b>				
Cash	\$ 11,827	\$ —	\$ —	\$ 11,827
Money market funds	84,313	—	—	84,313
<b>Total cash and cash equivalents</b>	<b>96,140</b>	<b>—</b>	<b>—</b>	<b>96,140</b>
<b>Short-term investments:</b>				
Commercial paper	\$ 25,336	\$ 6	\$ (51)	\$ 25,291
Corporate bonds	1,000	—	(1)	999
U.S. government-sponsored agency bonds	1,487	—	(8)	1,479
<b>Total short-term investments</b>	<b>27,823</b>	<b>6</b>	<b>(60)</b>	<b>27,769</b>
<b>Total cash equivalents and investments</b>	<b>\$ 123,963</b>	<b>\$ 6</b>	<b>\$ (60)</b>	<b>\$ 123,909</b>

	December 31, 2021			
	Amortized Cost	Gross Unrealized		Fair Value
		Gains	Losses	
<b>Cash and cash equivalents:</b>				
Cash	\$ 1,253	\$ —	\$ —	\$ 1,253
Money market funds	71,175	—	—	71,175
Commercial Paper	—	—	—	—
Corporate bonds	—	—	—	—
<b>Total cash and cash equivalents</b>	<b>72,428</b>	<b>—</b>	<b>—</b>	<b>72,428</b>
<b>Short-term investments</b>				
Commercial paper	\$ 31,936	\$ 1	\$ (2)	\$ 31,935
Corporate bonds	7,025	—	(3)	7,022
Asset backed securities	5,306	—	(2)	5,304
<b>Total short-term investments</b>	<b>44,267</b>	<b>1</b>	<b>(7)</b>	<b>44,261</b>
<b>Total cash equivalents and investments</b>	<b>\$ 116,695</b>	<b>\$ 1</b>	<b>\$ (7)</b>	<b>\$ 116,689</b>

Cash equivalents consist of money market funds with original maturities of three months or less at the time of purchase, and the carrying amount is a reasonable approximation of fair value. We invest our cash in high quality securities of financial and commercial institutions. These securities are carried at fair value, which is based on readily available market information, with unrealized gains and losses included in accumulated other comprehensive loss within stockholders' equity on our balance sheets. We use the specific identification method to determine the amount of realized gains or losses on sales of marketable securities. Realized gains or losses have been insignificant and are included in other income, net, in the statement of operations and comprehensive loss.

All of the short-term available-for sale securities held as of December 31, 2022 and 2021 had contractual maturities of less than one year. Our available-for-sale securities are subject to a periodic impairment review. We consider a debt security to be impaired when its fair value is less than its carrying cost, in which case we would further review the investment to determine whether it is other-than-temporarily impaired. When we evaluate an investment for other-than-temporary impairment, we review factors such as the length of time and extent to which fair value has been below cost basis, the financial condition of the issuer and any changes thereto, intent to sell, and whether it is more likely than not we will be required to sell the investment before the recovery of its cost basis. If an investment is other-than-temporarily impaired or subject to credit losses, we write it down through the statement of operations and comprehensive loss to its fair value and establish that value as a new cost basis for the investment. Our unrealized losses as of December 31, 2022 and 2021 were not material. We determined that none of our available-for-sale securities were other-than-temporarily impaired as of December 31, 2022 and 2021, and no investment was in a continuous unrealized loss position for more than one year. As such, we believe that it is more likely than not that the investments will be held until maturity or a forecasted recovery of fair value.

#### 4. FAIR VALUE MEASUREMENTS

Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs.

The three-level hierarchy for the inputs to valuation techniques is briefly summarized as follows:

Level 1 – Valuations are based on quoted prices in active markets for identical assets or liabilities and readily accessible to us at the reporting date.

Level 2 – Valuations based on inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 – Valuations based on unobservable inputs for which there is little or no market data, which require us to develop our own assumptions.



The following table sets forth the fair value of our financial assets and liabilities that are measured or disclosed on a recurring basis by level within the fair value hierarchy (in thousands):

	December 31, 2022			
	Total Fair Value	Level 1	Level 2	Level 3
<b>Assets:</b>				
Money market funds	\$ 84,313	\$ 84,313	\$ —	\$ —
Commercial paper	25,291	—	25,291	—
U.S. government-sponsored agency bonds	1,479	—	1,479	—
Corporate bonds	999	—	999	—
Total	<u>\$ 112,082</u>	<u>\$ 84,313</u>	<u>\$ 27,769</u>	<u>\$ —</u>
<b>Liabilities:</b>				
Derivative liabilities for exit fees	\$ 1,656	\$ —	\$ —	\$ 1,656
Total	<u>\$ 1,656</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,656</u>
	December 31, 2021			
	Total Fair Value	Level 1	Level 2	Level 3
<b>Assets:</b>				
Money market funds	\$ 71,175	\$ 71,175	\$ —	\$ —
Commercial paper	31,935	—	31,935	—
Corporate bonds	7,022	—	7,022	—
Asset-backed securities	5,304	—	5,304	—
Total	<u>\$ 115,436</u>	<u>\$ 71,175</u>	<u>\$ 44,261</u>	<u>\$ —</u>
<b>Liabilities:</b>				
Derivative liability for exit fee	\$ 698	\$ —	\$ —	\$ 698
Total	<u>\$ 698</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 698</u>

Where quoted prices are available in an active market, securities are classified as Level 1. We classify money market funds as Level 1. When quoted market prices are not available for the specific security, we estimate fair value by using benchmark yields, reported trades, broker/dealer quotes and issuer spreads. We classify U.S. government-sponsored agency bonds, U.S. treasury notes, corporate bonds, commercial paper, and asset-backed securities as Level 2. In certain cases, where there is limited activity or less transparency around inputs to valuation, securities or derivative liabilities, such as the 2018 Exit Fee and 2022 Exit Fee, as defined and discussed in *Note 10. Derivative Liabilities*, are classified as Level 3.

The carrying amounts reflected in the balance sheets for cash equivalents, short-term investments, accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at both December 31, 2022 and 2021, due to their short-term nature.

Based on our procedures under the expected credit loss model, including an assessment of unrealized losses in our portfolio, we concluded that any unrealized losses on our marketable securities were not attributable to credit and, therefore, we have not recorded an allowance for credit losses for these securities as of December 31, 2022 and 2021.

#### **Fair Value of Debt**

The principal amount outstanding under our term loan facilities is subject to a variable interest rate. Therefore, we believe the carrying amount of the term loan facility approximates fair value as of December 31, 2022 and 2021. See *Note 9. Borrowings* for a description of the Level 2 inputs used to estimate the fair value of the liability.

The carrying value of the deferred royalty obligation related to the sale of future royalties approximates its fair value as of December 31, 2022 and is based on our current estimates of future royalties and commercialization milestones expected to be

paid to us by Kyowa Kirin Co., Ltd. ("KKC") over the life of the agreement. See *Note 8. Deferred Royalty Obligation Related to the Sale of Future Royalties* for a description of the Level 3 inputs used to estimate the fair value of the liability.

## 5. INVENTORY

We began capitalizing inventory during the fourth quarter of 2021, at which time our intent to commercialize IBSRELA was established and we commenced preparation for the commercial launch of IBSRELA. Inventory as of December 31, 2021 was not material. Inventory as of December 31, 2022 consisted of the following (in thousands):

	<b>December 31, 2022</b>
Raw materials	\$ 22,299
Work in process	5,324
Finished goods	723
Total	<u>\$ 28,346</u>
Reported as:	
Inventory	\$ 3,282
Inventory, non-current	25,064
Total	<u>\$ 28,346</u>

Prepaid commercial manufacturing of \$13.6 million and \$9.4 million as of December 31, 2022 and 2021, respectively, consisted of prepayments to third party contract manufacturing organizations for the manufacture of IBSRELA for production orders which we expect work to commence within the next 12 months.

## 6. PRODUCT REVENUE, NET

We received approval from the FDA in September 2019 to market IBSRELA in the U.S. We began selling IBSRELA in the U.S. in March 2022. We recorded net revenue for IBSRELA of \$15.6 million during the twelve months ended December 31, 2022.

Sales to AmerisourceBergen Drug Corporation, Cardinal Health, and McKesson Corporation made up 26.8%, 23.1%, and 21.6%, respectively, of our gross product revenue during the twelve months ended December 31, 2022.

The activities and ending reserve balances for each significant category of discounts and allowances, which constitute variable consideration, were as follows (in thousands):

	<b>Discounts and Chargebacks</b>	<b>Rebates, Wholesaler and GPO Fees</b>	<b>Copay and Returns</b>	<b>Total</b>
Balance as of December 31, 2021	\$ —	\$ —	\$ —	\$ —
Activity related to 2022 sales	825	2,721	2,502	6,048
Credits/deductions issued	(683)	(1,277)	(1,244)	(3,204)
Balance as of December 31, 2022	<u>\$ 142</u>	<u>\$ 1,444</u>	<u>\$ 1,258</u>	<u>\$ 2,844</u>

There were no product sales or gross-to-net accruals during the twelve months ended December 31, 2021 or 2020.

## 7. COLLABORATION AND LICENSING AGREEMENTS

### *Kyowa Kirin Co., Ltd. ("KKC")*

#### *2019 KKC Agreement*

In November 2019, we entered into a research collaboration and option agreement with KKC ("2019 KKC Agreement"), to undergo research to identify two preclinical study-ready compounds for designation as development compounds, with one compound inhibiting the first undisclosed target ("Program 1") and a second inhibiting the second undisclosed target ("Program

2”). Pursuant to the 2019 KKC Agreement, upon completion of the research and designation by the research steering committee of one or more development candidates (“DCs”), KKC has the right to execute one or more separate collaborative agreements relating to the development and commercialization of one or both DCs in certain specified territories.

Under the terms of the 2019 KKC Agreement, KKC paid us a non-refundable, non-creditable upfront fee of \$10.0 million, in two installments as follows: the first installment of \$5.0 million within 30 days of November 11, 2019 (“Effective Date”), and the second installment of \$5.0 million on the first anniversary of the Effective Date. The original term of the 2019 KKC Agreement commenced on the Effective Date and was to end on the earliest of: (i) two years following the Effective Date, (ii) the nomination of a program DC for both programs, (iii) the nomination of one program DC and the decision by the parties to cease research for the other program, or (iv) the decision by the parties to cease research for both programs. We entered into three amendments to the 2019 KKC Agreement, which have resulted in the extension of the original term. Under the third amendment to the 2019 KKC Agreement entered into on June 28, 2022, the 2019 KKC Agreement ended on February 28, 2023.

We assessed the 2019 KKC Agreement in accordance with ASC 606 and concluded that the contract’s counterparty, KKC, is a customer. We also considered the modification guidance prescribed in ASC 606 and concluded that the 2019 KKC Agreement should be accounted for as a separate contract from the 2017 KKC Agreement, as defined and discussed below.

We identified various promises in the 2019 KKC Agreement, including the grant of an initial research license, the Program 1 research, the Program 2 research, the right to obtain certain development and commercialization rights with Program 1 in certain territories and the right to obtain development and commercialization rights with Program 2 in certain territories, and participation in a joint steering committee (“JSC”) and determined that KKC could not benefit from either of the research programs without the research license and participation in the JSC. As such, the combined license, research programs and participation in the JSC were deemed to be the highest level of goods and services that can be deemed distinct for each of the Program 1 research and Program 2 research. We concluded that the options to obtain additional development and commercialization rights that are exercisable by KKC under certain circumstances are not performance obligations of the contract at inception because the option fees reflect the standalone selling price of the options, and therefore, the options are not considered to be material rights.

At the outset of the 2019 KKC Agreement, we determined that the initial transaction price was \$10.0 million and that revenue associated with the combined performance obligations should be recognized as services are provided using the input method. Since transfer of control occurs over time, in management’s judgment this input method is the best measure of progress towards satisfying the performance obligations and reflects a faithful depiction of the transfer of goods and services. Revenue was recognized over the Program 1 and Program 2 research periods which concluded in 2021.

During the years ended December 31, 2022 and 2021, we recognized zero and \$4.2 million, respectively, as revenue under the 2019 KKC Agreement in the statement of operations and comprehensive loss. The transaction price had been fully allocated to revenue as of December 31, 2021 and there was no associated deferred revenue presented on the balance sheet as of December 31, 2022 or 2021. As of December 31, 2022 and 2021, we had no material future obligations under the 2019 KKC Agreement.

#### *2017 KKC Agreement*

In November 2017, we entered into an exclusive license agreement with KKC (“2017 KKC Agreement”), under which we granted KKC an exclusive license to develop and commercialize certain NHE3 inhibitors including tenapanor in Japan for the treatment of cardiorenal diseases and conditions, excluding cancer. We retained the rights to tenapanor outside of Japan, and also retained the rights to tenapanor in Japan for indications other than those stated above. Pursuant to the 2017 KKC Agreement, KKC is responsible for all costs and expenses incurred in the development and commercialization of tenapanor for all licensed indications in Japan. We are responsible for supplying the tenapanor drug substance for KKC’s use in development and commercialization throughout the term of the 2017 KKC Agreement, provided that KKC may exercise an option to manufacture the tenapanor drug substance under certain conditions. In October 2022, we entered into a Commercial Supply Agreement with KKC to further define the obligations of the parties with respect to the commercial supply of tenapanor drug substance (“2022 KKC Supply Agreement”). As detailed below under the heading “Deferred revenue” we have received advanced payments from KKC for the manufacturing of tenapanor drug substance that will be used to satisfy KKC needs.

We assessed these arrangements in accordance with Accounting Standards Update (“ASU”) No. 2014-09, *Revenue from Contracts with Customers (Topic 606) and related amendments (“ASC 606”)* and concluded that the contract counterparty, KKC, is a customer. Under the terms of the 2017 KKC Agreement, we received \$30.0 million in up-front license fees, which was recognized as revenue when the agreement was executed. Based on our assessment, management determined that the

license and the manufacturing supply services were the material performance obligations at the inception of the 2017 KKC Agreement and, as such, each of the performance obligations is distinct.

Under the terms of the 2017 KKC Agreement, KKC paid us an up-front license fee of \$30.0 million. We may be entitled to receive up to \$55.0 million in total development and regulatory milestones, of which \$20.0 million has been received and recognized as revenue as of December 31, 2022. We may also be eligible to receive approximately ¥8.5 billion for commercialization milestones, or approximately \$64.6 million at the currency exchange rate on December 31, 2022, as well as reimbursement of costs plus a reasonable overhead for the supply of product and royalties on net sales throughout the term of the agreement. As discussed in *Note 8. Deferred Royalty Obligation Related to the Sale of Future Royalties*, the future royalties and commercial milestone payments we may receive under the 2017 KKC Agreement will be remitted to HealthCare Royalty Partners IV, L.P. pursuant to a Royalty and Sales Milestone Interest Acquisition Agreement. The variable consideration related to the remaining milestone payments was fully constrained at December 31, 2022 and 2021.

