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

FORM 10-K

(Mark One)

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

FOR THE FISCAL YEAR ENDED DECEMBER 31 , 2024

OR

o **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)

DE LAWARE	**26-1303944**
(STATE OR OTHER JURISDICTION OF INCORPORATION OR ORGANIZATION)	**(I.R.S. EMPLOYER IDENTIFICATION NO.)**

400 FIFTH AVE. , SUITE 210 , WALTHAM , MA SSACHUSETTS 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 x No o

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yeso No x

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 x No o

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 x No o

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	x	Accelerated filer	o
Non-accelerated filer	o	Smaller reporting company	o
		Emerging growth company	o

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. o

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. x

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 o No x

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, 2024, based on the last reported sales price of the Registrant's common stock on the Nasdaq Global Market of $7.41 per share was $ 1,744,324,359 .

The number of shares of Registrant's Common Stock outstanding as of February 14, 2025, was 238,356,222 .

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the Registrant's Definitive Proxy Statement for its 2025 Annual Meeting of Stockholders, which will be filed with the Commission within 120 days of December 31, 2024, the close of the Registrant's 2024 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:

- 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, that could cause actual outcomes or results to differ materially from those expressed or implied by such forward-looking statements. 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.

SUMMARY OF PRINCIPAL RISKS ASSOCIATED WITH OUR BUSINESS

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

- We have incurred losses in each year since our inception, and we expect to continue to incur operating losses in the future as we incur additional expenses related to our ongoing operations and our pursuit of future business opportunities.
- We will require additional financing for the foreseeable future as we invest in the growth of IBSRELA and XPHOZAH in the U.S. and building a pipeline. The inability to access necessary capital when needed on acceptable terms, or at all, could force us to reduce our efforts to commercialize IBSRELA and/or XPHOZAH, or to delay or limit our pursuit of other future business opportunities.
- We have generated limited revenue from product sales and may never be profitable for a full fiscal year.
- We are substantially dependent on the successful commercialization of IBSRELA, and there is no guarantee that we will maintain sufficient market acceptance for IBSRELA, grow market share for IBSRELA, secure and maintain adequate coverage and reimbursement for IBSRELA, or generate sufficient revenue from product sales of IBSRELA.
- There is no guarantee that we will achieve sufficient market acceptance for XPHOZAH, or that we will be able to secure and maintain adequate coverage and reimbursement for XPHOZAH, or generate sufficient revenue from product sales of XPHOZAH.
- XPHOZAH is now included in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted.
- IBSRELA and/or 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 XPHOZAH could limit our ability to market those products and decrease our ability to generate revenue.
- We rely completely on third parties, including certain single-source suppliers, 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 XPHOZAH may be materially harmed.
- Our future results depend on CMOs, many of whom are our single source manufacturers.
- Our operating activities may be restricted as a result of covenants related to the indebtedness under our loan and security agreement with SLR, as amended, 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 financial statements and the related notes, as well as in other documents that we file with the U.S. SEC. 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, 2024
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PART I

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 minimally absorbed, 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. Tenapanor, branded as XPHOZAH®, is approved in the U.S. to reduce serum phosphorus in adults with chronic kidney disease on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

Refer to the *Summary of Abbreviated Terms* at the end of this Annual Report on Form 10-K for definitions of terms used throughout the document.

Strategy

We are committed to our mission of discovering, developing and commercializing first-in-class medicines that address unmet patient needs. Our principal strategy is to maintain our commercial momentum with our current products while identifying additional assets that leverage our core capabilities, including clinical, developmental and regulatory expertise and commercial excellence while maintaining a solid financial foundation, to support our future growth.

Our priorities include: (i) accelerating IBSRELA growth momentum; (ii) executing our XPHOZAH strategy to grow utilization; (iii) building a pipeline focused on areas of unmet patient need; and (iv) continuing to deliver strong commercial and financial performance.

We expect to continue to incur operating losses for the foreseeable future as we continue to invest in the commercialization of IBSRELA and XPHOZAH, incur manufacturing and development costs for tenapanor, and incur additional expenses related to our ongoing operations and our pursuit of future business opportunities. We have funded our operations primarily from the sale of common stock, product sales, funds from our collaboration partnerships, funds from our loan agreements with SLR, as well as sales of future royalties to HCR. We expect that we will increasingly rely on cash generated from operations to fund our operating plan while maintaining financial flexibility from our ability to source cash from future equity sales and debt financing.

Our Commercial Products

IBSRELA for IBS-C

IBSRELA, our first commercial product, is a first-in-class NHE3 inhibitor approved by the U.S. FDA for the treatment of IBS-C in adults. IBSRELA acts locally in the gut and is minimally absorbed. IBS-C is a gastrointestinal disorder characterized by both altered bowel habits and abdominal pain. 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. Throughout 2024, we continued to build on the commercial success of IBSRELA. We recognized approximately $158.3 million in net revenue related to sales of IBSRELA in the U.S. during the year ended December 31, 2024, an increase of $78.2 million compared to the year ended December 31, 2023.

We deploy a market-responsive commercial strategy for IBSRELA and have a commercial organization highly experienced in launching and commercializing 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 (secretagogues), 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 IBS-C patients currently being managed by high-writing healthcare providers. Central to our go to market strategy for IBSRELA has been our highly experienced specialty sales force, composed of many with existing relationships across their gastrointestinal target base, omnichannel digital initiatives and our patient services programs, including ArdelyxAssist, that support patient access to our therapies.

We believe competition for IBSRELA comes largely from 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 and prescription therapies, 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.

XPHOZAH to Reduce Serum Phosphorus in Adults with CKD on Dialysis as Add-on Therapy in Patients Who Have an Inadequate Response to Phosphate Binders or Who Are Intolerant of Any Dose of Phosphate Binder Therapy

XPHOZAH, our second commercial product, was approved by the U.S. FDA in October 2023. XPHOZAH is a first-in-class phosphate absorption inhibitor approved in the U.S. to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy. XPHOZAH has a differentiated 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. In addition, approximately 70% of patients treated with phosphate binders to treat hyperphosphatemia were unable to consistently maintain phosphorous levels <=5.5 mg/dL over a six-month period. XPHOZAH is the first therapy for phosphate management that blocks phosphate absorption at the primary site of uptake.

We recognized our first sales of XPHOZAH in the U.S. in December 2023. We recognized approximately $160.9 million in net revenue related to sales of XPHOZAH in the U.S. during the year ended December 31, 2024 – the first full year of commercialization of XPHOZAH.

For our commercial launch of XPHOZAH, we designed a market-responsive commercial strategy and built a commercial organization highly experienced and knowledgeable of the nephrology market. The dynamics of the hyperphosphatemia market reflect an established patient base, limited number of competitors all confined to a single mechanism of action (phosphate binders), concentrated number of prescribers and recognized unmet need. In addition, market research indicated a high level of awareness, interest and intent to adopt XPHOZAH upon approval and favorable response to the XPHOZAH product profile as a novel mechanism therapy. Central to our go to market strategy for XPHOZAH has been our highly experienced specialty sales force, many with existing relationships across their nephrology target base, innovative omnichannel digital initiatives and our patient services programs, including ArdelyxAssist, that support patient access to our therapies.

Beginning January 1, 2025, XPHOZAH, along with other oral ESRD related drugs without injectable or intravenous equivalents, are now included in the End-Stage Renal Disease Prospective Payment System, thereby eliminating coverage for XPHOZAH and these other ESRD related drugs under Medicare Part D as of such date. XPHOZAH patients with Medicare Part D accounted for approximately 60% of all XPHOZAH patients in 2024. Our strategy for XPHOZAH remains a targeted promotional focus on nephrology healthcare providers, with a focus on preserving access for patients determined to be appropriate candidates for XPHOZAH by their healthcare provider.

XPHOZAH is indicated to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy. 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 phosphate binders in development, including AP-301, developed by Alebund Pharmaceutical (Hong Kong) Limited and currently in Phase 3; VS-505, developed by Vidasym and currently in clinical development; TS-172, developed by Taisho Pharmaceuticals and currently in Phase 2; and OLC, developed by Unicycive Therapeutics, which has announced its plans to seek U.S. FDA approval via the 505(b)(2) pathway. OLC has demonstrated pharmacodynamic bioequivalence to Fosrenol. Additionally, Alebund is developing AP-306, an inhibitor of phosphate transporters NaPi-2b, PiT-1, and PiT-2, thus far studied in a Phase 2 clinical trial.