In April 2022, we entered into a second amendment to the 2017 KKC Agreement ("2022 Amendment"). Under the terms of the 2022 Amendment, we and KKC have agreed to a reduction in the royalty rate payable to us by KKC upon net sales of tenapanor for hyperphosphatemia in Japan. The royalty rate will be reduced from the high teens to low double digits for a two-year period of time following the first commercial sale in Japan, and then to mid-single digits for the remainder of the royalty term. As discussed in *Note 8. Deferred Royalty Obligation Related to the Sale of Future Royalties*, the future commercial milestones and royalties we may receive under the 2017 KKC Agreement will be remitted to HealthCare Royalty Partners IV, L.P. pursuant to a Royalty and Sales Milestone Interest Acquisition Agreement. As consideration for the reduction in the royalty rate, KKC agreed to pay us up to an additional \$40.0 million payable in two tranches, with the first payment due following KKC's filing with the Japanese Ministry of Health, Labour and Welfare of its application for marketing approval for tenapanor and the second payment due following KKC's receipt of regulatory approval to market tenapanor for hyperphosphatemia in Japan.

In October 2022, we announced that KKC submitted an NDA to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis, which resulted in payment to us from KKC for an aggregate of \$35.0 million for milestone payments and payments under the 2022 Amendment. We received these payments during the fourth quarter of 2022 and recorded them as licensing revenue on our statement of operations and comprehensive loss. The remaining variable consideration related to the reduction in the royalty rate was fully constrained at December 31, 2022. For the year ended December 31, 2021, \$5.0 million of licensing revenue was recorded upon the initiation of phase 3 clinical studies by KKC in Japan to evaluate tenapanor for hyperphosphatemia.

For the years ended December 31, 2022 and 2021, \$1.5 million and \$0.9 million, respectively, of product supply revenue was recorded for manufacturing supply of tenapanor and other materials to KKC for product development and clinical trials in Japan, in accordance with our agreement with the 2017 KKC Agreement.

For the years ended December 31, 2022 and 2021, \$35.0 million and \$5.0 million, respectively, of licensing revenue was recorded. The 2022 licensing revenue was earned upon KKC's submission of an NDA to the Japanese Ministry of Health, Labour and Welfare for tenapanor for the improvement of hyperphosphatemia in adult patients with CKD on dialysis. The 2021 licensing revenue was recorded upon the initiation of Phase 3 clinical studies by KKC in Japan to evaluate tenapanor for hyperphosphatemia.

#### ***Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. ("Fosun Pharma")***

In December 2017, we entered into an exclusive license agreement with Fosun Pharma ("Fosun Agreement") for the development, commercialization and distribution of tenapanor in China for both hyperphosphatemia and IBS-C. We assessed these arrangements in accordance with ASC 606 and concluded that the contract counterparty, Fosun Pharma, is a customer. Under the terms of the Fosun Agreement, we received \$12.0 million in up-front license fees which was recognized as revenue when the agreement was executed. Based on our assessment, we determined that the license and the manufacturing supply services represented the material performance obligations at the inception of the agreement and, as such, each of the performance obligations are distinct.

We may be entitled to additional development and commercialization milestones of up to \$110.0 million, as well as reimbursement of cost plus a reasonable overhead for the supply of product and tiered royalties on net sales ranging from the mid-teens to 20%. The variable consideration related to the remaining development milestone payments was fully constrained at December 31, 2022 and 2021.

We recorded no revenue related to the Fosun Agreement during the years ended December 31, 2022 and 2021.

***Knight Therapeutics, Inc. ("Knight")***

In March 2018, we entered into an exclusive license agreement with Knight Therapeutics, Inc., ("Knight Agreement") for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. We assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Knight, is a customer. Based on our assessment, we determined that the license and the manufacturing supply services were the material performance obligations at the inception of the agreement and, as such, each of the performance obligations are distinct.

Under the terms of the Knight Agreement, we received a \$2.3 million non-refundable, one-time upfront payment in March 2018 and may be eligible to receive additional development and commercialization milestone payments worth up to CAD22.2, or approximately \$16.3 million at the currency exchange rate on December 31, 2022. We are also eligible to receive royalties ranging from the mid-single digits to the low twenties throughout the term of the agreement, and a transfer price for manufacturing services. The variable consideration related to the remaining development milestone payments were fully constrained at December 31, 2022 and 2021.

For the years ended December 31, 2022 and 2021, \$31 thousand and \$13 thousand of licensing revenue was recorded, respectively, related to the Knight Agreement. For the years ended December 31, 2022 and 2021, no product supply revenue was recorded, respectively, related to the Knight Agreement.

***AstraZeneca AB ("AstraZeneca")***

In June 2015, we entered into a termination agreement with AstraZeneca ("AstraZeneca Termination Agreement") pursuant to which we have agreed to pay AstraZeneca (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should we elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, up to a maximum of \$75.0 million in aggregate for (i) and (ii). For the years ended December 31, 2022 and 2021, we recognized \$3.6 million and \$1.0 million, respectively, as cost of revenue related to the AstraZeneca Termination Agreement. To date in aggregate, we have recognized \$15.3 million of the \$75.0 million aggregate maximum related to the AstraZeneca Termination Agreement.

***Deferred Revenue***

The following tables present changes in our current and non-current deferred revenue balances during the reporting period. The December 31, 2022 deferred revenue current and non-current balances are attributable entirely to prepayments for product supply under the 2017 KKC Agreement, while the December 31, 2021 current deferred revenue balance is attributable to the 2019 KKC Agreement and the December 31, 2021 non-current deferred revenue balance is attributable prepayments for product supply under the 2017 KKC Agreement (in thousands):

<b>Deferred revenue - current</b>	<b>2022</b>	<b>2021</b>
Balance at Balance at January 1,	\$ —	\$ 4,177
Increases due to cash received, excluding amounts recognized as revenue during the period	42	—
Increases due to amounts reclassified from non-current, to be recognized in the next twelve months	3,961	—
Increases to amounts invoiced, for which cash has not yet been received	208	—
Decreases due to revenue recognized in the period for which cash has been received	—	(4,177)
Balance at December 31,	<u>\$ 4,211</u>	<u>\$ —</u>

<b>Deferred revenue - non-current</b>	<b>2022</b>	<b>2021</b>
Balance at Balance at January 1,	\$ 4,727	\$ —
Increases due to cash received during the period	7,794	3,242
Increases to amounts invoiced, for which cash has not yet been received	465	—
Increase due to unbilled prepayments recorded during the period	—	1,485
Decreases due to amounts reclassified as current, to be recognized in the next twelve months	(3,961)	—
Balance at December 31,	<u>\$ 9,025</u>	<u>\$ 4,727</u>

## 8. DEFERRED ROYALTY OBLIGATION RELATED TO THE SALE OF FUTURE ROYALTIES

In June 2022, we and HealthCare Royalty Partners IV, L.P. (“HCR”) entered into a Royalty and Sales Milestone Interest Acquisition Agreement (“HCR Agreement”). Under the terms of the HCR Agreement, HCR has agreed to pay us up to \$20.0 million in exchange for the royalty payments and commercial milestone payments (collectively the “Royalty Interest Payments”) that we may receive under our 2017 License Agreement with KKC based upon KKC’s net sales of tenapanor in Japan for hyperphosphatemia. As consideration for the sale of the Royalty Interest Payments, HCR paid to us a \$10.0 million upfront payment, and we are eligible to receive a \$5.0 million payment following KKC’s receipt of regulatory approval to market tenapanor for hyperphosphatemia in Japan, and another \$5.0 million payment in the event net sales by KKC in Japan exceed a certain annual target level by the end of 2025.

The HCR Agreement is effective until terminated by the mutual agreement of the parties and contains customary representations and warranties and customary affirmative and negative covenants, including, among others, requirements as to prosecution, maintenance, defense and enforcement of certain patent rights in Japan, restrictions regarding our ability to forgive, release or reduce any Royalty Interest Payments due to us under the 2017 KKC Agreement, to create or incur any liens with respect to the Royalty Interest Payments, the 2017 KKC Agreement or certain patents, or to sell, license or transfer certain patents in the field and territory described in the 2017 KKC Agreement.

In addition, the HCR Agreement contains customary events of default with respect to which we may incur indemnification obligations to HCR for any losses incurred by HCR and related parties as a result of the event of default, subject to a specified limitation of liability cap. Under the HCR Agreement, an event of default will occur if, among other things, any of the representations and warranties included in the HCR Agreement proves not to have been true and correct in all material respects, at the time it was made, we breach any of our covenants under the HCR Agreement, subject to specified cure periods with respect to certain breaches, we are in breach or default under the 2017 KKC Agreement in any manner which is likely to cause a material adverse effect on the Royalty Interest Payments, the occurrence of a termination of the 2017 KKC Agreement under certain circumstances or we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings, or we are unable to pay our debts as they become due.

We received the \$10.0 million upfront payment from HCR during June 2022 and recorded it as a deferred royalty obligation related to the sale of future royalties (“deferred royalty obligation”) on our balance sheet. Due to our ongoing manufacturing obligations under the 2017 KKC Agreement, we account for the proceeds as imputed debt and therefore will recognize royalties received under the arrangement as non-cash royalty revenue. Non-cash interest expense will be recognized over the life of the HCR Agreement using the effective interest method based on the imputed interest rate derived from estimated amounts and timing of future royalty payments to be received from KKC. As part of the sale, we incurred approximately \$0.4 million in transaction costs, which, along with the deferred royalty obligation, are being amortized to non-cash interest expense over the estimated life of the HCR Agreement using the effective interest method. As future royalties are remitted to us by KKC, and subsequently from us to HCR, the balance of the deferred royalty obligation will be effectively repaid over the life of the HCR Agreement. There are a number of factors that could materially affect the fair value of the deferred royalty obligation. Such factors include, but are not limited to, the amount and timing of potential future royalty payments to be received from KKC under the 2017 KKC agreement, changing standards of care, the introduction of competing products, manufacturing or other delays, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of the drug products, significant changes in foreign exchange rates as the royalties remitted to HCR are made in U.S. dollars while the underlying sales of the products by KKC are made in Japanese yen, and other events or circumstances that could result in reduced royalty payments from KKC, which are not within our control, and all of which would result in a reduction of non-cash royalty revenues and the non-cash interest expense over the life of the deferred royalty obligation. We periodically assess the estimated royalty payments from KKC and, to the extent that the amount or timing of such payments is materially different than our original estimates, we prospectively adjust the imputed interest rate and

the related amortization of the deferred royalty obligation. As of December 31, 2022, our effective interest rate used to amortize the liability is 34.4%.

During the twelve months ended December 31, 2022, we recognized approximately \$1.7 million of non-cash interest expense for the amortization of the deferred royalty obligation. As of December 31, 2022, we have received no royalty payments from KKC and, therefore, the deferred royalty obligation has not begun to be reduced.

## 9. BORROWINGS

### *Solar Capital and Western Alliance Bank Loan Agreement*

In May 2018, we entered into a loan and security agreement ("2018 Loan Agreement"), with Solar Capital Ltd. and Western Alliance Bank ("Lenders"). The 2018 Loan Agreement provided for a \$50.0 million term loan facility with a maturity date of November 1, 2022 ("2018 Term Loan"). The full amount of the 2018 Term Loan was funded on May 16, 2018. We received net proceeds from the loan of approximately \$49.3 million, after deducting the closing fee, legal expenses and issuance costs. In October 2020, we and the Lenders entered into an amendment to the 2018 Loan Agreement ("2020 Amendment") to extend the date through which we were permitted to make interest-only payments on the 2018 Term Loan by twelve months to December 1, 2021 subject to the repayment terms noted below.

Borrowings under the 2018 Term Loan bore interest at a floating per annum rate equal to 7.45% plus the one-month London Inter-bank Offered Rate ("LIBOR"). We were permitted to make interest-only payments on the 2018 Term Loan through June 1, 2020, or until we achieved our primary endpoint in the Phase 3 study of tenapanor for the treatment of hyperphosphatemia in end-stage renal disease patients on dialysis prior to June 1, 2020, in which case we would have been permitted to make interest-only payments on the 2018 Term Loan through December 1, 2020. In December 2019, we reported positive topline results for PHREEDOM, a long-term Phase 3 study evaluating the efficacy and safety of tenapanor as monotherapy for the treatment of hyperphosphatemia in adult patients with CKD on dialysis. The Lenders were in agreement that these positive data from the Phase 3 PHREEDOM study achieve the "Phase 3 Endpoint" required by the 2018 Term Loan to extend the interest only period by six months to December 1, 2020. Subsequent to the 2020 Amendment, the interest only period was extended an additional twelve months to December 1, 2021. Accordingly, beginning on December 1, 2021 through the maturity date, we would have been required to make monthly payments of interest plus repayment of the 2018 Term Loan in consecutive equal monthly installments of principal. If however, either the FDA did not approve our NDA for tenapanor for control of serum phosphorus in adult patients with CKD on dialysis on or before May 31, 2021 or the FDA issued a Complete Response Letter ("CRL") for tenapanor for the control of serum phosphorus in adult patients with CKD on dialysis, then we would begin principal payments on the earlier of June 1, 2021 or the first day of the month immediately following the date that the FDA issued a CRL to us.

In May and July 2021, we and the Lenders entered into additional amendments to the 2018 Loan Agreement ("the 2021 Amendments") which together extended the period of time that we were permitted to make interest-only payments on the 2018 Term Loan to December 1, 2021; provided that if we had not received FDA approval for our NDA for tenapanor for the control of serum phosphorus in adult patients with CDK on dialysis on or before October 25, 2021, the interest-only period would expire and principal repayments would be required to begin on November 1, 2021. If principal repayments were required to begin prior to December 1, 2021 under the 2021 Amendments, then the first such repayment was required to include all payments that would have been due if monthly principal repayment had begun on June 1, 2021. Accordingly, during November 2021, in compliance with the terms of our 2018 Loan Agreement, we began to repay principal on the 2018 Term Loan. As of the Closing Date for the 2022 Loan, as discussed below, we owed \$25.0 million in principal payments from the 2018 Loan, which we repaid in full at that time.

### *SLR Investment Corp. Loan Agreement*

On February 23, 2022 ("Closing Date"), we entered into a loan and security agreement ("2022 Loan Agreement") with SLR Investment Corp. as collateral agent ("Agent"), and the lenders listed in the 2022 Loan Agreement (collectively the "2022 Lenders"). The 2022 Loan Agreement provides for a senior secured loan facility, with \$27.5 million ("Term A Loan") funded on the Closing Date and an additional \$22.5 million that we may borrow on or prior to July 25, 2023; provided that (i) we have received approval by the FDA for our NDA for XPHOZAH by December 31, 2022, and (ii) we have achieved certain product revenue milestone targets described in the 2022 Loan Agreement ("Term B Loan", and collectively, the Term A Loan and the Term B Loan, the "2022 Loan"). On February 9, 2023, we entered into an amendment to the 2022 Loan Agreement with SLR Investment Corp. that extends the date by which we must receive approval by the FDA for our NDA for the control of serum phosphorus in adult patients with CKD on dialysis in order to borrow the additional \$22.5 million from December 31, 2022 to November 30, 2023 and extended the period during which we are permitted to make interest only payments until March 31,

2025 if we receive approval by the FDA for our NDA for XPHOZAH on or prior to November 30, 2023 or achieve a defined net product revenue threshold for 2023. The 2022 Term A Loan funds were used to repay the 2018 Loan with the 2018 Lenders. The 2022 Loan has a maturity date of March 1, 2027.

Borrowings under the 2022 Loan bear interest at a floating per annum rate equal to 7.95% plus the greater of (i) one tenth percent (0.10%) and (ii) the one-month rate published by the Intercontinental Exchange Benchmark Administration Ltd or its successor. We are permitted to make interest-only payments on the 2022 Loan through March 31, 2024 or if certain conditions described above are achieved, through March 31, 2025. Accordingly, beginning on April 1, 2024 or April 1, 2025, we will be required to make monthly payments of interest plus repay the 2022 Loan in consecutive equal monthly installments of principal over 36 months or 24 months, respectively. We were obligated to pay \$0.2 million, upon the closing of the Term A Loan, and we are obligated to pay \$0.1 million on the earliest of (i) the funding date of the Term B Loan, (ii) July 25, 2023, and (iii) the prepayment, refinancing, substitution, or replacement of the Term A Loan on or prior to July 25, 2023. We are obligated to pay a final fee equal to 4.95% of the aggregate original principal amount of the 2022 Loan funded upon the earliest to occur of the maturity date, the acceleration of the 2022 Loan, and the prepayment, refinancing, substitution, or replacement of the 2022 Loan. We may voluntarily prepay the outstanding 2022 Loan balance, subject to a prepayment premium of (i) 3% of the outstanding principal amount of the 2022 Loan if prepaid prior to or on the first anniversary of the Closing Date, (ii) 2% of the outstanding principal amount of the 2022 Loan if prepaid after the first anniversary of the Closing Date through and including the second anniversary of the Closing Date, or (iii) 1% of the outstanding principal amount of the 2022 Loan if prepaid after the second anniversary of the Closing Date and prior to the maturity date. The 2022 Loan is secured by substantially all of our assets, except for our intellectual property and certain other customary exclusions. Additionally, in connection with the 2022 Loan, we entered into an agreement, whereby we agreed to pay an exit fee in the amount of 2% of the 2022 Loan funded (“2022 Exit Fee”) upon (i) any change of control transaction or (ii) our achievement of net revenue from the sale of any products equal to or greater than \$100.0 million, measured on a six (6) months basis, tested monthly at the end of each month. Notwithstanding the prepayment or termination of the 2022 Loan, the 2022 Exit Fee will expire 10 years from the Closing Date.

The 2022 Loan Agreement contains customary representations and warranties and customary affirmative and negative covenants, including, among others, requirements as to financial reporting and insurance and restrictions on our ability to dispose of our business or property, to change our line of business, to liquidate or dissolve, to enter into any change in control transaction, to merge or consolidate with any other entity or to acquire all or substantially all the capital stock or property of another entity, to incur additional indebtedness, to incur liens on our property, to pay any dividends or other distributions on capital stock other than dividends payable solely in capital stock or to redeem capital stock. We have agreed to not allow our cash and cash equivalents to be less than the eighty percent (80%) of the outstanding 2022 Term Loan balance for any period in which our net revenue from the sale of any products, calculated on a trailing six (6) month basis and tested monthly, is less than sixty percent (60%) of the outstanding 2022 Loan balance.

In addition, the 2022 Loan Agreement contains customary events of default that entitle the Agent to cause our indebtedness under the 2022 Loan Agreement to become immediately due and payable, and to exercise remedies against us and the collateral securing the 2022 Term Loan, including our cash. Under the 2022 Loan Agreement, an event of default will occur if, among other things, we fail to make payments under the 2022 Loan Agreement, we breach any of our covenants under the 2022 Loan Agreement, subject to specified cure periods with respect to certain breaches, certain Lenders determine that a material adverse change has occurred, we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings, we are unable to pay our debts as they become due or we default on contracts with third parties which would permit the holder of indebtedness to accelerate the maturity of such indebtedness or that could have a material adverse change on us. Upon the occurrence and for the duration of an event of default, an additional default interest rate equal to 4% per annum will apply to all obligations owed under the 2022 Loan Agreement. We have classified the 2022 Loan balance as a current liability as of December 31, 2022 due to the determination of the existence of substantial doubt about our ability to continue operating as a going concern discussed in *Note 2. Summary of Significant Accounting Policies: Liquidity* and our assessment that the material adverse change clause under the 2022 Loan Agreement is not within our control. The lenders have not invoked the material adverse change clause as of the date of issuance of these financial statements.



As discussed in *Note 21. Subsequent Events*, on February 9, 2023, we entered into a second amendment (“Second Amendment”) to our Loan Agreement with the Lenders. The Second Amendment extends the interest-only term of the loan by twelve months to March 31, 2025 provided that we either (i) receive approval from the FDA for our NDA for the control of serum phosphorus in adult patients with CKD on dialysis on or prior to November 30, 2023 or (ii) achieve certain product revenue milestone targets as described in the Second Amendment for the year ending December 31, 2023. The Second Amendment also extends the period under which we may draw the Term B Loan from July 25, 2023 to December 20, 2023, and amends the milestone that we must achieve in order to draw the Term B Loan by extending the time period for the receipt of approval by the FDA of the NDA for the control of serum phosphorus in adult patients with CKD on dialysis until November 30, 2023. In addition, the Second Amendment replaces the floating per annum interest rate with 7.95% plus the greater of (a) one percent (1.00%) per annum and (b)(i) 0.022% plus (ii) 1-month CME Term SOFR reference rate as published by the CME Term SOFR Administrator on the CME Term SOFR Administrator’s Website.

As of December 31, 2022, our future payment obligations related to the 2022 Loan, excluding interest payments and the 2022 final fee, were as follows (in thousands) and may be condensed to the 24 months ending March 1, 2027 if certain conditions noted above to extend the interest-only period are achieved:

2023	\$	—
2024		7,639
2025		9,167
2026		9,167
2027		2,888
Thereafter		—
Total repayment obligations		<u>28,861</u>
Less: Unamortized discount and debt issuance costs		(1,110)
Less: Unaccreted value of final fee		<u>(1,040)</u>
Long-term debt		26,711
Less: Current portion of long-term debt		<u>(26,711)</u>
Long-term debt, net of current portion	\$	<u>—</u>

## 10. DERIVATIVE LIABILITIES

### 2018 Exit Fee

In May 2018, in connection with entering into the 2018 Loan Agreement, we entered into an agreement pursuant to which we agreed to pay \$1.5 million in cash (“2018 Exit Fee”) upon any change of control transaction in respect of the Company or if we obtain both (i) FDA approval of XPHOZAH and (ii) FDA approval of IBSRELA, which was obtained on September 12, 2019 (“2018 Exit Fee Agreement”). Notwithstanding the February 2022 prepayment of the 2018 Loan, our obligation to pay the 2018 Exit Fee will expire on May 16, 2028. We concluded that the 2018 Exit Fee is a freestanding derivative which should be accounted for at fair value on a recurring basis. The estimated fair value of the 2018 Exit Fee is recorded as a derivative liability and included in accrued expense and other current liabilities on the accompanying balance sheets. As of December 31, 2022 and 2021, the estimated fair value of the 2018 Exit Fee was \$1.2 million and \$0.7 million, respectively.

The fair value of the derivative liability was determined using a discounted cash flow analysis and is classified as a Level 3 measurement within the fair value hierarchy since our valuation utilized significant unobservable inputs. Specifically, the key assumptions included in the calculation of the estimated fair value of the derivative instrument include: (i) our estimates of both the probability and timing of a potential \$1.5 million payment to Solar Capital Ltd. and Western Alliance Bank as a result of the FDA approvals, and (ii) a discount rate which was derived from our estimated cost of debt, adjusted with current LIBOR. Generally, increases or decreases in the probability of occurrence would result in a directionally similar impact in the fair value measurement of the derivative instrument and it is estimated that a 10% increase (decrease), not to exceed 100%, in the probability of occurrence would result in a fair value fluctuation of no more than \$0.1 million.

**2022 Exit Fee**

In February 2022, in connection with entering into the 2022 Loan Agreement, we entered into an agreement, whereby we agreed to pay an exit fee in the amount of 2% of the 2022 Loan funded ("2022 Exit Fee") upon (i) any change of control transaction or (ii) our achievement of net revenue from the sale of any products equal to or greater than \$100.0 million, measured on a six (6) months basis ("Revenue Milestone"), tested monthly at the end of each month. Notwithstanding the prepayment or termination of the 2022 Loan, the 2022 Exit Fee will expire on February 23, 2032. We concluded that the 2022 Exit Fee is a freestanding derivative which should be accounted for at fair value on a recurring basis. The estimated fair value of the 2022 Exit Fee is recorded as a derivative liability and included in accrued expenses and other current liabilities on the accompanying balance sheets. As of December 31, 2022, the estimated fair value of the 2022 Exit Fee is \$0.4 million.

The fair value of the derivative liability was determined using a discounted cash flow analysis and is classified as a Level 3 measurement within the fair value hierarchy since our valuation utilized significant unobservable inputs. Specifically, the key assumptions included in the calculation of the estimated fair value of the 2022 derivative liability include: (i) our estimates of both the probability and timing of achieving the Revenue Milestone and (ii) the probability and timing of funding the Term B Loan, which is dependent upon (a) approval by the FDA for our NDA for the control of serum phosphorus in adult patients with CKD on dialysis by December 31, 2022, and (b) achievement of certain product revenue milestone targets. Generally, increases or decreases in the probability of occurrence would result in a directionally similar impact in the fair value measurement of the derivative liability and it is estimated that a 10% increase (decrease) in the probability of occurrence would not result in a material fair value fluctuation.

Changes in the fair value of recurring measurements included in Level 3 of the fair value hierarchy are presented as other income, net in our Statements of Operations and were as follows for the years ended December 31, 2022, 2021 and 2020 (in thousands):

	<u>2022</u>	<u>2021</u>	<u>2020</u>
Balance at January 1,	\$ 698	\$ 1,376	\$ 969
2022 Exit Fee addition at fair value	375	—	—
Changes in estimated fair value:			
2018 Exit Fee	510	(678)	407
2022 Exit Fee	73	—	—
Fair value of exit fee derivative liabilities at December 31,	<u>\$ 1,656</u>	<u>\$ 698</u>	<u>\$ 1,376</u>

**11. LEASES**

We have recorded right-of-use operating lease assets under three lease agreements. We have evaluated our facility leases and determined that, effective upon the adoption of Topic 842, the leases evaluated are all operating leases. We have performed an evaluation of our other contracts with suppliers and collaborators in accordance with Topic 842 and have determined that, except for the facility leases described below, none of our contracts contain a lease.

We have recorded a right-of-use operating lease asset located in Fremont, California under a lease agreement entered into in September 2008 that was amended multiple times to add space and to extend the lease term through March 2025. The office space consists of 72,500 square feet. We do not have an option to renew the lease at our current Fremont location beyond March 2025.

We have recorded a right-of-use operating lease asset located in Waltham, Massachusetts under a lease agreement entered into in October 2018. The office space consisted of 3,520 square feet with the lease terminating in September 2021. We did not renew the lease at our original Waltham, Massachusetts facility. During April 2021 and May 2021, we recorded right-of-use operating lease assets for a new facility in Waltham, Massachusetts under a lease agreement entered into during December 2020 with lease commencement dates during April and May 2021. The office space consists of 12,864 square feet with the lease terminating in June 2026. We have an option to extend the lease term for one additional five year period. This option to extend the lease term has not been included in the calculation since currently the exercise of the option is uncertain and therefore deemed not probable. We recorded a \$1.6 million right-of-use asset and lease liability for the Waltham lease upon commencement of the lease.

We have recorded a right-of-use operating lease asset located in Milwaukee, Wisconsin under a lease agreement entered into in October 2020 with a lease commencement date in November 2020. The office space consists of 4,768 square feet with the lease terminating in February 2026. We have an option to extend the lease term by one additional five-year period. This option to extend the lease term has not been included in the calculation since currently the exercise of the option is uncertain and therefore deemed not probable. We recorded a \$0.4 million right-of-use asset and lease liability for the Milwaukee lease upon commencement of the lease.

All of our leases are operating leases and each contain customary rent escalation clauses. Certain of the leases have both lease and non-lease components. We have elected to account for each separate lease component and the non-lease components associated with that lease component as a single lease component for all classes of underlying assets.

The following table provides additional details of our facility leases presented in our balance sheets (dollars in thousands):

Facilities	December 31,	
	2022	2021
Right-of-use assets	\$ 9,295	\$ 12,752
Current portion of lease liabilities	3,894	3,492
Operating lease liability, net of current portion	5,855	9,748
Total	\$ 9,749	\$ 13,240
Weighted-average remaining life (years)	2.4	3.4
Weighted-average discount rate	6.8 %	6.9 %

The lease costs, which are included in operating expenses in our statements of operations, were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Operating lease expense	\$ 4,257	\$ 3,671	\$ 2,608
Cash paid for operating lease	\$ 4,292	\$ 3,438	\$ 3,065

The following table summarizes our undiscounted cash payment obligations for our operating lease liabilities as of December 31, 2022 (in thousands):

Ending December 31,	
2023	\$ 4,440
2024	4,589
2025	1,321
2026	252
Thereafter	—
Total undiscounted operating lease payments	10,602
Imputed interest expenses	(853)
Total operating lease liabilities	9,749
Less: Current portion of operating lease liability	(3,894)
Operating lease liability, net of current portion	\$ 5,855

## 12. STOCKHOLDERS' EQUITY

In July 2020, we filed a Form S-3 registration statement, which became effective in August 2020 ("2020 Registration Statement"), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$100.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies LLC ("Jefferies"), deemed to be "at-the-market offerings" ("2020 Open Market Sales Agreement"). Pursuant to the 2020 Open Market Sales Agreement, Jefferies, as sales agent, received a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2020 Open Market Sales Agreement. As of December 31, 2021, we had sold 23.3 million shares and received the maximum gross proceeds of \$100.0 million pursuant to the 2020 Open Market Sales Agreement.