Our Commercial Strategy

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 XPHOZAH. We have executed 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 enter into collaboration agreements with third parties for the development and commercialization of tenapanor for certain indications in their respective territories. In exchange for granting the respective licenses, we receive upfront payments upon contract execution, are eligible to receive development and regulatory milestones upon achievement of respective events, and are eligible to receive sales-based royalties and commercial milestones. We also enter into supply agreements with our partners to supply drug substance or finished product for a fee.

We have an exclusive license agreement with Kyowa Kirin for the development, commercialization and distribution of tenapanor in Japan for cardiorenal indications. We supply tenapanor drug substance to satisfy Kyowa Kirin commercial needs. In February 2024, Kyowa Kirin announced the launch of tenapanor, marketed as PHOZEVEL®, for CKD patients with hyperphosphatemia in Japan. 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 license, as amended, will be remitted to HCR pursuant to the HCR Agreement.

We have an exclusive license agreement with Fosun Pharma for the development and commercialization of tenapanor in China for both hyperphosphatemia and IBS-C. Fosun Pharma received approval from the Hong Kong Department of Health for the marketing application for tenapanor for the treatment of IBS-C in 2023. A New Drug Application for tenapanor for hyperphosphatemia has been submitted in China with Fosun Pharma.

We have an exclusive license agreement with Knight for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. IBSRELA was launched in Canada in March 2021.

We have an exclusive license agreement with METiS for the development and commercialization of a portfolio of TGR5 agonist compounds that we discovered and developed for all therapeutic areas.

Corporate Financings

In January 2023, we filed a registration statement on Form S-3, which became effective in January 2023, 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. As of December 31, 2024, we have completed sales pursuant to the 2023 Open Market Sales Agreement resulting in the issuance of 16.8 million shares of our common stock and receipt of gross proceeds of $70.0 million at a weighted average sales price of approximately $4.17.

We have a loan and security agreement (as amended, the 2022 Loan Agreement) with SLR. The 2022 Loan Agreement provides a total of $200.0 million, of which $150.0 million has been drawn as of December 31, 2024 to support our ongoing operations and the commercial launches of IBSRELA and XPHOZAH.

As of December 31, 2024, we had cash, cash equivalents and short-term investments totaling $250.1 million, an increase of $65.8 million, or 35.7%, from our cash position as of December 31, 2023.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our products, 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 products or drug 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 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 includes five issued U.S. patents, three issued patents in each of Israel and Mexico, two issued patents in each of the 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, are wholly owned by us, and are predicted, without extension or adjustment, to expire in December 2029. The term of U.S. patent no. 8,541,448, which claims the composition of matter of tenapanor, 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 are wholly owned by us and 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.

Manufacturing

To date, we have relied upon third-party CMOs to manufacture both the API and final drug product dosage forms of our commercial products, as well as our clinical trial material, and we expect that we will continue to rely upon CMOs for the manufacture of commercial product for IBSRELA, commercial product for XPHOZAH and clinical trial materials. 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 API to Kyowa Kirin to support their development and commercialization of tenapanor in Japan. We expect that we will continue to 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 FFDCA and the FDA's implementing regulations. If we fail to comply with applicable U.S. 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 U.S. 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 U.S. FDA enforcement action could have a material adverse effect on us. U.S. 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 U.S. 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 U.S. FDA's current GLP regulations;
- submission to the U.S. FDA of an IND application which must become effective before human clinical trials in the U.S. may begin;
- approval by an independent 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 GCP regulations to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the U.S. FDA of an NDA;
- satisfactory completion of a U.S. FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP regulations;
- satisfactory completion of a potential review by an U.S. FDA advisory committee, if applicable; and
- U.S. 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 any product candidates that we may seek to advance 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 U.S. FDA. Additional preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the U.S. FDA, unless the U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. FDA in support of an NDA so long as the clinical trial is conducted in compliance with GCP and if the U.S. 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 U.S. 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 U.S. FDA, or if the U.S. FDA considers such an inspection to be necessary, the U.S. 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 U.S. 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 U.S. 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 cGMP 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 U.S. 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 U.S. FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The U.S. 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 U.S. 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 U.S. 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 U.S. FDA requests for additional information or clarification. The U.S. FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The U.S. FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

After the U.S. 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 U.S. FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The U.S. FDA could also approve the NDA with a 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 U.S. 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 U.S. FDA has the authority to prevent or limit further marketing of a drug based on the results of these post-market programs. Once the U.S. FDA approves an NDA, or supplement thereto, the U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. FDA. Nonclinical and clinical data may be interpreted by the U.S. 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 U.S. 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 U.S. 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 U.S. FDA approvals would be subject to continuing regulation by the U.S. 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 U.S. FDA and certain state agencies and are subject to periodic announced and unannounced inspections by the U.S. 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 U.S. FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the U.S. 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 U.S. 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 U.S. 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 U.S. FDA does not regulate the behavior of physicians in their choice of treatments. The U.S. 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 FFDCA describes three types of marketing applications that may be submitted to the U.S. 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 U.S. 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 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 U.S. 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 U.S. 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 U.S. FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. 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 an NCE that has not been previously approved by the U.S. FDA. A drug is an NCE if the U.S. 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 U.S. 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 U.S. 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 U.S. 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 U.S. FDA, including the 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 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 are 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 U.S. 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 is marketed to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy. In January 2011, CMS implemented a new PPS for dialysis treatment. Under the ESRD PPS, 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. Beginning January 1, 2025, XPHOZAH, along with other oral ESRD related drugs without injectable or intravenous equivalents, are now included in the ESRD PPS, thereby eliminating coverage for XPHOZAH and these other ESRD related drugs under Medicare Part D as of such date. While it is too early to project the full impact that bundling may have on XPHOZAH and our business, we may be unable to sell XPHOZAH to dialysis providers on a profitable basis.

Healthcare Reform

In March 2010, Congress passed the Patient Protection and ACA, a healthcare reform measure. 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 AMP;
- 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 (which was replaced by a new discount program in 2025, as discussed below), under which they were required 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.

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 eliminated the statutory Medicaid drug rebate cap beginning January 1, 2024. The rebate was previously capped at 100% of a drug's AMP.

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 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 (which began in 2025). Under the IRA, small molecule drugs and biologics first become eligible for price negotiation seven and eleven years, respectively, after FDA approval. The IRA permits the Secretary of the HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has issued and will continue to issue guidance implementing the IRA. CMS has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and the list of the subsequent 15 drugs that will be subject to negotiation, although the Medicare drug price negotiation program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant. 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. Some states have enacted legislation creating so-called prescription drug affordability boards, which ultimately may attempt to impose price limits on certain drugs in these states. 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 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. CMS, the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the AMP and the best price 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 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 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. VA FSS pricing program. Under the VA/FSS program, manufacturers must report the 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.

Human Capital

The future success of our company depends on our ability to attract, retain and further develop top talent. Throughout our transition to a commercial organization 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, 2024, we had 395 full-time employees, 77 of whom were engaged directly in development and manufacturing, 252 in sales and marketing and 66 in general and administrative activities. During 2024, our employee base increased by approximately 128, or 48%.

Inclusion and Diversity

Our culture is supported by an unwavering commitment to inclusion and diversity. As of December 31, 2024, approximately 61% of our workforce was female; 33% of our executive leadership team was female and 55% of our employees in managerial roles were female. As of December 31, 2024, minorities represented 31% of our workforce, and 37% 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.

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 believe they help 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. We continue to offer hybrid and remote working opportunities for our team members employed in areas within the organization where such flexible work options are possible. 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) with company match contribution, 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.

We file electronically with the 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, 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.

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 losses in each year since our inception, and we expect to continue to incur operating losses in the future as we incur additional expenses related to our ongoing operations and our pursuit of future business opportunities.

In March 2022, we commenced the commercialization of our first product, IBSRELA ® (tenapanor) for the treatment of IBS-C in adult patients. In November 2023, we commenced the commercialization of XPHOZAH® (tenapanor) for the reduction of serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

We 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 additional expenses related to our ongoing operations and pursuit of future business opportunities. As of December 31, 2024, we had an accumulated deficit of $885.3 million.

We expect to continue to incur operating losses for the foreseeable future as we incur expenses related to our ongoing operations and our pursuit of future business opportunities.

There are no assurances that our efforts to meet our operating cash flow requirements will be successful. If our current cash, cash equivalents 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, our liquidity, financial condition, and business prospects will be materially affected.

Our prior losses, combined with any 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 may be subject to limitations, pursuant to Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. 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 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 growth of IBSRELA and XPHOZAH in the U.S. and building a pipeline. The inability to access necessary capital when needed on acceptable terms, or at all, could force us to reduce our efforts to commercialize IBSRELA and/or XPHOZAH, or to delay or limit our pursuit of other future business opportunities.

We believe that we will continue to expend substantial resources for the foreseeable future, including costs associated with our efforts to commercialize IBSRELA and XPHOZAH; conducting pediatric clinical trials for IBSRELA; manufacturing for IBSRELA and XPHOZAH; investments to build a pipeline; and research and development related to potential new product candidates. The inability to access necessary capital when needed on acceptable terms, or at all, could force us to reduce our efforts to commercialize IBSRELA and/or XPHOZAH or otherwise delay or limit our pursuit of future business opportunities. 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 and XPHOZAH;
- the extent to which access to XPHOZAH is impacted by the elimination of Medicare Part D coverage for XPHOZAH on January 1, 2025, and the extent to which this change will interfere with the shared decision-making between healthcare professionals and their patients, regardless of insurance coverage;
- the extent to which the elimination of separate payment for XPHOZAH for Medicare beneficiaries under Medicare Part D will influence the payment decisions of other payors and the extent to which payment for XPHOZAH will continue to be made as a pharmacy benefit for non-Medicare patients;
- the availability of adequate third-party reimbursement for IBSRELA;
- the manufacturing, selling and marketing costs associated with IBSRELA and 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 royalties we may receive as a result of sales of tenapanor by our collaboration partners in China, and Canada, if any;
- the extent to which IBSRELA and XPHOZAH are commercialized in other ex-U.S. territories;
- the cash requirements necessary to expand our business;
- the cash requirements for the discovery and/or development of other potential product candidates;
- 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, and 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, as amended to date.

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 XPOHZAH, delay or limit additional clinical trials for tenapanor, or delay or limit our pursuit of other future business opportunities.

We have generated limited revenue from product sales and may never be profitable for a full fiscal year.

We have generated limited revenue from product sales and have incurred significant net losses in each year since inception. We began selling IBSRELA in the U.S. in March 2022 and we began selling XPHOZAH in the U.S. in November 2023. We have no other products approved for sale.

There can be no assurances that we will generate sufficient product revenue from sales of IBSRELA and 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 ISBRELA and XPHOZAH and to increase market share for both products;
- maintaining sufficient market acceptance of IBSRELA as a viable treatment option for IBS-C;
- obtaining market acceptance of XPHOZAH;
- the extent to which access to XPHOZAH is impacted by the elimination of Medicare Part D coverage for XPHOZAH on January 1, 2025, and the extent to which this change will interfere with the shared decision-making between healthcare professionals and their patients, regardless of insurance coverage;
- the extent to which the elimination of separate payment for XPHOZAH for Medicare beneficiaries under Medicare Part D will influence the payment decisions of other payors and the extent to which payment for XPHOZAH will continue to be made as a pharmacy benefit for non-Medicare patients;
- our ability to obtain an adequate level of coverage and reimbursement for IBSRELA by third-party payors;
- 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 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 XPHOZAH, our revenue will be dependent, in part, upon the size of the markets in the U.S., the label for which approval was granted, accepted price for the product, and the ability to secure and maintain adequate reimbursement. Beginning January 1, 2025, XPHOZAH, along with other oral ESRD related drugs without injectable or intravenous equivalents, are now included in the ESRD PPS, thereby eliminating coverage for XPHOZAH and these other ESRD related drugs under Medicare Part D as of such date. The inclusion of XPHOZAH in the ESRD PPS creates additional uncertainty as to our ability to generate revenue from sales of XPHOZAH. See "*—XPHOZAH is now included in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted*" below.

Additionally, if the number of adult patients for IBSRELA and/or XPHOZAH is not as significant as we estimate, coverage and reimbursement for either IBSRELA or XPHOZAH 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 sales of IBSRELA or XPHOZAH. Even if we achieve profitability on a quarterly basis in the future, we may not be able to sustain profitability for a full fiscal year. 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 maintain sufficient market acceptance for IBSRELA, grow market share for IBSRELA, secure and maintain 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;
- whether IBSRELA will be subject to price negotiations under the IRA, and the timing and impact of those price negotiations on the revenue from product sales of IBSRELA;
- the size of the treatable patient population;
- our ability to continue to increase the market share of IBSRELA;
- 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 continue to secure and maintain 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 maintain market acceptance, continue to increase market share, obtain and maintain sufficient third-party coverage or reimbursement, or achieve commercial success would adversely affect our results of operations.

There is no guarantee that we will achieve sufficient market acceptance for XPHOZAH, or that we will be able to secure and maintain adequate coverage and reimbursement for XPHOZAH, or generate sufficient revenue from product sales of XPHOZAH. The inclusion of XPHOZAH in the ESRD PPS creates additional uncertainty as to the commercial opportunity for XPHOZAH.

We began selling XPHOZAH in the U.S. in November 2023. The overall commercial success of XPHOZAH will depend on a number of factors, including the following:

- the extent to which access to XPHOZAH is impacted by the elimination of Medicare Part D coverage for XPHOZAH on January 1, 2025, and the extent to which this change will interfere with the shared decision-making between healthcare professionals and their patients, regardless of insurance coverage;
- the extent to which the elimination of separate payment for XPHOZAH for Medicare beneficiaries under Medicare Part D will influence the payment decisions of other payors and the extent to which payment for XPHOZAH will continue to be made as a pharmacy benefit for non-Medicare patients;

- 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 XPHOZAH;
- whether or not the content and breadth of the label that has been approved by the U.S. FDA for XPHOZAH will materially and adversely impact our ability to commercialize the product for the approved indication;
- 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;
- 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.

There is no guarantee that we will achieve sufficient market acceptance for XPHOZAH, or that we will be able to secure and maintain adequate coverage and reimbursement for XPHOZAH, or generate sufficient revenue from product sales of XPHOZAH. The inclusion of XPHOZAH in the ESRD PPS creates additional uncertainty as to the commercial opportunity for XPHOZAH. See "*—XPHOZAH is now included in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted*" below.

XPHOZAH is now included in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted.

In January 2011, the CMS, an agency within the United States Department of Health and Human Services responsible for administering the Medicare program, implemented the ESRD PPS, a new PPS for dialysis treatment. Under the ESRD PPS, 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 drugs defined by CMS to be part of the renal dialysis service. CMS included XPHOZAH in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted.

The extent to which the inclusion of XPHOZAH in the ESRD PPS will materially and adversely impact our XPHOZAH business is dependent on the following:

- the extent to which access to XPHOZAH is impacted by the elimination of Medicare Part D coverage for XPHOZAH on January 1, 2025, and the extent to which this change will interfere with the shared decision-making between healthcare professionals and their patients, regardless of insurance coverage; and
- the extent to which the elimination of separate payment for XPHOZAH for Medicare beneficiaries under Medicare Part D will influence the payment decisions of other payors and the extent to which payment for XPHOZAH will continue to be made as a pharmacy benefit for non-Medicare patients.

IBSRELA and/or 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 XPHOZAH could cause us or regulatory authorities to interrupt, delay or halt the commercialization of the product. Despite marketing approval for IBSRELA and XPHOZAH, the prevalence and/or severity of side effects caused by IBSRELA and/or XPHOZAH could result in a number of potentially significant negative consequences, 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 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 XPHOZAH, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

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 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 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 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. 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.

In the U.S., 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. Beginning January 1, 2025, XPHOZAH, along with other oral ESRD related drugs without injectable or intravenous equivalents, are now included in the ESRD PPS, thereby eliminating coverage for XPHOZAH and these other ESRD related drugs under Medicare Part D as of such date. See "*—XPHOZAH is now included in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted*" above.

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 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, including certain single-source suppliers, 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 XPHOZAH 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. Our success depends upon our ability to enter into new supplier agreements and maintain our relationships with suppliers who are critical and necessary to the production of our drug supply.

The facilities used by our CMOs to manufacture our drug supply are subject to inspection by the U.S. FDA. Our ability to control the manufacturing process of our product candidates is limited to the contractual requirements and obligations we impose on our CMOs. Although they are contractually required to do so, we are completely dependent on our CMOs for compliance with the regulatory requirements, known as cGMP requirements, 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 CMOs 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 CMOs fail to adhere to applicable cGMP 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 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 XPHOZAH may be materially harmed.

Our future results depend on CMOs, many of whom are our single source manufacturers.