In August 2021, we filed an additional prospectus supplement under the 2020 Registration Statement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under an additional sales agreement we entered into with Jefferies ("2021 Open Market Sales Agreement"), pursuant to which we may, from time to time, sell up to \$150.0 million in shares of our common stock through Jefferies. We are required to sell shares under the 2021 Open Market Sales Agreement. Pursuant to the 2021 Open Market Sales Agreement, Jefferies, as our sales agent, receives a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2021 Open Market Sales Agreement. During the twelve months ended December 31, 2022, we sold 64.1 million shares and received gross proceeds of \$73.1 million at a weighted average sales price of approximately \$1.14 per share under the 2021 Open Market Sales Agreement. As of December 31, 2022 we sold a total of 79.8 million shares and received gross proceeds of \$98.1 million at a weighted average sales price of approximately \$1.23 per share under the 2021 Open Market Sales Agreement. During the period January 1, 2023 to January 12, 2023, we received additional gross proceeds of \$20.0 million for the sale of an additional 7.7 million shares which were sold at a weighted average sales price of approximately \$2.60 per share under the 2021 Open Market Sales Agreement. There have been no other sales under the 2021 Open Market Sales Agreement after December 31, 2022.

In January 2023, we filed a Form S-3 registration statement, which became effective in January 2023 ("2023 Registration Statement"), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies LLC ("Jefferies"), deemed to be "at-the-market offerings" ("2023 Open Market Sales Agreement"). Pursuant to the 2023 Open Market Sales Agreement, Jefferies, as sales agent, may receive a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2023 Open Market Sales Agreement. There have been no sales of our common stock under the 2023 Open Market Sales Agreement.

## 13. EQUITY INCENTIVE PLANS

### *2008 Plan*

We granted options under our 2008 Stock Incentive Plan ("2008 Plan") until June 2014 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2008 Plan. The 2008 Plan provided for the granting of incentive and non-qualified stock options, and stock purchase rights to employees, directors and consultants at the discretion of the board of directors. Stock options granted generally vested over a period of four years from the date of grant. In connection with the board of directors and stockholders' approval of the 2014 Plan, all remaining shares available for future award under the 2008 Plan were transferred to 2014 Plan, as discussed below, and the 2008 Plan was terminated.

### *2014 Plan*

The 2014 Equity Incentive Award Plan ("2014 Plan") became effective on June 18, 2014. Under the 2014 Plan, 1.4 million shares of common stock were initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, stock appreciation rights ("SARs"), restricted stock awards, service-based restricted stock unit ("RSU") awards, performance-based restricted stock unit ("PRSU") awards, deferred stock awards, deferred stock unit awards, dividend equivalent awards, stock payment awards and performance awards. In addition, 35 thousand shares that had been available for future awards under the 2008 Plan as of June 18, 2014, were added to the initial reserve available under the 2014 Plan, bringing the total reserve upon the effective date of the 2014 Plan to 1.5 million shares. The number of shares initially reserved for

issuance or transfer pursuant to awards under the 2014 Plan will be increased by (i) the number of shares represented by awards outstanding under 2008 Plan on June 18, 2014, that are either forfeited or lapse unexercised or that are repurchased for the original purchase price thereof, up to a maximum of 1.2 million shares, and (ii) if approved by the administrator of the 2014 Plan, an annual increase on the first day of each fiscal year ending in 2024 equal to the lesser of (A) four percent (4.0%) of the shares of stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (B) such smaller number of shares of stock as determined by our board of directors; provided, however, that no more than 10.7 million shares of stock may be issued upon the exercise of incentive stock options.

### 2016 Plan

In November 2016, our board of directors approved the 2016 Employment Commencement Incentive Plan (“Inducement Plan”) under which 1.0 million shares were reserved. In January 2021, January 2022 and December 2022, 0.5 million, 2.0 million and 3.0 million shares, respectively, were added to the Inducement Plan. As of December 31, 2022, 2.1 million shares of our common stock were subject to inducement grants that were issued pursuant to the Inducement Plan.

### Stock Options

A summary of our stock option activity and related information during the twelve months ended December 31, 2022 is as follows (in thousands, except per share dollar amounts and years):

	Shares Available for Grant	Options Issued and Outstanding		Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
		Number of Shares	Weighted-Average Exercise Price per Share		
Balance at December 31, 2021	4,974	10,417	\$ 7.00		
Options authorized	10,207	—	\$ —		
Options granted	(5,392)	5,392	\$ 0.96		
Options exercised	—	(14)	\$ 0.99		
Options canceled	1,832	(1,832)	\$ 5.80		
Issuance of common stock for services	(712)	—	\$ —		
Balance at December 31, 2022	10,909	13,963	\$ 4.83	7.3	\$ 10,156
Vested and expected to vest at December 31, 2022		13,963	\$ 4.83	7.3	\$ 10,156
Exercisable at December 31, 2022		8,283	\$ 6.32	6.3	\$ 2,727

The aggregate intrinsic value represents the difference between the total pre-tax value (i.e., the difference between our stock price and the exercise price) of stock options outstanding as of December 31, 2022, based on our common stock closing price of \$2.85 per share, which would have been received by the option holders if all their in-the-money options had been exercised as of that date.

The intrinsic value of options exercised during the years ended December 31, 2022, 2021 and 2020, was \$30 thousand, \$1.7 million, and \$2.7 million, respectively.

The weighted-average grant-date estimated fair value of options granted during the years ended December 31, 2022, 2021 and 2020 was \$0.63, \$3.92 and \$4.82 per share, respectively. The estimated grant date fair value of employee stock options was calculated using the Black-Scholes option-pricing model, based on the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Expected term (years)	4.9	5.0	6.0
Expected volatility	92.1 %	77.0 %	83.0 %
Risk-free interest rate	2.2 %	4.7 %	1.1 %
Dividend yield	— %	— %	— %

**Expected Term**—We have limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock-option grants. As such, the expected term was initially estimated using the simplified method whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option. Beginning in 2021, we estimate the expected term of our options based upon historical exercises and post-vesting termination behavior, which has not resulted in a material difference as compared to using the simplified method.

**Expected Volatility**—Since January 1, 2017, we use the historic volatility of our own stock over the retrospective period corresponding to the expected remaining term of the options, or the period since our shares were first quoted on The Nasdaq Global Market, if that is shorter, to compute our expected stock price volatility.

**Risk-Free Interest Rate**—The risk-free interest rate assumption is based on the zero-coupon U.S. treasury instruments on the date of grant with a maturity date consistent with the expected term of our stock option grants.

**Dividend Yield**—To date, we have not declared or paid any cash dividends and does not have any plans to do so in the future. Therefore, we use an expected dividend yield of zero.

### **Restricted Stock Units**

A summary of our RSUs activity and related information for the twelve months ended December 31, 2022 is as follows (in thousands, except per share dollar amounts):

	Number of RSUs	Weighted-Average Grant Date Fair Value Per Share
Non-vested restricted stock units at December 31, 2021	3,529	\$ 2.04
Granted	2,195	\$ 0.89
Vested	(3,956)	\$ 1.34
Forfeited	(362)	\$ 2.23
Non-vested restricted stock units at December 31, 2022	<u>1,406</u>	<u>\$ 2.17</u>

The total estimated fair value of RSUs vested during the years ended December 31, 2022, 2021 and 2020 was \$2.6 million, \$0.8 million and zero, respectively.

In July 2018, we granted 0.9 million PRSUs to our employees that vested upon the achievement of certain performance conditions, subject to the employees' continued service relationship with us through the achievement date. During 2020, we granted an additional 30 thousand PRSUs subject to the same performance conditions. All 0.9 million of these PRSUs vested in September 2020.

### **Issuance of Common Stock for Services**

During the years ended December 31, 2022, 2021 and 2020, we issued approximately 0.7 million, 26 thousand and 42 thousand shares, respectively, of common stock to members of the board of directors who elected to receive stock in lieu of their cash fees under our Non-Employee Director Compensation Program. The shares issued during the years ended December 31, 2022, 2021 and 2020 were valued at \$0.4 million, \$0.2 million and \$0.3 million for each year, respectively, based on the fair value of the common stock on the date of grant.

### **Employee Stock Purchase Plan**

We adopted the 2014 Employee Stock Purchase Plan ("ESPP") and initially reserved approximately 0.2 million shares of common stock as of its effective date of June 18, 2014. If approved by the administrator of the ESPP, on the first day of each calendar year, ending in 2024, the number of shares in the reserve will increase by an amount equal to the lesser of (i) one percent (1.0%) of the shares of common stock outstanding on the last day of the immediately preceding fiscal year and (ii) such number of shares of common stock as determined by the board of directors; provided, however, no more than 2.2 million shares of our common stock may be issued under the ESPP.

A summary of our ESPP activity during the twelve months ended December 31, 2022 is as follows (in thousands, except per share dollar amounts):

	Shares Available for Grant	Number of Shares Purchased	Average Purchase Price per Share	Gross Proceeds
Balance at December 31, 2021	899	1,048		
Shares purchased	(308)	308	\$ 0.63	\$ 195
Balance at December 31, 2022	591	1,356		

The following table illustrates the weighted-average assumptions for the Black-Scholes option-pricing model used in determining the fair value of ESPP purchase rights granted to our employees:

	Year Ended December 31,		
	2022	2021	2020
Expected term (years)	0.5	0.5	0.5
Expected volatility	97.2 %	123.0 %	79.4 %
Risk-free interest rate	1.9 %	0.7 %	0.5 %
Dividend yield	— %	— %	— %

### Stock-based Compensation Expense

Stock-based compensation expense recognized for stock options, RSUs, PRSUs and our ESPP are recorded as operating expenses in our statements of operations and comprehensive loss, as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Selling, general and administrative	\$ 7,525	\$ 7,923	\$ 6,522
Research and development	3,225	4,116	4,061
Total	\$ 10,750	\$ 12,039	\$ 10,583

A summary of our total unrecognized stock-based compensation expense, net of estimated forfeitures, as of December 31, 2022 is as follows (dollars in thousands):

	December 31, 2022	
	Unrecognized Compensation Expense	Average Remaining Vesting Period (Years)
Stock options grant	\$ 9,434	2.55
RSU grants	\$ 2,937	2.95
ESPP	\$ 22	0.2

## 14. RESTRUCTURING

During 2021, we implemented restructuring plans in August and October following the receipt of a Complete Response Letter (“CRL”) from the U.S. FDA relating to our new drug application (“NDA”) for XPHOZAH and following the conclusion of an End of Review Type A meeting with the FDA, respectively. Both restructuring plans were substantially completed in December 2021 and most of the cash payments related to the reduction in workforce were disbursed prior to December 31, 2021.

Impacted employees were eligible to receive severance benefits and additional Company funded COBRA premiums, contingent upon an impacted employee’s execution (and non-revocation) of a separation agreement, which included a general release of claims against us. In connection with restructuring, we incurred restructuring charges of \$6.2 million, which were recorded during the twelve months ended December 31, 2021, related to one-time termination notice and severance payments and other employee-related costs. We did not incur any significant contract termination costs pursuant to restructuring. Of the

charges, \$2.7 million was recorded in research and development expenses, and \$3.5 million was recorded in selling, general and administrative expense in the accompanying statements of operations and comprehensive loss. Most of the cash payments related to the reduction in workforce were disbursed during the twelve months ended December 31, 2021. We reported the remaining estimated restructuring liability of zero and \$0.5 million as accrued compensation and benefits in our balance sheet as of December 31, 2022 and 2021, respectively.

In addition, in October, 2021, our Board approved, and management has implemented a retention program consisting of cash payments and grants of RSUs to our employees, including our executives, not impacted by the reduction in force.

## 15. PROPERTY AND EQUIPMENT, NET

Property and equipment consist of the following (in thousands):

	December 31,	
	2022	2021
Laboratory equipment	\$ 46	\$ 7,474
Office equipment and furniture	2,089	2,034
Leasehold improvements	8,745	8,745
Property and equipment, gross	10,880	18,253
Less: accumulated depreciation	(9,657)	(15,891)
Total property and equipment, net	\$ 1,223	\$ 2,362

We recognized depreciation expense in the amount of \$0.7 million, \$1.4 million, and \$1.8 million for the years ended December 31, 2022, 2021 and 2020, respectively.

During the year ended December 31, 2022, following the elimination of our internal research organization in the fourth quarter of 2021, we sold laboratory equipment with total net carrying value of \$0.5 million and received cash proceeds of \$1.8 million, resulting in a gain of \$1.3 million which has been reported within other income, net on our statement of operations and comprehensive loss.

## 16. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Accrued payments due to AstraZeneca	\$ 3,385	\$ 69
Accrued gross to net revenue liabilities	1,991	—
Accrued contract manufacturing expenses	1,657	2,485
Derivative liability for exit fees	1,656	698
Accrued non-clinical research and development expenses	1,188	265
Accrued professional and consulting services	808	597
Accrued sales and marketing expenses	587	256
Accrued clinical expenses	223	2,522
Other	885	474
Total accrued expenses and other current liabilities	\$ 12,380	\$ 7,366



## 17. INCOME TAXES

The components of our provision for income taxes for the years ended December 31, 2022, 2021 and 2020, are as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
<b>Current:</b>			
State	\$ 8	\$ 4	\$ 2
Foreign	—	—	—
Total current	8	4	2
<b>Deferred:</b>			
Federal	—	—	—
Total deferred	—	—	—
Provision for income taxes	<u>\$ 8</u>	<u>\$ 4</u>	<u>\$ 2</u>

A reconciliation of the statutory federal income tax rate to our effective tax rate is as follows:

	Year Ended December 31,		
	2022	2021	2020
Income tax at the federal statutory rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	1.9	0.4	0.7
Tax credits	1.5	1.0	1.3
Executive compensation disallowed under IRC Sec 162(m)	(1.6)	(1.1)	(0.5)
Stock based compensation	(2.3)	(1.3)	(0.1)
Other	(0.8)	—	(0.1)
Change in valuation allowance	(19.7)	(20.0)	(22.3)
Income tax provision	<u>— %</u>	<u>— %</u>	<u>— %</u>

Deferred income taxes reflect the 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. Significant components of our deferred tax assets are as follows as of December 31, 2022 and 2021 (in thousands):

	December 31,	
	2022	2021
<b>Deferred tax assets:</b>		
Amortization and depreciation	\$ 64,111	\$ 61,098
Net operating loss carryforwards	86,547	74,989
Tax credits	14,411	13,827
Stock-based compensation	5,244	4,054
Other	7,486	3,867
Gross deferred tax assets	177,799	157,835
Valuation allowance	(175,670)	(155,141)
Deferred tax assets net of valuation allowance	2,129	2,694
<b>Deferred tax liabilities:</b>		
Right-of-use asset	(2,129)	(2,689)
Other	—	(5)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

Realization of deferred tax assets is dependent on future taxable income, if any, the timing and the amount of which are uncertain. We assess the available positive and negative evidence to estimate whether sufficient future taxable income will be generated to permit use of the existing deferred tax assets. A significant component of objective negative evidence evaluated was our cumulative loss incurred over the three-year period ended December 31, 2022. Such objective evidence limits the

ability to consider other subjective evidence, such as our projections for future growth. On the basis of this evaluation, as of December 31, 2022, December 31, 2021 and December 31, 2020, a full valuation allowance has been recorded against our net deferred tax asset. The valuation allowance increased by \$20.5 million in 2022 primarily due to increases in net operating losses. The amount of the deferred tax asset considered realizable, however, could be adjusted if estimates of future taxable income during the carryforward period are reduced or increased or if objective negative evidence in the form of cumulative losses is no longer present and additional weight is given to subjective evidence such as our projections for growth.