Many of our CMOs are currently single source manufacturers. While we try to obtain multiple sources whenever possible, similar to other commercial pharmaceutical companies, three stages of our manufacturing process are currently completed by a single source, which exposes us to a number of risks related to our supply chain, including delivery failure and drug shortages. To date, we have no qualified alternative sources for these single source CMOs.

Our manufacturing and commercial supply agreements with our CMOs, including our single source CMOs, contain or are likely to contain pricing provisions that are subject to adjustment based on factors outside of our control, including changes in market prices. Substantial increases in the prices for necessary materials and equipment, whether due to supply chain or logistics issues or due to inflation, would increase our operating costs and could reduce our margins. Any attempts to increase the announced or expected prices of IBSRELA and/or XPHOZAH in response to increased costs could be viewed negatively by the public and could adversely affect our business, prospects, financial condition, and results of operations.

Further, we currently and may in the future rely on foreign CMOs and CROs. Such foreign CMOs and CROs may be subject to U.S. legislation, sanctions, trade restrictions and other foreign regulatory requirements which could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies.

An inability to continue to source product from any of these CMOs, which could be due to regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a CMO, labor disputes or shortages, unexpected demands, or quality issues, could adversely affect our ability to satisfy demand for our products, which could adversely and materially affect our product sales and operating results, which could significantly harm our business. Furthermore, qualifying alternate suppliers or developing our own manufacturing capability for certain highly customized stages of our manufacturing process may be time consuming and costly. There can be no assurance that our business, financial condition and results of operations will not be materially and adversely affected by supply chain disruptions. Any disruption in the supply chain, whether or not from a single source CMO, could temporarily disrupt production of our drug supply until an alternative supplier is fully qualified by us or until such CMO is able to perform. There can be no assurance that we would be able to successfully retain an alternative CMO on a timely basis, on acceptable terms, or at all. Changes in business conditions, force majeure, governmental changes, and other factors beyond our control or which we do not presently anticipate, could also affect our CMOs' ability to deliver components to us on a timely basis. Any of the foregoing could materially and adversely affect our results of operations, financial condition and prospects.

Our operating activities may be restricted as a result of covenants related to the indebtedness under our loan and security agreement with SLR, as amended, 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 (the 2022 Loan Agreement) with SLR as collateral agent and the lenders listed in the 2022 Loan Agreement (collectively, the 2022 Lenders). The 2022 Loan Agreement was subsequently amended in August 2022 (the First Amendment), February 2023 (the Second Amendment), October 2023 (the Third Amendment) and October 2024 (Fourth Amendment). The loan was funded in the amount of $27.5 million on February 23, 2022 and additional amounts of $22.5 million, $50.0 million and $50.0 million were drawn on October 19, 2023, March 1, 2024, and October 29, 2024, respectively. In addition, we have the option to draw up to an additional $50.0 million by June 30, 2025. Until we have repaid all funded indebtedness, the 2022 Loan 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.

In addition, we may be required to repay the outstanding indebtedness under the loan facility if an event of default occurs 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; 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 XPHOZAH, or delay or limit clinical trials for tenapanor or other product candidates. The Lenders 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

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.

Competition for IBSRELA largely comes from three prescription products marketed for certain patients with IBS-C that we are aware of, including 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.

XPHOZAH is indicated to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy. 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 phosphate binders in development, including AP-301, developed by Alebund Pharmaceutical (Hong Kong) Limited and currently in Phase 3; VS-505, developed by Vidasym and currently in clinical development; TS-172, developed by Taisho Pharmaceuticals and currently in Phase 2; and OLC, developed by Unicycive Therapeutics, which has announced its plans to seek U.S. FDA approval via the 505(b)(2) pathway. OLC has demonstrated pharmacodynamic bioequivalence to Fosrenol. Additionally, Alebund is developing AP-306, an inhibitor of phosphate transporters NaPi-2b, PiT-1, and PiT-2, thus far studied in a Phase 2 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 our commercialization activities 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.

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 and 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.

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

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and our commercialization of IBSRELA and XPOHZAH. For example, we may be sued if any product we develop and/or commercialize 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 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, sales and marketing, clinical, medical, business development, manufacturing, finance and administrative 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., 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 CCPA requires covered businesses that process the personal information of California residents to, among other things: (i) provide certain disclosures to California residents regarding the business's collection, use, and disclosure of their personal information; (ii) receive and respond to requests from California residents to access, delete, and correct their personal information, or to opt out of certain disclosures of their personal information; and (iii) enter into specific contractual provisions with service providers that process California resident personal information on the business's behalf. Additional compliance investment and potential business process changes may also be required. Similar laws have passed in other states and are continuing to be at the state and 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, 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 FTC also has authority to initiate enforcement actions against entities that mislead customers about HIPAA compliance, make deceptive statements about privacy and data sharing in privacy policies, fail to limit third-party use of personal health information, fail to implement policies to protect personal health information or engage in other unfair practices that harm customers or that may violate Section 5(a) of the FTC Act. 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 FTC Act. The 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, including on websites, to regulate the presentation of website content. 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 GDPR went into effect in May 2018 and imposes strict requirements for processing the personal data of individuals within the 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. and the efficacy and longevity of current transfer mechanisms between the EEA, and the United States remains uncertain. Case law from the Court of Justice of the European Union states that reliance on the standard contractual clauses - a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism - alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. On July 10, 2023, the European Commission adopted its Adequacy Decision in relation to the new DPF, rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing data transfers within required time frames.

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. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a data transfer mechanism from the United Kingdom to U.S. entities self-certified under the DPF. 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.

In addition, we use AI Technologies in our business. The regulatory framework for AI Technologies is rapidly evolving as many federal, state, and foreign government bodies and agencies have introduced or are currently considering additional laws and regulations. Additionally, existing laws and regulations may be interpreted in ways that would affect the operation of AI Technologies. As a result, 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 market perception of their requirements may have on our business and may not always be able to anticipate how to respond to these laws or regulations.

It is possible that new laws and regulations will be adopted in the United States and in other non-U.S. jurisdictions, or that existing laws and regulations, including competition and antitrust laws, may be interpreted in ways that would limit our ability to use AI Technologies for our business, or require us to change the way we use AI Technologies in a manner that negatively affects the performance of our products, services, and business and the way in which we use AI Technologies. We may need to expand resources to adjust our products or services in certain jurisdictions if the laws, regulations, or decisions are not consistent across jurisdictions. Further, the cost to comply with such laws, regulations, or decisions and/or guidance interpreting existing laws, could be significant and would increase our operating expenses (such as by imposing additional reporting obligations regarding our use of AI Technologies). Such an increase in operating expenses, as well as any actual or perceived failure to comply with such laws and regulations, could adversely affect our business, financial condition and results of operations.

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, clinical trial data and personal information (collectively, Confidential 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 Confidential 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. There can also be no assurance that our and our collaborators', CROs', CMOs, contractors', consultants' and other service providers' cybersecurity risk management program and processes, including policies, controls or procedures, will be fully implemented, complied with or effective in protecting our systems, networks and Confidential Information.

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. Any adverse impact to the availability, integrity or confidentiality of our or third-party systems or Confidential Information can result in legal claims or proceedings (such as class actions), regulatory investigations and enforcement actions, fines and penalties, negative reputational impacts that cause us to lose existing or future customers, and/or significant incident response, system restoration or remediation and future compliance costs, 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 Kyowa Kirin 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; in Canada with Knight for commercialization of tenapanor for IBS-C and hyperphosphatemia; and with METiS for the development and commercialization of a portfolio of TGR5 agonist compounds for all therapeutic areas. 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.

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.

In the conduct of additional clinical trials, we could encounter delays in our 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 U.S. 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 U.S. 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 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 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 GCPs for clinical studies. GLPs and GCPs are regulations and guidelines enforced by the U.S. FDA, the Competent Authorities of the Member States of the 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 U.S. FDA, the European Medicines Agency 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.

Our CMOs manufacture tenapanor API outside of the U.S., our collaboration partners outside of the U.S. have sought and obtained and may continue to seek and obtain approval to commercialize tenapanor outside of the U.S., and as a result a variety of risks associated with international operations could materially adversely affect our business.

Our collaboration partners have sought and obtained and may continue to seek and obtain marketing approval for tenapanor outside the U.S. Furthermore, we may seek and obtain marketing approval for IBSRELA or XPHOZAH in other territories outside of 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;
- changes in laws or policies governing the terms of foreign trade, and in particular increased trade restrictions, tariffs or taxes on imports or exports from or to countries where we manufacture or, sell, or our partners sell, our products to may affect the prices of and demand for our products;
- 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 supporting access to systems such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or time consuming to restore some business of our business functions. The disaster recovery and business continuity plans we have in place currently are not holistic in coverage and may prove inadequate 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 XPHOZAH, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, IBSRELA and 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 after a drug is approved by the U.S. 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 U.S. 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 U.S. 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 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 U.S. 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 U.S. 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 U.S. 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, policy changes, and other events that may otherwise affect the U.S. FDA's ability to perform routine functions. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the U.S. FDA, have had to furlough critical U.S. FDA employees and stop critical activities.