As of December 31, 2022, we had net operating loss carryforwards for federal income tax purposes of approximately \$433.6 million, of which approximately \$283.4 million can be carried forward indefinitely and the remaining net operating losses expire beginning in 2030, if not utilized. Federal research and development tax credit carryforwards of approximately \$17.2 million that expire beginning in 2027, if not utilized, and foreign tax credit carryforwards of approximately \$1.2 million that expire in 2027, if not utilized.

In addition, we had net operating loss carryforwards for California income tax purposes of approximately \$89.8 million that expire beginning of 2030, if not utilized, and state research and development tax credit carryforwards of approximately \$8.6 million which can be carried forward indefinitely. We had approximately \$0.1 million of minimum tax credit carryovers for California income tax purposes. The minimum tax credits have no expiration date. We had other state net operating losses of approximately \$19.0 million that begin to expire in 2031.

The future utilization of net operating loss and tax credit carryforwards and credits may be subject to an annual limitation, pursuant to Internal Revenue Code Sections 382 and 383, as a result of ownership changes that may have occurred previously or that could occur in the future. Due to the existence of the valuation allowance, limitations under Section 382 and 383 will not impact our effective tax rate.

Under the Tax Cuts and Jobs Act of 2017, research and development costs are no longer fully deductible and are required to be capitalized and amortized for U.S. tax purposes effective January 1, 2022. The mandatory capitalization requirement did not have a material impact on our deferred tax assets and did not result in a cash tax liability as we have historically elected to capitalize research and development expenses for tax purposes.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	December 31,		
	2022	2021	2020
Balance at beginning of year	\$ 24,426	\$ 23,624	\$ 24,538
Additions based on tax positions related to current year	460	1,613	474
Subtractions related to lapse of statute of limitation	(811)	—	—
Subtractions based on tax positions related to prior year	—	(811)	(1,388)
Balance at end of year	<u>\$ 24,075</u>	<u>\$ 24,426</u>	<u>\$ 23,624</u>

We recognize a tax benefit from an uncertain tax position when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on the technical merits. Income tax positions must meet a more likely than not recognition at the effective date to be recognized. None of our unrecognized tax benefits would impact the effective tax rate if recognized, because the benefit would be offset by an increase in the valuation allowance.

We have elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2022, 2021 and 2020, we did not recognize accrued interest and penalties related to unrecognized tax benefits. Although the timing and outcome of an income tax audit is highly uncertain, we do not anticipate that the amount of existing unrecognized tax benefits will significantly change during the next 12 months.

We file a U.S. federal income tax return and income tax returns in various state and local jurisdictions. Due to our net operating loss and tax credit carryforwards, the income tax returns remain open to U.S. federal and state tax examinations. We are not currently under examination in any tax jurisdiction.

## 18. GEOGRAPHIC INFORMATION AND CONCENTRATIONS

Revenues are attributed to geographical areas based on the location at which we earned revenue for product sales of IBSRELA or the domicile of our collaboration partners. A summary of our revenue by geographic areas for the years ended December 31, 2022, 2021 and 2020, is as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
United States (1)	\$ 15,600	\$ —	\$ —
International:			
Asia Pacific (2)	36,527	10,084	6,765
North America (3)	31	13	806
<b>Total revenue</b>	<b>\$ 52,158</b>	<b>\$ 10,097</b>	<b>\$ 7,571</b>

(1) Revenues from the United States are comprised of amounts earned from sales of IBSRELA.

(2) Revenues from Asia Pacific are primarily comprised of amounts earned in accordance with the 2017 KKC Agreement and the 2019 KKC Agreement.

(3) Revenues from North America are comprised of amounts earned from Canada in accordance with the Knight Agreement.

Revenues from Customers and collaboration partnerships accounting for more than 10% of total revenues during the years ended December 31, 2022, 2021 and 2020 were as follows:

	Year Ended December 31,		
	2022	2021	2020
KKC	70.0 %	100 %	89 %
Knight	0.1 %	— %	11 %
AmerisourceBergen Drug Corporation	11.1 %	— %	— %

Historically, we have not experienced credit losses from our accounts receivable. We have not recorded a reserve for credit losses as of December 31, 2022 and 2021.

## 19. NET LOSS PER SHARE

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period, less shares subject to repurchase, and excludes any dilutive effects of stock-based awards and warrants. Diluted net loss per common share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, and unvested restricted common stock and stock units. As we had net losses for the years ended December 31, 2022, 2021 and 2020, all potential common shares were determined to be anti-dilutive.

The following table sets forth the computation of net loss per common share (in thousands, except per share dollar amounts):

	Year Ended December 31,		
	2022	2021	2020
<b>Numerator:</b>			
Net loss	\$ (67,207)	\$ (158,165)	\$ (94,313)
<b>Denominator:</b>			
Weighted average common shares outstanding - basic and diluted	158,690	104,206	89,582
<b>Net loss per share - basic and diluted</b>	<b>\$ (0.42)</b>	<b>\$ (1.52)</b>	<b>\$ (1.05)</b>

For the years ended December 31, 2022, 2021 and 2020, the total numbers of securities that could potentially dilute net income per share in the future that were not considered in the diluted net loss per share calculations because the effect would have been anti-dilutive were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Options to purchase common stock	13,522	11,871	9,247
Restricted stock units	2,694	1,602	26
ESPP shares issuable	166	207	94
Warrants to purchase common stock	—	—	932
<b>Total</b>	<b>16,382</b>	<b>13,680</b>	<b>10,299</b>

The number of potential common shares that would have been included in diluted income per share had it not been for the anti-dilutive effect caused by the net loss, computed by converting these securities using the treasury stock method during the years ended December 31, 2022, 2021 and 2020, was approximately 0.6 million, 1.1 million and 2.1 million, respectively.

## 20. COMMITMENTS AND CONTINGENCIES

### *Guarantees and Indemnifications*

We indemnify each of our officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at our request in such capacity, as permitted under Delaware law and in accordance with our certificate of incorporation and bylaws. The term of the indemnification period lasts as long as an officer or director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity.

The maximum amount of potential future indemnification is unlimited; however, we currently hold director and officer liability insurance, which allows the transfer of risk associated with our exposure and may enable us to recover a portion of any future amounts paid. We believe that the fair value of these indemnification obligations is minimal. Accordingly, we have not recognized any liabilities relating to these obligations for any period presented.

### *Legal Proceedings and Claims*

On July 30 and August 12, 2021, two putative securities class action lawsuits were commenced in the U.S. District Court for the Northern District of California naming as defendants Ardelyx and two current officers captioned *Strezsak v. Ardelyx, Inc., et al.*, Case No. 4:21-cv-05868-HSG, and *Siegel v. Ardelyx, Inc., et al.*, Case No. 5:21-cv-06228-HSG (together, the “Securities Class Actions”). The complaints allege that the defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 thereunder, by making false and misleading statements and omissions of material fact related to tenapanor. The plaintiffs seek to represent all persons who purchased or otherwise acquired Ardelyx securities between August 6, 2020, and July 19, 2021. The plaintiffs seek damages and interest, and an award of costs, including attorneys’ fees. On July 19, 2022, the court consolidated the two putative class actions and appointed a lead plaintiff and lead counsel. The lead plaintiff filed an amended complaint on September 29, 2022. Defendants filed a motion to dismiss the amended complaint on December 2, 2022. In January and February 2023, in lieu of filing a response to defendant’s motion to dismiss, plaintiffs filed a motion seeking leave to further amend their complaint and defendants filed an opposition to the motion for leave to further amend the complaint. A hearing on the motion for leave to further amend the complaint is scheduled for mid-May 2023. We believe the plaintiff’s claims are without merit and we have not recorded any accrual for a contingent liability associated with these legal proceedings.

On December 7, 2021 and March 29, 2022, two verified shareholders derivative lawsuits were filed in the U.S. District Court for the Northern District of California purportedly on behalf of Ardelyx against certain of Ardelyx’s executive officers and members of our board of directors, captioned *Go v. Raab, et al.*, Case No. 4:21-cv-09455-HSG, and *Morris v. Raab, et al.*, Case No. 4:22-cv-01988-JSC. The complaints allege that the defendants’ violations of Section 14(a) of the Securities Exchange Act of 1934, as amended, breaches of fiduciary duties, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets, for personally making and/or causing Ardelyx to make materially false and misleading statements regarding the Company’s business, operations and prospects. The complaint seeks contribution under Sections 10(b) and 21D of the Securities Exchange Act of 1934 from two executive officers. On January 19, and April 27, 2022, the court granted the parties’ stipulation to stay the Go and Morris actions, respectively, until resolution of the anticipated motion(s) to dismiss in the Securities Class Actions. On October 25, 2022, the parties filed a stipulation to consolidate and stay the Go and Morris actions,

and on October 27, 2022, the court consolidated the Go and Morris action and stayed the consolidated action pending resolution of the anticipated motion(s) to dismiss in the Securities Class Action. We believe the plaintiff's claims are without merit and we have not recorded any accrual for a contingent liability associated with these legal proceedings.

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. As of December 31, 2022, there is no litigation pending that would reasonably be expected to have a material adverse effect on our results of operations and financial condition, and no contingent liabilities were accrued as of December 31, 2022.

## **21. SUBSEQUENT EVENTS**

In January 2023, we filed a Form S-3 registration statement, which became effective in January 2023 ("2023 Registration Statement"), containing (i) a base prospectus for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$250.0 million of our common stock, preferred stock, debt securities, warrants and/or units, from time to time in one or more offerings; and (ii) a prospectus supplement for the offering, issuance and sale by us of up to a maximum aggregate offering price of \$150.0 million of our common stock that may be issued and sold, from time to time, under a sales agreement with Jefferies LLC ("Jefferies"), deemed to be "at-the-market offerings" ("2023 Open Market Sales Agreement"). Pursuant to the 2023 Open Market Sales Agreement, Jefferies, as sales agent, may receive a commission of up to 3.0% of the gross sales price for shares of common stock sold under the 2023 Open Market Sales Agreement.

On February 9, 2023, we entered into a second amendment ("Second Amendment") to our Loan Agreement with the Lenders. The Second Amendment extends the interest-only term of the loan by twelve months to March 31, 2025 provided that we either (i) receive approval from the FDA for our NDA for the control of serum phosphorus in adult patients with CKD on dialysis on or prior to November 30, 2023 or (ii) achieve certain product revenue milestone targets as described in the Second Amendment for the year ending December 31, 2023. The Second Amendment also extends the period under which we may draw the Term B Loan from July 25, 2023 to December 20, 2023, and amends the milestone that we must achieve in order to draw the Term B Loan by extending the time period for the receipt of approval by the FDA of the NDA for the control of serum phosphorus in adult patients with CKD on dialysis until November 30, 2023. In addition, the Second Amendment replaces the floating per annum interest rate with 7.95% plus the greater of (a) one percent (1.00%) per annum and (b)(i) 0.022% plus (ii) 1-month CME Term SOFR reference rate as published by the CME Term SOFR Administrator on the CME Term SOFR Administrator's Website.

## **ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

## **ITEM 9A. CONTROLS AND PROCEDURES**

### ***Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures***

As of December 31, 2022, management, with the participation of our Chief Executive Officer ("CEO") and Chief Financial and Operations Officer ("CFOO"), performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including the CEO and the CFOO, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our CEO and CFOO concluded that, as of December 31, 2022, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

***Management’s Annual Report on Internal Control Over Financial Reporting***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed by, or under the supervision of, our CEO and CFO, and effected by our Board of Directors, management and other personnel, 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that accurately and fairly reflect in reasonable detail the transactions and dispositions of the assets of our company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- Provide reasonable assurances regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material adverse effect on our financial statements.

Our management assessed our internal control over financial reporting as of December 31, 2022, the end of the period covered by this Annual Report on Form 10-K. Management based its assessment on criteria established in “Internal Control—Integrated Framework (2013)” issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on management’s assessment of our internal control over financial reporting, management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

***Changes in Internal Control over Financial Reporting***

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

**ITEM 9B. OTHER INFORMATION**

None.

**ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS**

Not Applicable.

### **PART III**

#### **ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2023 Annual Meeting of Stockholders (“Proxy Statement”), which will be filed not later than 120 days after the end of our fiscal year ended December 31, 2022, under the headings “Executive Officers,” “Election of Directors,” “Corporate Governance,” and “Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our website at [www.ardelyx.com](http://www.ardelyx.com). The Code of Business Conduct and Ethics is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. If we make any amendment to, or waiver from, a provision of our Code of Conduct that we are required to disclose under SEC rules, we intend to satisfy that disclosure requirement by posting such information to our website at [www.ardelyx.com](http://www.ardelyx.com). The contents of our websites are not intended to be incorporated by reference into this Form 10-K or in any other report or document we file with the SEC, and any references to our websites are intended to be inactive textual references only.

#### **ITEM 11. EXECUTIVE COMPENSATION**

The information required by this item regarding executive compensation will be incorporated by reference to the information set forth in the sections titled “Executive Compensation” in our Proxy Statement.

#### **ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The information required by this item regarding security ownership of certain beneficial owners and management will be incorporated by reference to the information set forth in the section titled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our Proxy Statement.

#### **ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The information required by this item regarding certain relationships and related transactions and director independence will be incorporated by reference to the information set forth in the sections titled “Certain Relationships and Related Party Transactions” and “Election of Directors”, respectively, in our Proxy Statement.

#### **ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

The information required by this item regarding principal accountant fees and services will be incorporated by reference to the information set forth in the section titled “Principal Accountant Fees and Services” in our Proxy Statement.

**PART IV****ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES**

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements at Item 8 herein.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

See the Exhibit Index immediately following this page.

**ITEM 16. FORM 10-K SUMMARY**

None.

**Exhibit Index**

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	<a href="#">Amended and Restated Certificate of Incorporation</a>	8-K	6/24/2014	3.1	
3.2	<a href="#">Amended and Restated Bylaws</a>	8-K	6/24/2014	3.2	
4.1	Reference is made to Exhibits 3.1 and 3.2				
4.2	<a href="#">Form of Common Stock Certificate</a>	S-1/A	6/18/2014	4.2	
4.4	<a href="#">Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934</a>	10-K	3/8/2021	10.31	
10.1(a)	<a href="#">Termination Agreement, dated June 2, 2015, by and between AstraZeneca AB and Ardelyx, Inc.</a>	10-Q	8/12/2015	10.1	
10.1(b)	<a href="#">Amendment No. 1 to Termination Agreement and to Manufacturing and Supply Agreement, dated November 2, 2015 by and between AstraZeneca AB and Ardelyx, Inc.</a>	10-K	3/4/2016	10.1(d)	
10.2(a)	<a href="#">Lease, dated August 8, 2008, by and between 34175 Ardenwood Venture, LLC and Ardelyx, Inc.</a>	S-1	5/19/2014	10.4(a)	
10.2(b)	<a href="#">First Amendment to Lease, dated December 20, 2012, by and between 34175 Ardenwood Venture, LLC and Ardelyx, Inc.</a>	S-1	5/19/2014	10.4(b)	
10.2(c)	<a href="#">Second Amendment to Lease, dated September 5, 2014, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC</a>	8-K	9/9/2014	10.1	
10.2(d)	<a href="#">Third Amendment to Lease, dated April 28, 2016, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC</a>	10-Q	8/8/2016	10.3	
10.2(e)	<a href="#">Fourth Amendment to Lease, dated May 25, 2021, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC</a>				X
10.2(f)	<a href="#">Fifth Amendment to Lease, dated May 25, 2021, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC</a>	8-K	6/1/2021	10.1	
10.3	<a href="#">Lease Agreement, dated December 30, 2020, by and between Ardelyx, Inc. and Prospect Fifth Ave, LLC.</a>	10-K	3/8/2021	10.31	
10.4(a)#	<a href="#">Ardelyx, Inc. 2008 Stock Incentive Plan, as amended</a>	S-1	5/19/2014	10.5(a)	



Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.4(b)#	<a href="#">Form of Stock Option Grant Notice and Stock Option Agreement under the 2008 Stock Incentive Plan, as amended</a>	S-1	5/19/2014	10.5(b)	
10.4(c)#	<a href="#">Form of Restricted Stock Purchase Grant Notice and Restricted Stock Purchase Agreement under the 2008 Stock Incentive Plan, as amended</a>	S-1	5/19/2014	10.5(c)	
10.5(a)#	<a href="#">Ardelyx, Inc. 2014 Equity Incentive Award Plan</a>	S-8	7/14/2014	99.3	
10.5(b)#	<a href="#">Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan</a>	S-1/A	6/9/2014	10.6(b)	
10.5(c)#	<a href="#">Form of Restricted Stock Award Agreement and Restricted Stock Unit Award Grant Notice under the 2014 Equity Incentive Award Plan</a>	S-1/A	6/9/2014	10.6(c)	
10.6#	<a href="#">Ardelyx, Inc. 2014 Employee Stock Purchase Plan</a>	S-8	7/14/2014	99.6	
10.7(a)#	<a href="#">Ardelyx, Inc. 2016 Employment Commencement Incentive Plan</a>	S-8	11/10/2016	99.1	
10.7(b)#	<a href="#">Form of Stock Option Grant Notice and Stock Option Agreement under the 2016 Employment Commencement Incentive Plan</a>	S-8	11/10/2016	99.2	
10.7(c)#	<a href="#">Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2016 Employment Commencement Incentive Plan</a>	S-8	11/10/2016	99.3	
10.7(d)#	<a href="#">Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2016 Employment Commencement Incentive Plan</a>	S-8	11/10/2016	99.4	
10.8	<a href="#">Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated June 2, 2015</a>	S-3	7/13/2015	99.1	
10.9	<a href="#">Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated July 14, 2016</a>	10-Q	8/8/2016	10.2	
10.10#	<a href="#">Form of Indemnification Agreement for directors and officers</a>	S-1/A	6/9/2014	10.7	
10.11#	<a href="#">Amended and Restated Executive Employment Agreement, dated June 6, 2014, by and between Ardelyx, Inc. and Michael Raab</a>	S-1/A	6/9/2014	10.8	
10.12#	<a href="#">Offer Letter, dated December 28, 2009, by and between Ardelyx, Inc. and David Rosenbaum, Ph.D.</a>	S-1/A	6/9/2014	10.13	
10.13(a)#	<a href="#">Second Amended and Restated Change in Control and Severance Agreement by and between Ardelyx, Inc. and David P. Rosenbaum, Ph.D.</a>	10-Q	5/8/2018	10.1	
10.13(b)#	<a href="#">Amendment Number One to Second Amended and Restated Change in Control Severance Agreement and Retention Agreement dated December 1, 2021 between Ardelyx, Inc. and David Rosenbaum</a>	10-K	2/28/2022	10.20	
10.14#	<a href="#">Offer Letter, dated November 21, 2012, by and between Ardelyx, Inc. and Elizabeth Grammer, Esq.</a>	S-1/A	6/9/2014	10.14	
10.15#	<a href="#">Second Amended and Restated Change in Control and Severance Agreement by and between Ardelyx, Inc. and Elizabeth Grammer.</a>	10-Q	5/8/2018	10.0	
10.16#	<a href="#">Offer Letter, dated April 27, 2020, by and between Ardelyx, Inc. and Susan Rodriguez</a>	10-Q	8/6/2020	10.1	
10.17#	<a href="#">Change in Control Severance Agreement dated June 2, 2020, by and between Ardelyx, Inc. and Susan Rodriguez</a>	10-Q	8/6/2020	10.2	
10.18#	<a href="#">Offer Letter, dated June 2, 2020, by and between Ardelyx, Inc. and Justin Renz</a>	10-Q	8/6/2020	10.3	
10.19#	<a href="#">Change in Control Severance Agreement, dated June 8, 2020, by and between Ardelyx, Inc. and Justin Renz</a>	10-Q	8/6/2020	10.4	
10.20(a)#	<a href="#">Non-Employee Director Compensation Program</a>	S-1/A	6/9/2014	10.21	
10.20(b)#	<a href="#">Description of amendments to Non-Employee Director Compensation Program</a>	8-K	3/9/2017	N/A	
10.20(c)#	<a href="#">Amended and Restated Non-Employee Director Compensation Program.</a>	10-Q	5/7/2019	10.1	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.20(d)#	<a href="#">Second Amended and Restated Non-Employee Director Compensation Program</a>	10-Q	8/4/2022	10.3	
10.21(a)††	<a href="#">License Agreement, dated November 27, 2017, by and between Kyowa Hakko Kirin Co., Ltd. and Ardelyx, Inc.</a>	10-K	3/14/2018	10.35	
10.21(b)	<a href="#">Amendment Number 1 to License Agreement, dated as of November 27, 2017, by and among Ardelyx, Inc., and Kyowa Kirin Co., Ltd.</a>				X
10.21(c)††	<a href="#">Amendment Number 2 to License Agreement, dated as of April 11, 2022, by and among Ardelyx, Inc., and Kyowa Kirin Co., Ltd.</a>	8-K	4/11/2022	10.1	
10.22††	<a href="#">License Agreement, dated December 11, 2017, by and between Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. and Ardelyx, Inc.</a>	10-K	3/14/2018	10.36	
10.23††	<a href="#">Royalty and Sales Milestone Interest Acquisition Agreement dated June 29, 2022, by and between Ardelyx, Inc. and Healthcare Royalty Partners IV, L.P.</a>	10-Q	8/4/2022	10.1	
10.24(a)	<a href="#">Loan and Security Agreement dated February 23, 2022, by and between Ardelyx, Inc. and SLR Investment Corp.</a>	10-Q	5/5/2022	10.1	
10.24(b)	<a href="#">First Amendment to the Loan and Security Agreement dated August 1, 2022, by and between Ardelyx, Inc. and SLR Investment Corp.</a>	10-Q	8/4/2022	10.2	
10.24(c)	<a href="#">Second Amendment to the Loan and Security Agreement dated February 9, 2023, by and between Ardelyx, Inc. and SLR Investment Corp.</a>				X
10.25	<a href="#">Exit Fee Agreement dated February 23, 2022, by and between Ardelyx, Inc. and SLR Investment Corp.</a>	10-Q	5/5/2022	10.2	
10.26	<a href="#">Exit Fee Agreement, dated May 16, 2018, by and between the Company and Solar Capital Ltd. and Western Alliance Bank.</a>	10-Q	8/7/2018	10.2	
10.27(a)††	<a href="#">Manufacturing Services Agreement, dated May 18, 2020, between Ardelyx, Inc. and Patheon Pharmaceuticals Inc.</a>	10-Q	8/6/2020	10.5	
10.27(b)††	<a href="#">First Amendment to the Manufacturing Services Agreement dated February 27, 2023, between Ardelyx, Inc. and Patheon Pharmaceuticals Inc.</a>				X
10.29	<a href="#">Open Market Sales Agreement, dated August 31, 2021 between Ardelyx, Inc. and Jefferies LLC.</a>	8-K	8/13/2021	10.1	
10.30	<a href="#">Open Market Sales Agreement, dated January 18, 2023 between Ardelyx, Inc. and Jefferies LLC.</a>	S-3	1/19/2023	1.2	
23.1	<a href="#">Consent of Independent Registered Public Accounting Firm</a>			—	X
31.1	<a href="#">Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended</a>			—	X
31.2	<a href="#">Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended</a>			—	X
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>			—	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document			—	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document			—	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document			—	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document			—	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document			—	X

- † Confidential treatment granted as to portions of this Exhibit. The confidential portions of this Exhibit have been omitted and are marked by asterisks.
- †† Certain portions of this exhibit have been redacted pursuant to Item 601(b)(10) of Regulation S-K. A copy of the omitted portions will be furnished supplementally to the Securities and Exchange Commission upon request.
- # Indicates management contract or compensatory plan.

## SIGNATURES

Pursuant to the requirements 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.

**Ardelyx, Inc.**

Date: March 2, 2023

By: /s/ Robert Felsch

**Robert Felsch**  
**Senior Vice President and Chief Accounting Officer**  
**(Principal Accounting Officer)**

## POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Michael Raab, Justin Renz, and Robert Felsch, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Michael Raab</u> Michael Raab	President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i>	March 2, 2023
<u>/s/ Justin Renz</u> Justin Renz	Chief Financial and Operations Officer <i>(Principal Financial Officer)</i>	March 2, 2023
<u>/s/ Robert Felsch</u> Robert Felsch	Chief Accounting Officer <i>(Principal Accounting Officer)</i>	March 2, 2023
<u>/s/ David Mott</u> David Mott	Chairman of the Board of Directors	March 2, 2023
<u>/s/ Robert Bazemore</u> Robert Bazemore	Director	March 2, 2023
<u>/s/ William Bertrand, Jr.</u> William Bertrand, Jr., J.D.	Director	March 2, 2023
<u>/s/ Muna Bhanji</u> Muna Bhanji, R.Ph	Director	March 2, 2023
<u>/s/ Geoffrey A. Block</u> Geoffrey A. Block, M.D.	Director	March 2, 2023
<u>/s/ Onaiza Cadoret-Manier</u> Onaiza Cadoret-Manier	Director	March 2, 2023
<u>/s/ Jan M. Lundberg</u> Jan M. Lundberg, Ph.D.	Director	March 2, 2023
<u>/s/ Richard Rodgers</u> Richard Rodgers	Director	March 2, 2023

**FOURTH AMENDMENT TO LEASE**

THIS FOURTH AMENDMENT TO LEASE (this "Fourth Amendment") is entered into as of this 11<sup>th</sup> day of May, 2018 (the "Execution Date"), by and between 34175 ARDENWOOD VENTURE, LLC, a Delaware limited liability company ("Landlord"), and ARDELYX, INC., a Delaware corporation ("Tenant," formerly known as Nteryx, Inc.).

**RECITALS**

A. WHEREAS, Landlord and Tenant entered into that certain Lease dated as of August 8, 2008, as amended by that certain First Amendment to Lease dated as of December 20, 2012, as further amended by that certain Second Amendment to Lease dated as of September 5, 2014, and as further amended by that certain Third Amendment to Lease dated as of April 28, 2016 (collectively, and as the same may have been further amended, amended and restated, supplemented or modified from time to time, the "Existing Lease"), whereby Tenant leases certain premises (the "Existing Premises") from Landlord at 34175 Ardenwood Boulevard in Fremont, California (the "Building");

B. WHEREAS, Tenant desires to amend its notice address under the Lease; and

C. WHEREAS, Landlord and Tenant desire to modify and amend the Existing Lease only in the respects and on the conditions hereinafter stated.

**AGREEMENT**

NOW, THEREFORE, Landlord and Tenant, in consideration of the mutual promises contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, agree as follows:

I. Definitions. For purposes of this Fourth Amendment, capitalized terms shall have the meanings ascribed to them in the Existing Lease unless otherwise defined herein. The Existing Lease, as amended by this Fourth Amendment, is referred to collectively herein as the "Lease." From and after the date hereof, the term "Lease," as used in the Existing Lease, shall mean the Existing Lease, as amended by this Fourth Amendment.

2. Notices. Notwithstanding anything in the Lease to the contrary, notices delivered to Tenant pursuant to the Lease should be sent to:

Ardelyx, Inc.  
34175 Ardenwood Blvd.  
Fremont, California 94555 Attn: Director of Facilities

With a copy to:

Ardelyx, Inc.  
34175 Ardenwood Blvd.

Fremont, California 94555 Attn: General Counsel

And a copy to:

Solar Capital Ltd.  
500 Park Avenue, 3,d Floor New York, NY 10022 Attn:  
Anthony Storino

3. Broker. Tenant represents and warrants that it has not dealt with any broker or agent in the negotiation for or the obtaining of this Fourth Amendment, and agrees to reimburse, indemnify, save, defend (at Landlord's option and with counsel reasonably acceptable to Landlord, at Tenant's sole cost and expense) and hold harmless the Landlord Parties for, from and against any and all cost or liability for compensation claimed by any such broker or agent, other than Broker, employed or engaged by it or claiming to have been employed or engaged by it.