Disruptions at the U.S. 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 U.S. FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the U.S. 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 CMOs 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 U.S. FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some, or all, of our CMOs 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 CMOs 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 CMOs 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 CMOs. 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 U.S. 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 U.S. FDA and other regulations related to the promotion of our products for unapproved uses, other sales practices, as well as the design and implementation of our patient assistance programs, 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 and the design and implementation of patient assistance programs are complex and subject to substantial interpretation by the U.S. FDA and other government agencies. With respect to the commercialization of IBSRELA and/or 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 U.S. 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, other sales practices, as well as the design and implementation of patient assistance programs, 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 U.S. 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 FFDCA, 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 U.S. 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 U.S. FDA or other regulations relating to the promotion of our products and/or the design and implementation of our patient assistance programs, 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 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 U.S. 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, CMOs 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, CMOs 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: U.S. FDA regulations, including those laws that require the reporting of true, complete and accurate financial and other information to the U.S. 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. Before the Marketing Authorization is granted, the European Medicines Agency 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 U.S. FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the U.S. 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 U.S. 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 U.S. 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, including the False Claims Act, 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 Act;
- 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 Payments Sunshine Act 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, U.S. FDA regulations and guidance are often revised or reinterpreted by the U.S. 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 MDRP 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, which was replaced by a new manufacturer discount program on January 1, 2025 (as discussed below), in which manufacturers were required 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.

Moreover, beginning January 1, 2025, XPHOZAH, along with other oral ESRD related drugs without injectable or intravenous equivalents, are now included in the ESRD PPS, thereby eliminating coverage under Medicare Part D as of such date. See "*—XPHOZAH is now included in the ESRD PPS, effective January 1, 2025, which means coverage for XPHOZAH for Medicare beneficiaries is no longer available under Medicare Part D, and as a result the revenue that we may generate on sales of XPHOZAH will be negatively and materially impacted*" above.

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 eliminated the statutory Medicaid drug rebate cap beginning January 1, 2024. The rebate was previously capped at 100% of a drug's AMP.

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 IRA was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare which will start to take effect 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 (which began on January 1, 2025). Under the IRA, small molecule drugs and biologics first become eligible for price negotiation seven and eleven years, respectively, after U.S. FDA approval. The IRA permits the Secretary of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. CMS has published the negotiated prices for the initial ten drugs, which will first be effective in 2026, and the list of the subsequent 15 drugs that will be subject to negotiation. Each year thereafter, more Part B and Part D products will become subject to the HHS price negotiation program, although the program is currently subject to legal challenges. While the impact of the IRA on the pharmaceutical industry cannot yet be fully determined, it is likely to be significant. 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 MDRP 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.

We participate in the 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 CMS, the federal agency that administers the MDRP and Medicare programs. For the MDRP, these data include the AMP and the best price 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 best price, 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 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 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. VA/FSS pricing program. Under the VA/FSS program, we are obligated to report the 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 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 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 ultimately be found to 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 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 we are not able to successfully enforce our intellectual property rights, the commercial value of IBSRELA and XPHOZAH or other product candidates may be adversely affected and we may not be able to compete effectively in our market.

The enforceability of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions, the answers to which 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 issue, third parties may challenge the validity, enforceability, scope or infringement thereof, which may result in such patents being narrowed, invalidated, held unenforceable or not infringed. 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 unchallenged, our patents and patent applications may not prevent others from designing around our patent 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 and XPHOZAH 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.

Even where laws provide intellectual property and/or regulatory 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, unenforceable and/or not infringed. In patent litigation in the U.S. and other jurisdictions, defendant counterclaims alleging invalidity, unenforceability and/or noninfringement are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including novelty, nonobviousness and 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, unenforceability and noninfringement 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, unenforceability or non-infringement of our intellectual property related to a product or a product candidate, we could lose part, and possibly all, of the patent protection on such product or product candidate. Such a loss of patent protection could have a material adverse impact on our business. Moreover, our competitors could counterclaim that we infringe their intellectual property and may attempt to prevent us from commercializing a product.

Although the composition and use of IBSRELA are currently claimed by four (4) issued patents that are listed in the U.S. FDA's Orange Book, we cannot assure that we will be successful in defending against third parties asserting that any of our patents are invalid, unenforceable or not infringed by the third parties' products, or in competing against third parties seeking to introduce generic versions of IBSRELA or any of our future products.

In the U.S., the Hatch-Waxman Act provides non-patent regulatory exclusivity for five years from the date of the first U.S. FDA approval of a drug containing an NCE. The U.S. FDA is prohibited during those five years from approving an ANDA that references the NDA that has been granted NCE exclusivity. However, if any patents are listed in the U.S. FDA Orange Book for such NCE-containing drug, a generic manufacturer may file an ANDA that references a NDA product with granted NCE exclusivity after four years from the first NDA approval date provided it is accompanied by a Paragraph IV certification asserting that each Orange Book listed patent is invalid, unenforceable, or that the generic product does not infringe the Orange Book listed patents. The Hatch-Waxman Act does not prevent a third party from filing, or the U.S. FDA from approving, another full NDA (i.e., not an ANDA) for an already-approved drug where the third party has conducted its own pre-clinical and clinical trials to independently demonstrate safety and effectiveness without reliance on the original NDA data.

In cases where NCE exclusivity has been granted for an NDA, as in the case of IBSRELA, if an ANDA sponsor has provided a Paragraph IV certification to the U.S. FDA when filing an ANDA, the ANDA sponsor must also send a notice thereof to the NCE NDA owner. The NCE NDA owner may then initiate a patent infringement lawsuit in response to the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the NCE NDA owner's receipt of a notice of the Paragraph IV certification automatically prevents the U.S. FDA from approving the ANDA until the earlier of 30 months after the NCE NDA owner's receipt of the Paragraph IV certification notice or a final decision in the infringement case in favor of the ANDA sponsor. There can be no assurances that an ANDA that references our IBSRELA NDA and includes a Paragraph IV certification will not be filed, or that we will be successful in enforcing our Orange Book listed patents against such ANDA sponsor.

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 could 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 exclusivity for tenapanor, if we do not obtain patent term extension in foreign countries under similar legislation, our business may be materially harmed. Furthermore, we have obtained patent term adjustment in the U.S. under the American Inventors Protection Act extending the patent term for certain patents covering tenapanor.

U.S. Patent No. 8,541,448 covering tenapanor was subject to patent term adjustment under the American Inventors Protection Act for delays by the USPTO in granting the patent. Additionally, following the approval by the U.S. FDA for our NDA to market tenapanor for IBS-C, this patent was granted patent term extension under the Hatch-Waxman Act and together with patent term adjustment provides us with exclusivity for tenapanor and uses thereof until August 1, 2033. The Hatch-Waxman Act allows a maximum of one patent to be extended per U.S. FDA approved product. Extension and/or adjustment of patent term (collectively, Patent Restoration) also may be available in certain foreign countries upon regulatory approval of our product candidates. Despite seeking Patent Restoration for tenapanor in all countries where it is available, it may not be granted 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 patent protection subject to Patent Restoration, as well as the scope of patent protection during any such Patent Restoration, afforded by the governmental authority could be less than we request or could change due to changes to applicable Patent Restoration laws or regulations or interpretations thereof.

If we are unable to obtain Patent Term Restoration in any particular country, or the term of any such extension is less than we request, or is changed due to changes in applicable laws or regulations or interpretations thereof, the period during which we will have exclusive rights to our product in such country could be shortened and our competitors may obtain approval of competing products following our non-extended/adjusted patent expiration, and our revenue could be reduced, possibly materially.

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 new 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 EU Patent Package regulations were passed with the goal of providing a single pan-European Unitary Patent and a new UPC, for litigation involving European patents. Implementation of the EU Patent Package entered into force on June 1, 2023. Under the UPC, all European patents, including those issued prior to ratification of the EU 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.

In addition, geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's conflict in Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

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.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

We consider proprietary trade secrets, confidential know-how and unpatented know-how to be important to our business. We seek to protect our confidential proprietary information, in part, by entering into confidentiality agreements and invention assignment agreements with parties who have access to them, including our employees, consultants, scientific advisors, contractors, CROs, contract manufacturers, collaborators and other third parties, that are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties that may have or have had access to our trade secrets or proprietary technology, and we cannot be certain 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 and other confidential proprietary technology, or independently develop substantially equivalent information and techniques. For example, any of these parties with whom we have entered into such confidentiality or invention assignment agreements may breach the agreements and disclose our proprietary information, including trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know, whether the steps we have taken to protect our intellectual property will be effective.

Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. We may not be able to obtain adequate remedies in the event of such unauthorized use. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive and time consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Trade secrets will also over time be disseminated within the industry through independent development, the publication of journal articles and the movement of personnel skilled in the art from company to company or academic institutions to industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors and consultants to publish data potentially relating to our trade secrets and proprietary information, our agreements may contain certain limited publication rights. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are incorporated (inadvertently or not) into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of such information may be greatly reduced and our competitive position, business, financial condition, results of operations and prospects would be harmed.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our current or future registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive, cancelled or determined to be infringing on other marks. We may not be able to protect or

preserve our rights to these trademarks and trade names or may be forced to stop using those names, which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Although these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our competitive position, business, financial condition, results of operations and prospects.

Moreover, any name we have proposed to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark.

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 to defend 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 continue to 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 and XPHOZAH;
- results of regulatory inspections of our facilities or those of our CMOs, or specific label restrictions or patient populations for XPHOZAH's use, or changes or delays in the regulatory review process;
- announcements regarding coverage and reimbursement for XPHOZAH alone or with other oral ESRD related drugs without injectable or intravenous equivalents;
- announcements relating to our current or future collaboration partnerships;
- announcements of therapeutic innovations or new products or strategic transactions 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 and XPOHZAH, 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;
- U.S. 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 will experience additional dilution and, as a result, our stock price may decline.

We are no longer a "smaller reporting company" and as a result we are or will be subject to certain enhanced disclosure requirements which will require us to incur significant expenses and expend time and resources.

We are no longer a "smaller reporting company," and, as a result, we are or will be required to comply with various disclosure and compliance requirements that did not previously apply to us. Compliance with these additional requirements increases our legal and financial compliance costs and causes management and other personnel to divert attention from operational and other business matters to these additional public company reporting requirements. In addition, if we are not able to comply with changing requirements in a timely manner, the market price of our stock could decline and we could be subject to delisting proceedings by the Nasdaq Global Market, or sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

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 SEC which generally require, among other things, our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. 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. Adverse developments that affect financial institutions, transactional counterparties, or other third parties, or concerns or rumors about these events, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the U.S. Federal Deposit Insurance Corporation as receiver. Similarly, other institutions have been and may continue to be swept into receivership. We currently have no borrowing or deposit exposure to directly impacted institutions and have not experienced an adverse impact to our liquidity or to our business operations, financial condition, or results of operations as a result of these recent events. However, uncertainty may remain over liquidity concerns in the broader financial services industry, and there may be unpredictable impacts to our business and our industry. 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 future business opportunities. Additionally, the terms of our Loan Agreement 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 1C. CYBERSECURITY

Cybersecurity Risk Management and Strategy

We have developed and implemented a cybersecurity program intended to manage risk, and protect the confidentiality, integrity, and availability of our critical systems and information.

We design, assess and benchmark our program based on the National Institute of Standards and Technology Cybersecurity Framework.

Our cybersecurity risk management program is integrated into our overall enterprise risk management program, and shares common methodologies, reporting channels and governance processes that apply across the enterprise risk management program, in areas such as legal, compliance, strategic, operational and financial risk.

Key elements of our cybersecurity program include but are not limited to the following:

- risk assessments designed to help identify material risks from cybersecurity threats to our critical systems and information;
- a security team principally responsible for managing (1) our cybersecurity risk assessment processes, (2) our security controls and (3) our response to cybersecurity incidents;
- the use of external service providers, where appropriate, to assess, test or otherwise assist with aspects of our security processes;
- cybersecurity awareness training of our employees, including incident response personnel and senior management;
- a cybersecurity incident response plan that includes procedures for responding to cybersecurity incidents; and
- a third-party risk management process for service providers, suppliers and vendors that have access to our critical systems and information based on our assessment of their criticality to our operations and respective risk profile.

We have not identified risks from known cybersecurity threats, including as a result of any prior cybersecurity incidents, that have materially affected us, including our operations, business strategy, results of operations, or financial condition. We face risks from cybersecurity threats that, if realized are reasonably likely to materially affect us, including our operations, business strategy, results of operations or financial condition. For more information, see the section titled "Risk Factors— *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*."

Cybersecurity Governance

Our board of directors considers cybersecurity risk as part of its risk oversight function and has delegated to the Audit and Compliance Committee (Committee) oversight of cybersecurity risks, including oversight of management's implementation of our cybersecurity risk management program, maintains a strategic role in coordinating cyber risk initiatives and policies, and confirming their efficacy.

The Committee receives annual reports from management on our cybersecurity posture. In addition, management updates the Committee where it deems appropriate regarding any cybersecurity incidents it considers to be significant or potentially significant.

The Committee reports to the full board of directors regarding its activities, including those related to cybersecurity. The board of directors also receives periodic briefings from management on our cybersecurity program. The board members receive presentations on cybersecurity topics from our Chief Information Officer, internal security staff or external experts as part of the board of directors' continuing education on topics that impact public companies.

Our Chief Information Officer has over 20 years of experience in overseeing cybersecurity and risk management. In addition, our Chief Legal and Administrative Officer has over 25 years of risk management experience and our Chief Financial and Operations Officer has over 20 years of experience in overseeing risk management and cybersecurity. This team is responsible for assessing and managing our material risks from cybersecurity threats and has primary responsibility for our overall cybersecurity risk management program and supervises both our internal cybersecurity personnel and our retained external cybersecurity consultants. Our management team's experience includes experience running cybersecurity programs at similarly situated commercial biotechnology organizations and navigating the associated risk landscape.

Our management team takes steps to stay informed about and monitor efforts to prevent, detect, mitigate, and remediate cybersecurity risks and incidents through various means, which may include briefings from internal security personnel, threat intelligence and other information obtained from governmental, public or private sources, including external consultants engaged by us and alerts and reports produced by security tools deployed in the IT environment.

ITEM 2. PROPERTIES

We do not own any real estate or other physical properties materially important to our operations. Our Waltham, Massachusetts headquarters is leased for three suites, two of which expire on July 31, 2026, and one expires on April 30, 2027. In addition, we have lease agreements to lease office space and/or laboratory space in Fremont, California, Milwaukee, Wisconsin and Newark, California which expire in March 2025, February 2029 and May 2028, respectively.

ITEM 3. LEGAL PROCEEDINGS

See information under the "Legal Proceedings and Claims" caption in *Note 19. Commitments And Contingencies* which we incorporated here by reference.

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

As of December 31, 2024, there were 24 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," "we," "us," "our" and "the Company" refer to Ardelyx, Inc.

EXECUTIVE SUMMARY AND FINANCIAL HIGHLIGHTS

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 minimally absorbed, first-in-class, oral, small molecule therapy. Tenapanor, branded as IBSRELA®, is approved in the U.S. for the treatment of adults with IBS-C. Tenapanor, branded as XPHOZAH®, is approved in the U.S. to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

Below is a summary of our product sales, net by product for the years ended December 31 and total cash, cash equivalents and short-term investments as of December 31:

(in thousands)	2024	2023
IBSRELA product sales, net	$ 158,286	$ 80,062
XPHOZAH product sales, net	160,910	2,464
Total product sales, net	$ 319,196	$ 82,526
Cash, cash equivalents and short-term investments	$ 250,100	$ 184,299

IBSRELA and XPHOZAH product sales have continually grown since their respective commercial launches. IBSRELA net sales growth was attributed to patient demand for this first-in-class therapy as well as increased product awareness achieved through the IBSRELA field-based team. XPHOZAH's commercial launch has been met with a strong response from the prescribing community and net sales continued to increase during 2024, the first full year of commercialization. As of January 1, 2025, we no longer receive reimbursement for XPHOZAH from Medicare Part D following the decision by the Centers of Medicare and Medicaid Services to eliminate Medicare Part D reimbursement to transition oral only therapies, including XPHOZAH, into the End Stage Renal Disease Prospective Payment System. Patient access to XPHOZAH remains through a prescription written by a qualifying healthcare provider through our ArdelyxAssist specialty pharmacy partner. Patients who do not have affordable access will be evaluated for eligibility to receive XPHOZAH fulfilled by our Ardelyx patient assistance program.