4. No Default. Tenant represents, warrants and covenants that, to the best of Tenant's knowledge, Landlord and Tenant are not in default of any of their respective obligations under the Existing Lease and no event has occurred that, with the passage of time or the giving of notice (or both) would constitute a default by either Landlord or Tenant thereunder.

5. Effect of Amendment. Except as modified by this Fourth Amendment, the Existing Lease and all the covenants, agreements, terms, provisions and conditions thereof shall remain in full force and effect and are hereby ratified and affirmed. In the event of any conflict between the terms contained in this Fourth Amendment and the Existing Lease, the terms herein contained shall supersede and control the obligations and liabilities of the parties.

6. Successors and Assigns. Each of the covenants, conditions and agreements contained in this Fourth Amendment shall inure to the benefit of and shall apply to and be binding upon the parties hereto and their respective heirs, legatees, devisees, executors, administrators and permitted successors and assigns and sublessees. Nothing in this Section shall in any way alter the provisions of the Lease restricting assignment or subletting.

7. Miscellaneous. This Fourth Amendment becomes effective only upon execution and delivery hereof by Landlord and Tenant. The captions of the paragraphs and subparagraphs in this Fourth Amendment are inserted and included solely for convenience and shall not be considered or given any effect in construing the provisions hereof. All exhibits hereto are incorporated herein by reference. Submission of this instrument for examination or signature by Tenant does not constitute a reservation of or option for a lease, and shall not be effective as a lease, lease amendment or otherwise until execution by and delivery to both Landlord and Tenant.

8. Authority. Tenant guarantees, warrants and represents that the individual or individuals signing this Fourth Amendment have the power, authority and legal capacity to sign this Fourth Amendment on behalf of and to bind all entities, corporations, partnerships, limited liability

companies, joint venturers or other organizations and entities on whose behalf such individual or individuals have signed.

9. Counterparts: Facsimile and PDF Signatures. This Fourth Amendment may be executed in one or more counterparts, each of which, when taken together, shall constitute one and the same document. A facsimile or portable document format (PDF) signature on this Fourth Amendment shall be equivalent to, and have the same force and effect as, an original signature.

[REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]



IN WITNESS WHEREOF, Landlord and Tenant have executed this Fourth Amendment as of the date and year first above written.

**LANDLORD:**

34175 ARDENWOOD VENTURE, LLC,  
a Delaware limited liability company

By: /s/ Kevin M. Simonsen

Name: Kevin M. Simonsen  
Title: Sr. Vice President, Sr. Counsel

**TENANT:**

ARDELYX, INC.,  
a Delaware corporation

By: /s/ Mark Kaufmann

Name: Mark Kaufmann  
Title: Chief Financial Officer

AMENDMENT NO. 1 to  
LICENSE AGREEMENT

This FIRST AMENDMENT (the "Amendment"), effective as of the date last signed below (the "Amendment Date"), amends that certain License Agreement dated November 27, 2017 (together with all exhibits, amendments and attachments thereto, the "Original Agreement") by and between Kyowa Kirin Co., Ltd. (f/k/a Kyowa Hakko Kirin Co., Ltd.), a Japanese corporation with a place of business at 1—9— 2 Otemachi, Chiyoda—ku, Tokyo 100-0004, Japan ("KKC"), and Ardelyx, Inc., a Delaware corporation having its principal place of business at 34175 Ardenwood Boulevard, Fremont, California United States of America 94555 ("Ardelyx"). KKC and Ardelyx shall each be hereinafter referred to as a "Party" and collectively as the "Parties". Capitalized terms used but not otherwise defined herein shall have the meanings ascribed to them in the Original Agreement.

WHEREAS, KKC has no further need for Licensed Product supply from Ardelyx and desires only to receive API supply in accordance with the Original Agreement and the MSA; and

WHEREAS, the Parties wish to amend the Original Agreement to reflect the foregoing;

NOW, THEREFORE, in consideration of the premises and the terms and conditions contained herein, the Parties agree as follows:

1. **Development Product Supply.** The Parties agree that Ardelyx shall have no further obligation to supply to KKC, and KKC shall have no further obligation to purchase from Ardelyx, any Development Product Supply pursuant to Section 5.01(a) of the Original Agreement. KKC acknowledges and agrees that: (a) Ardelyx has fulfilled all of its obligations with respect to Development Product Supply under the Original Agreement, as amended by this Amendment, and that (b) other than provisions which expressly survive termination or expiration, all of Ardelyx's obligations under the Original Agreement with respect to Development Product Supply shall expire automatically on the Amendment Date. Notwithstanding the foregoing, if KKC requests Ardelyx to supply to KKC the Lead Licensed Product and placebos that are manufactured for the US market in order for KKC to conduct the CMC Development of the Lead Licensed Product and placebos by KKC in the Territory, the Parties shall discuss KKC's request in good faith.
2. **Amendment.** In connection with the foregoing, Exhibit F to the Original Agreement is hereby amended to delete the tables listed under clauses (i)-(iii) and to insert the following language in their place: "As set forth in Exhibit C to the MSA dated April 9, 2018, as amended."
3. **Commercial Product Supply.** KKC has elected to assume responsibility for Manufacture of Licensed Products and does not desire Ardelyx to provide Temporary Commercial Product Supply pursuant to Section 5.01(b) of the Original Agreement. The Parties therefore agree that: (a) Ardelyx shall have no obligation to supply Temporary Commercial Product Supply, and (b) each occurrence of the term "Temporary Commercial Product Supply" throughout the Original Agreement is hereby omitted and surrounding language adjusted to reflect such omission.
4. **Third Party Manufacturers.** The Parties acknowledge that Ardelyx may in its discretion provide assistance to KKC in engaging one or more of Ardelyx's Third Party contractors (each an "Ardelyx Contractor") to perform Manufacturing activities for KCC. The Parties agree that, in connection with KKC's engagement of any Ardelyx Contractor, each Party will use Commercially Reasonable Efforts to avoid interference with the other Party's own supply requirements from such Ardelyx Contractor.

Without limiting the foregoing, KKC shall obtain Ardelyx's prior written approval for any Manufacturing services to be scheduled in the same physical location being used for Manufacture of Ardelyx's own supply requirements by such Ardelyx Contractor.

5. Miscellaneous. This Amendment shall be governed and construed in accordance with the laws of the State of New York, without giving effect to the conflict of law rules thereof that would require application of the laws of any other jurisdiction. Except as expressly amended hereby, the Original Agreement remains unchanged and in full force and effect. The Original Agreement together with this Amendment shall be construed as a single instrument. This Amendment may be executed in any number of counterparts, each of which shall be deemed an original and all of which taken together shall be deemed to constitute one and the same instrument.

\*\*\*

IN WITNESS WHEREOF, the Parties have caused this First Amendment to License Agreement to be executed by their duly authorized representatives as of the Amendment Date.

Kyowa Kirin Co., Ltd.    Ardelyx, Inc.  
/s/ Yasuo Fujii    /s/ Michael Raab

Name: Yasuo Fujii    Name: Michael Raab  
Title: Executive Officer, Director,    Title: CEO  
Business Development Department  
Date: June 17, 2020    Date: June 23, 2020



## SECOND AMENDMENT TO LOAN AND SECURITY AGREEMENT

THIS SECOND AMENDMENT TO LOAN AND SECURITY AGREEMENT (this “**Amendment**”) is entered into as of February 9, 2023, by and among SLR INVESTMENT CORP., a Maryland corporation with an office located at 500 Park Avenue, 3<sup>rd</sup> Floor, New York, NY 10022 (“**SLR**”), as collateral agent (in such capacity, together with its successors and assigns, “**Collateral Agent**”), the Lenders listed on Schedule 1.1 thereto or otherwise a party thereto from time to time including SLR in its capacity as a Lender (each a “**Lender**” and collectively, the “**Lenders**”), and ARDELYX, INC., a Delaware corporation with offices located at 400 Fifth Avenue, Suite 210, Waltham, MA 02451 (the “**Borrower**”).

A. Collateral Agent, Borrower and Lenders have entered into that certain Loan and Security Agreement dated as of February 23, 2022 (as amended, supplemented or otherwise modified from time to time, including but not limited to that certain First Amendment to Loan and Security Agreement dated as of August 1, 2022, collectively, the “**Loan Agreement**”) pursuant to which Lenders have provided to Borrower certain loans in accordance with the terms and conditions thereof; and

B. Borrower, Collateral Agent and the Required Lenders have agreed to amend the defined term “Term B Milestone”, subject to, and in accordance with, the terms and conditions set forth herein, and in reliance upon the representations and warranties set forth herein.

### Agreement

NOW, THEREFORE, in consideration of the promises, covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, Borrower, the Required Lenders and Collateral Agent hereby agree as follows:

1. **Definitions.** Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.
2. **Amendments to Loan Agreement.**

**1.1 Section 13.1 (Definitions).** The following terms and their respective definitions hereby are added or amended and restated in their entirety, as applicable, to Section 1.4 of the Loan Agreement as follows:

“**1-Month CME Term SOFR**” is the 1-month CME Term SOFR reference rate as published by the CME Term SOFR Administrator on the CME Term SOFR Administrator’s Website.

“**Amortization Date**” means April 1, 2024; provided, that upon achievement of the Interest-Only Extension Milestone, the Amortization Date shall automatically be extended to April 1, 2025.

“**Applicable Rate**” means a per annum interest rate equal to the greater of (a) one percent (1.00%) per annum and (b)(i) 0.022% plus (ii) 1-month CME Term SOFR reference rate as published by the CME Term SOFR Administrator on the CME Term SOFR Administrator’s Website (or on any successor or substitute page of the CME Term SOFR Administrator, or any successor to or substitute for the CME Term SOFR Administrator, as determined by Collateral Agent in a manner consistent with other loans in Collateral Agent’s portfolio), which determination by Collateral Agent shall be conclusive in the absence of manifest error; provided that if, at any time, Lenders notify Collateral Agent that Lenders have determined that (x) Lenders are unable to determine or ascertain such rate, or (y) the applicable regulator has made public statements to the effect that the rate published by the CME Term SOFR Administrator is no longer used for determining interest rates for loans, then the Applicable Rate shall be equal to an alternate benchmark rate and spread agreed between Collateral Agent and Borrowers, giving due consideration to (i) market convention or (ii) selection, endorsement or recommendation by a Relevant Governmental Body. Such alternative benchmark rate and spread shall be binding unless the Required Lenders object within five (5) days following notification of such amendment.

“**CME Term SOFR Administrator**” is CME Group Benchmark Administration Limited, as administrator of the forward-looking term SOFR, or any successor administrator of 1-Month CME Term SOFR selected by the Collateral Agent in its reasonable discretion.

“**CME Term SOFR Administrator’s Website**” is the website of the CME Group Benchmark Administrator at <http://www.cmegroup.com>, or any successor source.

“**Interest-Only Extension Milestone**” is Collateral Agent’s receipt of satisfactory evidence that Borrower has either (i) received FDA approval of Tenapanor for use in certain patients with Hyperphosphatemia on or prior to November 30, 2023 or (ii) achieved a minimum of Seventy-Five Million Dollars (\$75,000,000) in Net Product Revenue calculated for Borrower’s fiscal year ending December 31, 2023.

“**Term B Draw Period**” is the period commencing on the date of the occurrence of the Term B Milestone and ending on December 20, 2023.

“**Term B Milestone**” is Collateral Agent’s receipt of satisfactory evidence that Borrower (i) has received FDA approval of Tenapanor for use in certain patients with Hyperphosphatemia on or prior to November 30, 2023 and (ii) has achieved a minimum of Thirty Million Dollars (\$30,000,000) in Net Product Revenue calculated on a trailing six (6) month basis.

**1.2 Section 13.1 (Definitions).** The following term and its definitions hereby is deleted from Section 1.4 of the Loan Agreement:

“SOFR”

**1.3 Section 2.2 (Term Loans).** Section 2.2(b) of the Loan Agreement is hereby amended and restated to read as follows:

“(b) Repayment. Borrower shall make monthly payments of interest only commencing on the first (1st) Payment Date following the Funding Date of each Term Loan, and continuing on the Payment Date of each successive month thereafter through and including the Payment Date immediately preceding the Amortization Date. Borrower agrees to pay, on the Funding Date of each Term Loan, any initial partial monthly interest payment otherwise due for the period between the Funding Date of such Term Loan and the first Payment Date after such Funding Date. Commencing on the Amortization Date, and continuing on the Payment Date of each month thereafter, Borrower shall (i) make monthly payments of interest, to each Lender in accordance with its Pro Rata Share, as calculated by Collateral Agent (which calculations shall be deemed correct absent manifest error) based upon the effective rate of interest applicable to the Term Loan, as determined in Section 2.3(a) plus (ii) make consecutive equal monthly payments of principal to each Lender in accordance with its Pro Rata Share in accordance with their respective Pro Rata Shares, as calculated by Collateral Agent (which calculations shall be deemed correct absent manifest error) based upon: (A) the respective principal amounts of such Lender’s Term Loans outstanding, and (B) a repayment schedule equal to (I) if the Amortization Date is April 1, 2024, thirty-six (36) months and (II) if the Amortization Date is April 1, 2025, twenty-four (24) months. All unpaid principal and accrued and unpaid interest with respect to each such Term Loan is due and payable in full on the Maturity Date. The Term Loans may only be prepaid in accordance with Sections 2.2(c) and 2.2(d).”

### **3. Limitation of Amendment.**

**1.1** The amendment set forth in Section 2 above is effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right, remedy or obligation which Lenders or Borrower may now have or may have in the future under or in connection with any Loan Document, as amended hereby.

1.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents are hereby ratified and confirmed and shall remain in full force and effect.

4. **Representations and Warranties.** To induce Collateral Agent and the Required Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and the Required Lenders as follows:

1.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct in all material respects as of such date) and (b) no Event of Default has occurred and is continuing;

1.2 Borrower has the power and due authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

1.3 The organizational documents of Borrower delivered to Collateral Agent on the Effective Date, and updated pursuant to subsequent deliveries by or on behalf of the Borrower to the Collateral Agent, remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

1.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not contravene (i) any material law or regulation binding on or affecting Borrower, (ii) any material contractual restriction with a Person binding on Borrower, (iii) any applicable order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (iv) the organizational documents of Borrower;

1.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower, except as already has been obtained or made;

1.6 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

5. **Loan Document.** Borrower, Lenders and Collateral Agent agree that this Amendment shall be a Loan Document. Except as expressly set forth herein, the Loan Agreement and the other Loan Documents shall continue in full force and effect without alteration or amendment. This Amendment and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements.