The increase in our cash, cash equivalents and short-term investment was attributed to higher product sales, net and incremental borrowings. During 2024, we amended the 2022 Loan Agreement with SLR and drew an additional $100.0 million in debt as discussed in *Note 9. Borrowing*. We expect that we will increasingly rely on cash generated from operations to fund our operating plan. We believe our existing cash, cash equivalents and short-term investments, and cash generated from operations will be sufficient to satisfy our anticipated cash needs for operations for at least the next few years. Our access to additional capital, including our ability to source cash from future equity sales and debt financing, provides us financial flexibility to execute our principal strategy as discussed below.

Strategy

We are committed to our mission of discovering, developing and commercializing first-in-class medicines that address unmet patient needs. Our principal strategy is to maintain our commercial momentum with our current products while identifying additional assets that leverage our core capabilities, including clinical, developmental and regulatory expertise and commercial excellence while maintaining a solid financial foundation, to support our future growth.

Our priorities include: (i) accelerating IBSRELA growth momentum; (ii) executing our XPHOZAH strategy to grow utilization; (iii) building a pipeline focused on areas of unmet patient need; and (iv) continuing to deliver strong commercial and financial performance.

RECENT ACCOUNTING PRONOUNCEMENTS

A summary of recent accounting pronouncements that we have adopted or may expect to adopt is included 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 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. The preparation of financial statements requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities and the reported amounts of revenues and expenses. Our critical accounting policies are those that significantly affect our financial condition and results of operations and require the most difficult, subjective or complex judgments, often because of the need to make estimates about the effect of matters that are inherently uncertain.

While we believe that our estimates, assumptions and judgments are reasonable, they are based on information available when the estimate or assumption was made. Actual results may differ significantly. Additionally, changes in our assumptions, estimates or assessments due to unforeseen events or otherwise could have a material impact on our financial position or results of operations.

Revenue Recognition

The application of ASC 606 *Revenue from Contracts with Customers* substantially impacts our reported results, particularly product sales, net, which requires certain estimates in determining the transaction price. Total revenues are recognized following a five-step model: (i) identify the customer contract; (ii) identify the contract's performance obligations; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations; and (v) recognize revenue when or as a performance obligation is satisfied.

Product Sales, Net

GTN adjustments are primarily a function of sales volume, payor mix, contractual or legislative discounts and rebates. The transaction price for product sales, net is reduced for estimates of variable consideration related to GTN adjustments for discounts and chargebacks, rebates, wholesaler and GPO fees, copay assistance and returns. Except for certain wholesaler and GPO fees and discounts, which are based on contracts, these adjustments involve estimation and judgment. The GTN adjustments for rebates, copay assistance and chargebacks are impacted by our estimate of payor mix, which requires significant judgment. We consider legal interpretations of applicable laws and regulations, historical experience, current contract prices under applicable programs, unbilled claims, processing time lags and inventory levels in the distribution channel in determining our estimates. Estimates are assessed each period and adjusted as required to revise information or actual experience.

Discounts and chargebacks:

Our U.S. business participates in programs with government entities, the most significant of which are the U.S. Department of Defense and the U.S. Department of Veterans Affairs, and other parties, including covered entities under the 340B program, whereby pricing on products is extended below wholesaler list price to participating entities. These entities purchase products through wholesalers at the lower program price and the wholesalers then charge us the difference between their acquisition cost and the lower program price. Accounts receivable is reduced for the estimated amount of unprocessed chargeback claims attributable to a sale (typically within a two to four week time lag).

Our Customers may also receive prompt pay discounts for payment within a specified period, generally approximating two percent of the invoiced sales price. Our payment terms are generally 30 to 60 days. We expect discounts to be earned when offered and we deduct the full amount of these discounts from product sales when revenue is recognized.

Accounts receivable is reduced for the estimated amount of fees and cash discount at the time of sale and the discount is typically taken by the customer within contractual terms.

Rebates, wholesaler and GPO fees:

Our U.S. business participates in state government Medicaid and Medicare programs and other qualifying Federal and state government programs requiring discounts and rebates to participating state and local government entities. All discounts and rebates provided through these programs are included in our Medicaid and Medicare rebate accruals. Medicaid rebates have also been extended to drugs used in managed Medicaid plans. The estimated amount of unpaid or unbilled rebates and discounts is presented as a liability. Settlement of Medicare and Medicaid accruals can lag for multiple quarters due to extensive time delays between recording an accrual and subsequent receipt of an invoice. Due to this lag, adjustments can incorporate revision of several prior quarters. Through December 31, 2024, we paid a 70% discount to CMS when the Medicare Part D beneficiaries were in the coverage gap. Beginning in 2025, as part of the Medicare Part D redesign within the IRA, there is a $2,000 cap for out-of-pocket costs for Medicare Beneficiaries and manufacturers are responsible for 10% of costs up to the cap and 20% after the cap is reached.

Wholesaler and GPO administrative fees are a significant portion of our GTN adjustments, however, since they are based on contracts, they require inherently less estimation.

Copay assistance and returns:

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. We also estimate the amount of copay assistance that we will provide to patients associated with product we have sold but has not yet been dispensed to commercial patients, which requires significant estimation and judgment. Our estimates are recorded in accrued expenses and other current liabilities on the balance sheets.

Considering the timing of our respective product launches, and limited experiences with returns, we are primarily reliant on historical sales returns of similar products, such as those within the same product line, similar therapeutic area, similar distribution model, estimated levels of inventory in the distribution channel and projected demand. We increasingly rely on our products' actual returns history and other factors, including levels of our inventory in the distribution channel and estimated shelf life, to estimate our returns. Our estimates are recorded in accrued expenses and other current liabilities on the balance sheets.

Use of Information from External Sources:

Information from external sources is used to estimate GTN adjustments. Our estimate of inventory at the wholesalers is based on the historical inventory experience, as well as our analysis of third-party information, including written and oral information obtained from certain wholesalers with respect to their inventory levels and sell-through to customers and our internal information. The inventory information received from wholesalers is a product of their recordkeeping process and excludes inventory held by intermediaries to whom they sell, such as retailers and hospitals. We also use information from external sources to identify prescription trends, patient demand and average selling prices. Our estimates are subject to inherent limitations of estimates that rely on third-party information, as certain third-party information was itself in the form of estimates and reflect other limitations including lags between the date as of which third-party information is generated and the date on which we receive third-party information.

RESULTS OF OPERATIONS

Revenue

Our revenue to date has been generated primarily through a combination of product sales and payments in connection with license, research and development collaborative agreements with our various collaboration partners. 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 many factors as described in Part I, Item 1A, "Risk Factors," of this Annual Report on Form 10-K.

Below is a summary of our total revenues:

	Year Ended December 31,			Change 2024 vs. 2023		Change 2023 vs. 2022	
($ in thousands)	**2024**	**2023**	**2022**	**$**	**%**	**$**	**%**
Product sales, net	$ 319,196	$ 82,526	$ 15,600	$ 236,670	287 %	$ 66,926	429 %
Product supply revenue	11,649	6,121	1,527	5,528	90 %	4,594	301 %
Licensing revenue	78	35,809	35,031	(35,731)	(100)%	778	2 %
Non-cash royalty revenue related to the sale of future royalties	2,692	—	—	2,692	(a)	—	(a)
Total revenues	$ 333,615	$ 124,456	$ 52,158	$ 209,159	168 %	$ 72,298	139 %

(a) Percent change is not meaningful.

Below is a summary of our product sales, net by product:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Product sales, net			
IBSRELA	$ 158,286	$ 80,062	$ 15,600
XPHOZAH	160,910	2,464	—
Total product sales, net	$ 319,196	$ 82,526	$ 15,600

Product sales, net:

The increase in IBSRELA product sales, net in 2024 and 2023 was due to higher demand since its commercial launch in March 2022, reflecting continued increase in awareness and prescriber experience. In addition, the increase in 2024 was attributable to the completion of our field-base team expansion.

The increase in XPHOZAH product sales, net in 2024 and 2023 was due to higher demand since its commercial launch in November 2023. As of January 1, 2025, we no longer receive reimbursement for XPHOZAH from Medicare Part D following the decision by the Centers of Medicare and Medicaid Services to eliminate Medicare Part D reimbursement to transition oral only therapies, including XPHOZAH, into the End Stage Renal Disease Prospective Payment System. Patient access to XPHOZAH remains through a prescription written by a qualifying healthcare provider through our ArdelyxAssist specialty pharmacy partner. Patients who do not have affordable access will be evaluated for eligibility to receive XPHOZAH fulfilled by our Ardelyx patient assistance program.