6. **Release by Borrower.**

1.1 **FOR GOOD AND VALUABLE CONSIDERATION**, Borrower hereby forever relieves, releases, and discharges Collateral Agent and each Lender and their respective present or former employees, officers, directors, agents, representatives, attorneys, and each of them, from any and all claims, debts, liabilities, demands, obligations, promises, acts, agreements, costs and expenses, actions and causes of action, of every type, kind, nature, description or character whatsoever, whether known or unknown, suspected or unsuspected, absolute or contingent, arising out of or in any manner whatsoever connected with or related to facts, circumstances, issues, controversies or claims existing or arising from the Effective Date through and including the date of execution of this Amendment solely to the extent such claims arise out of or are in any manner whatsoever connected with or related to the Loan Documents, the Recitals hereto, any instruments, agreements or documents executed in connection with any of the foregoing or the origination, negotiation, administration, servicing and/or enforcement of any of the foregoing (collectively "**Released Claims**").

1.2 By entering into this release, Borrower recognizes that no facts or representations are ever absolutely certain and it may hereafter discover facts in addition to or different from those which it presently knows

or believes to be true, but that it is the intention of Borrower hereby to fully, finally and forever settle and release all matters, disputes and differences, known or unknown, suspected or unsuspected in relation to the Released Claims; accordingly, if Borrower should subsequently discover that any fact that it relied upon in entering into this release was untrue, or that any understanding of the facts was incorrect, Borrower shall not be entitled to set aside this release by reason thereof, regardless of any claim of mistake of fact or law or any other circumstances whatsoever. Borrower acknowledges that it is not relying upon and has not relied upon any representation or statement made by Collateral Agent or Lenders with respect to the facts underlying this release or with regard to any of such party's rights or asserted rights.

**1.3** This release may be pleaded as a full and complete defense and/or as a cross-complaint or counterclaim against any action, suit, or other proceeding that may be instituted, prosecuted or attempted in breach of this release. Borrower acknowledges that the release contained herein constitutes a material inducement to Collateral Agent and the Lenders to enter into this Amendment, and that Collateral Agent and the Lenders would not have done so but for Collateral Agent's and the Lenders' expectation that such release is valid and enforceable in all events.

**7. Effectiveness.** This Amendment shall be deemed effective as of the date hereof upon (i) the due execution and delivery of this Amendment by each party hereto, (ii) the due execution and delivery to Collateral Agent and Lenders of a certificate of Borrower in substantially the form of Annex I hereto executed by the Secretary of Borrower with appropriate insertions and attachments, and (iii) Borrower's payment of a non-refundable amendment fee, fully earned as of the date hereof, in an amount equal to Fifty-Five Thousand Dollars (\$55,000) to be shared among the Lenders in accordance with their respective Pro Rata Shares.

**8. Counterparts.** This Amendment may be executed in any number of counterparts, each of which shall be deemed an original, and all of which, taken together, shall constitute one and the same instrument. Delivery by electronic transmission (e.g. ".pdf") of an executed counterpart of this Amendment shall be effective as a manually executed counterpart signature thereof.

**9. Electronic Execution.** The words "execution," "execute", "signed," "signature," and words of like import in or related to any document to be signed in connection with this Amendment and the transactions contemplated hereby (including without limitation assignments, assumptions, amendments, waivers and consents) shall be deemed to include electronic signatures, the electronic matching of assignment terms and contract formations on electronic platforms approved by the Collateral Agent, or the keeping of records in electronic form, each of which shall be of the same legal effect, validity or enforceability as a manually executed signature or the use of a paper-based recordkeeping system, as the case may be, to the extent and as provided for in any applicable law, including the Federal Electronic Signatures in Global and National Commerce Act, the New York State Electronic Signatures and Records Act, or any other similar state laws based on the Uniform Electronic Transactions Act.

**10. Governing Law.** THIS AMENDMENT AND THE RIGHTS AND OBLIGATIONS OF THE PARTIES HEREUNDER SHALL IN ALL RESPECTS BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH, THE INTERNAL LAWS OF THE STATE OF NEW YORK (WITHOUT REGARD TO THE CONFLICT OF LAWS PRINCIPLES THAT WOULD RESULT IN THE APPLICATION OF ANY LAW OTHER THAN THE LAW OF SUCH STATE), INCLUDING ALL MATTERS OF CONSTRUCTION, VALIDITY AND PERFORMANCE, REGARDLESS OF THE LOCATION OF THE COLLATERAL, PROVIDED, HOWEVER, THAT IF THE LAWS OF ANY JURISDICTION OTHER THAN NEW YORK SHALL GOVERN IN REGARD TO THE VALIDITY, PERFECTION OR EFFECT OF PERFECTION OF ANY LIEN OR IN REGARD TO PROCEDURAL MATTERS AFFECTING ENFORCEMENT OF ANY LIENS IN COLLATERAL, SUCH LAWS OF SUCH OTHER JURISDICTIONS SHALL CONTINUE TO APPLY TO THAT EXTENT.

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**IN WITNESS WHEREOF**, the parties hereto have caused this Second Amendment to Loan and Security Agreement to be executed as of the date first set forth above.

**BORROWER:**

ARDELYX, INC.

By /s/ Justin Renz  
Name: Justin Renz  
Title: Chief Financial and Operations Officer

**COLLATERAL AGENT AND LENDER:**

SLR INVESTMENT CORP.

By /s/ Anthony J. Storino  
Name: Anthony J. Storino  
Title: Authorized Signatory

**LENDERS:**

SLR SENIOR INVESTMENT CORP.  
SCP PRIVATE CREDIT INCOME FUND SPV, LLC  
SCP PRIVATE CREDIT INCOME BDC SPV LLC  
SCP PRIVATE CORPORATE LENDING FUND SPV LLC  
SCP SF DEBT FUND L.P.  
SLR HC FUND SPV, LLC  
SLR HC BDC LLC

By /s/ Anthony J. Storino\_\_  
Name: Anthony J. Storino  
Title: Authorized Signatory

**[Signature Page to Second Amendment to Loan and Security Agreement]**

Annex I

**CORPORATE BORROWING CERTIFICATE**

**BORROWER:** ARDELYX, INC.   **DATE:** February 7, 2023

**LENDER:** SLR INVESTMENT CORP., as Collateral Agent and Lender

I hereby certify, solely in my capacity as an officer of Borrower and not in my individual capacity, as follows, as of the date set forth above:

1. I am the Secretary or other officer of Borrower. My title is as set forth below.
2. Borrower's exact legal name is set forth above. Borrower is a corporation existing under the laws of the State of Delaware.
3. Attached hereto as Exhibit A and Exhibit B, respectively, are true, correct and complete copies of (i) Borrower's Certificate of Incorporation (including amendments), as filed with the Secretary of State of the state in which Borrower is incorporated as set forth in paragraph 2 above; and (ii) Borrower's Bylaws. Neither such Certificate of Incorporation nor such Bylaws have been amended, annulled, rescinded, revoked or supplemented, and such Certificate of Incorporation and such Bylaws remain in full force and effect as of the date hereof.
4. The following resolutions were duly and validly adopted by Borrower's board of directors (or a duly authorized committee thereof) at a duly held meeting of such directors (or pursuant to a unanimous written consent or other authorized corporate action). Such resolutions are in full force and effect as of the date hereof and have not been in any way modified, repealed, rescinded, amended or revoked, and the Lenders may rely on them until each Lender receives written notice of revocation from Borrower.

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**RESOLVED**, that **any one** of the following officers or employees of Borrower, whose names, titles and signatures are below, may act on behalf of Borrower:

<u>Name</u>	<u>Title</u>	<u>Signature</u>	<u>Authorized to Add or Remove Signatories</u>
Michael Raab	Chief Executive Officer	/s/ Michael Raab	X
Justin Renz	Chief Financial & Operating Officer	/s/ Justin Renz	X
			<input type="checkbox"/>
			<input type="checkbox"/>

**RESOLVED FURTHER**, that **any one** of the persons designated above with a checked box beside his or her name may, from time to time, add or remove any individuals to and from the above list of persons authorized to act on behalf of Borrower.

**RESOLVED FURTHER**, that such individuals may, on behalf of Borrower:

**Borrow Money.** Borrow money from the Lenders.

**Execute Loan Documents.** Execute any loan documents any Lender requires, including that certain Second Amendment to Loan and Security Agreement dated on or about even date herewith.

**Grant Security.** Grant Collateral Agent a security interest in any of Borrower's assets (excluding intellectual property).

**Negotiate Items.** Negotiate or discount all drafts, trade acceptances, promissory notes, or other indebtedness in which Borrower has an interest and receive cash or otherwise use the proceeds.

**Pay Fees.** Pay fees under the Loan Agreement or any other Loan Document.

**Further Acts.** Designate other individuals to request advances, pay fees and costs and execute other documents or agreements (including documents or agreement that waive Borrower's right to a jury trial) they believe to be necessary to effectuate such resolutions.

**RESOLVED FURTHER**, that all acts authorized by the above resolutions and any prior acts relating thereto are ratified.

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5. The persons listed above are Borrower's officers or employees with their titles and signatures shown next to their names.

**By: /s/ Justin Renz**  
**Name: Justin Renz**  
**Title: Chief Financial and Operating Officer**

*\*\*\* If the Secretary or other certifying officer executing above is designated by the resolutions set forth in paragraph 4 as one of the authorized signing officers, this Certificate must also be signed by a second authorized officer or director of Borrower.*

I, the CEO of Borrower, hereby certify as to paragraphs 1 through 5 above, as February 9, 2023 on the date set forth above.

**By: /s/ Michael Raab**  
**Name: Michael Raab**  
**Title: Chief Executive Officer**

**EXHIBIT A**

**Certificate of Incorporation (including amendments)**

**EXHIBIT B**

**Bylaws**

Certain confidential information contained in this document, marked by [\*\*\*], has been omitted because it is both (i) not material and (ii) is the type that the registrant treats as private or confidential.

**First Amendment to Manufacturing Services Agreement  
Between Ardelyx, Inc. and Patheon Pharmaceuticals Inc.**

**THIS AMENDMENT NO. 1 (“Amendment 1”)** is entered into by and between **Ardelyx, Inc.** a Delaware corporation with a principal place of business at 400 5th Ave., Suite 210, Waltham, MA 02451, USA (“**Client**”) and **Patheon Pharmaceuticals Inc.**, located at 2110 East Galbraith Road, Cincinnati, OH 45237, USA (“**Patheon**”).

**WHEREAS**, Patheon and Client entered into that certain Manufacturing Services Agreement dated May 18, 2020 (the “**MSA**”);

**AND WHEREAS**, Patheon and Client wish to amend the MSA as set forth in this Amendment. All capitalized terms used but not defined in this Amendment shall have the respective meanings set forth in the MSA;

**NOW, THEREFORE**, in consideration of the foregoing recitals that are hereby incorporated by reference hereunder and made a part of this Amendment 1 as if expressly set forth below, the promises and agreements contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties wish to amend the MSA as follows:

1. The Amendment 1 shall take effect as of the date last signed below (“**Amendment Effective Date**”).
2. Appendix 1 “Commercial Supply Pricing” of the MSA is deleted in its entirety and shall be replaced as set forth in Exhibit 1 hereto.
3. Section 2.2(a) of the MSA is hereby augmented such that, as of the Amendment Effective Date, the Minimum [\*\*\*] Requirement will be based on [\*\*\*]. The Parties agree that a [\*\*\*] shall count as [\*\*\*] for purposes of calculating [\*\*\*] contemplated in such Section 2.2(a).
4. Except as expressly provided in this Amendment 1, the MSA shall remain unchanged.

Certain confidential information contained in this document, marked by [\*\*\*], has been omitted because it is both (i) not material and (ii) is the type that the registrant treats as private or confidential.

**IN WITNESS WHEREOF**, the Parties hereto have executed or caused this Amendment 1 to be executed by their respective officers or other representatives duly authorized as of the Amendment Effective Date.

**Ardelyx, Inc.**

By: /s/ Justin Renz  
Print Name: Justin Renz  
Title: Chief Financial and Operations Manager  
Date: 1/24/2023

**Patheon Pharmaceuticals Inc.**

By: /s/ Alan Bensman  
Print Name: Alan Bensman  
Title: General Manager, Cincinnati  
Date: 2/27/2023

Certain confidential information contained in this document, marked by [\*\*\*], has been omitted because it is both (i) not material and (ii) is the type that the registrant treats as private or confidential.



**EXHIBIT 1**  
**Commercial Supply Pricing**

[\*\*\*]

Certain confidential information contained in this document, marked by [\*\*\*], has been omitted because it is both (i) not material and (ii) is the type that the registrant treats as private or confidential.

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement on Form S-8 (No. 333-197408) pertaining to the 2008 Stock Incentive Plan, as amended, the 2014 Equity Incentive Award Plan and the 2014 Employee Stock Purchase Plan of Ardelyx, Inc.
2. Registration Statements on Form S-8 (Nos. 333-202663 and 333-230156) pertaining to the 2014 Equity Incentive Award Plan and the 2014 Employee Stock Purchase Plan of Ardelyx, Inc.
3. Registration Statements on Form S-3 (Nos. 333-205630, 333-213085, 333-239764 and 333-269297) of Ardelyx, Inc.
4. Registration Statements on Form S-8 (Nos. 333-210079, 333-216154, 333-223694 and 333-237057) pertaining to the 2014 Equity Incentive Award Plan of Ardelyx, Inc.
5. Registration Statement on Form S-8 (No. 333-214538) pertaining to the 2016 Employment Commencement Incentive Plan of Ardelyx, Inc.
6. Registration Statement on Form S-8 (No. 333-254187) pertaining to the 2014 Equity Incentive Award Plan, the 2014 Employee Stock Purchase Plan and the 2016 Employment Commencement Incentive Plan of Ardelyx, Inc.
7. Registration Statement on Form S-8 (333-263145) pertaining to the 2014 Equity Incentive Award Plan and the 2016 Employment Commencement Incentive Plan of Ardelyx, Inc.

of our report dated March 2, 2023, with respect to the financial statements of Ardelyx, Inc. included in this Annual Report (Form 10-K) of Ardelyx, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP  
San Mateo, California

March 2, 2023





**CERTIFICATION PURSUANT TO  
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906  
OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report of Ardelyx, Inc. (the "Company") on Form 10-K for the period ending December 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Michael Raab, President and Chief Executive Officer of the Company, and Justin Renz, Chief Financial & Operations Officer of the Company, respectively, do each hereby 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 result of operations of the Company.

Date: March 2, 2023

By: \_\_\_\_\_ /s/ Michael Raab

**Michael Raab**  
**President, Chief Executive Officer and Director**  
**(Principal Executive Officer)**

Date: March 2, 2023

By: \_\_\_\_\_ /s/ Justin Renz

**Justin Renz**  
**Chief Financial & Operations Officer**  
**(Principal Financial Officer)**