Product supply revenue:

The increase in product supply revenue in 2024 and 2023 was due to product supply shipments to our collaboration partners, primarily Kyowa Kirin, under our respective commercial supply agreements in support of non-US launches.

Licensing revenue:

Licensing revenue is primarily impacted by the timing of regulatory and commercial milestone achievements from our out-licensing partners, as well as sales-based royalties received from Knight. The 2023 licensing revenue included $30.0 million in payments received under the Kyowa Kirin Agreement, following Kyowa Kirin's submission to the Japanese MHLW for the NDA for tenapanor in the improvement of hyperphosphatemia in adult patients with CKD on dialysis; and a $5.0 million payment under the Fosun Agreement, following the NDA acceptance by China's Center for Drug Evaluation of the NMPA for tenapanor in the control of serum phosphorus in adult patients with CKD on hemodialysis and the U.S. FDA approval of XPHOZAH to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

Non-cash royalty revenue:

Non-cash royalty revenue in 2024 was attributable to royalties from Kyowa Kirin for sales of PHOZEVEL in Japan since its launch in February 2024, which we remitted to HCR upon receipt in accordance with the HCR Agreement.

GTN Adjustments

We recognize product sales net of GTN adjustments that are further described in *Note 6. Revenue* and the "Critical Accounting Policies and Estimates" caption in Part II, Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations." Reconciliation of gross product sales to product sales, net by GTN adjustment category is as follows:

	Year Ended December 31,		
($ in thousands)	**2024**	**2023**	**2022**
Gross product sales	$ 429,053	$ 113,861	$ 21,648
GTN adjustments	(109,857)	(31,335)	(6,048)
Product sales, net	$ 319,196	$ 82,526	$ 15,600
GTN adjustment percentage	25.6 %	27.5 %	27.9 %

GTN adjustments are primarily a function of sales volume, payor mix, contractual or legislative discounts and rebates. Adjustments to provisions for product sales made in prior periods due to changes in estimates were not significant for any of the years presented. The decrease in GTN adjustment percentage in 2024 was primarily due to a higher percentage of sales which had a more favorable GTN rate. The reduction was mainly due to lower sales subjected to copay assistance and contractual chargebacks which had higher GTN adjustment percentages. We expect GTN adjustment percentages to increase in the future due to unfavorable payor mix shifts associated with loss of XPHOZAH Medicare Part D reimbursement beginning January 1, 2025.

The activities and ending reserve balances for each significant category of GTN adjustments on product sales, net, which constitute variable consideration, were as follows:

(in thousands)	Discounts and chargebacks	Rebates, wholesaler and GPO fees	Copay assistance and returns	Total
Balance as of December 31, 2022	$ 142	$ 1,444	$ 1,258	$ 2,844
Provisions	5,341	15,365	10,629	31,335
Credits/payments	(5,005)	(12,575)	(7,971)	(25,551)
Balance as of December 31, 2023	478	4,234	3,916	8,628
Provisions	15,099	65,833	28,925	109,857
Credits/payments	(13,934)	(55,592)	(21,671)	(91,197)
Balance as of December 31, 2024	$ 1,643	$ 14,475	$ 11,170	$ 27,288

Adjustments to prior period provisions recorded in the current period were not material.

Expenses

Below is a summary of our cost of goods sold, operating expenses, interest expense, non-cash interest expense related to the sale of future royalties and other income, net:

	Year Ended December 31,			Change 2024 vs. 2023		Change 2023 vs. 2022	
($ in thousands)	2024	2023	2022	$	%	$	%
Cost of product sales	$ 6,851	$ 2,323	$ 566	$ 4,528	195 %	$ 1,757	310 %
Other cost of revenue	43,705	15,472	3,551	28,233	182 %	11,921	336 %
Total cost of goods sold	$ 50,556	$ 17,795	$ 4,117	$ 32,761	184 %	$ 13,678	332 %
Research and development	$ 52,317	$ 35,536	$ 35,201	$ 16,781	47 %	$ 335	1 %
Selling, general and administrative	258,692	134,401	76,599	124,291	92 %	57,802	75 %
Total operating expenses	$ 311,009	$ 169,937	$ 111,800	$ 141,072	83 %	$ 58,137	52 %
Interest expense	$ (13,006)	$ (4,950)	$ (3,400)	$ (8,056)	163 %	$ (1,550)	46 %
Non-cash interest expense related to the sale of future royalties	(7,088)	(3,924)	(1,673)	(3,164)	81 %	(2,251)	135 %
Other income, net	9,174	6,630	1,633	2,544	38 %	4,997	306 %

Cost of Goods Sold

Cost of product sales consists of the cost of commercial goods sold to our Customers and includes 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. Other cost of revenue consists of the cost of materials sold to our international partners under product supply agreements, certain costs related to capacity expansion at current and future CMOs, as well as payments due to AstraZeneca based on sales of tenapanor. See the “AstraZeneca” caption in *Note 7. Collaboration And Licensing Agreements* for further detail.

Cost of product sales:

The increase in cost of product sales in 2024 and 2023 was due to higher product sales. A portion of the costs of IBSRELA and XPHOZAH units recognized as revenue during the years ended December 31, 2024 and 2023 were expensed as research and development expenses in periods prior to the commencement of capitalization of inventory costs for each respective product as discussed in *Note 2. Summary Of Significant Accounting Policies.* The cost associated with inventory sold but previously expensed as research and development was $6.3 million, $4.4 million and $1.9 million in 2024, 2023 and 2022, respectively. The value of inventory on hand as of December 31, 2024 and 2023 that was previously expensed as research and development was approximately $15.6 million and $21.8 million, respectively.

Other cost of revenue:

The increase in other cost of revenue in 2024 and 2023 was primarily due to higher AstraZeneca royalties, driven by higher product sales, net of tenapanor. In 2023, AstraZeneca royalties attributed to licensing revenue had a greater impact on the obligation than royalties from product sales, net. Other cost of revenue related to the AstraZeneca Termination Agreement was $34.7 million, $12.4 million and $3.6 million in 2024, 2023 and 2022, respectively. The remaining future royalty obligation to AstraZeneca was $12.1 million as of December 31, 2024. In addition, the increase in other cost of revenue was due to higher product supply revenue and costs associated with that revenue.

Research and Development

Research and development activities include research and early discovery, preclinical and clinical development, drug formulation and medical support to marketed products. External R&D expenses include research and development expenses incurred under agreements with outside consultants, third-party CROs and investigative sites where a substantial portion of our clinical studies are conducted, and with CMOs where our clinical supplies are produced; employee-related expenses, which include salaries, bonuses, benefits, travel and stock-based compensation; expenses associated with supplies and materials consumed in connection with our research operations; 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.

Below is a summary of our research and development expenses:

	Year Ended December 31,			Change 2024 vs. 2023		Change 2023 vs. 2022	
($ in thousands)	**2024**	**2023**	**2022**	**$**	**%**	**$**	**%**
External R&D and other expenses	$ 20,723	$ 15,213	$ 17,011	$ 5,510	36 %	$ (1,798)	(11)%
Employee-related expenses	27,541	17,391	15,065	10,150	58 %	2,326	15 %
Facilities, equipment, depreciation and other expenses	4,053	2,932	3,125	1,121	38 %	(193)	(6)%
Total research and development expenses	$ 52,317	$ 35,536	$ 35,201	$ 16,781	47 %	$ 335	1 %

The increase in R&D expenses in 2024, including other R&D expenses, primarily reflected increased medical engagement with scientific communities in the areas of gastroenterology and nephrology related to our marketed products. The increase in external R&D expenses was also attributable to clinical trial and pharmacovigilance activities. The increase in employee-related R&D expenses was the result of increases in headcount and personnel costs, including an increase in stock-based compensation expenses totaling $6.0 million and $0.4 million in 2024 and 2023, respectively.

R&D expenses in 2023 remained relatively stable as compared to 2022, however, the focus of 2023 activities primarily shifted towards medical and pharmacovigilance efforts supporting our marketed products. Whereas, in 2022, activities focused more on clinical activities in preparation for the respective regulatory approvals.

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.

The increase in selling, general and administrative expenses in 2024 and 2023 was primarily due to increased commercialization and administrative costs to support net sales growth of IBSRELA and XPHOZAH and to support our strategy. The increases consisted of external spending for disease awareness initiatives, patient affordability, access support and related patient awareness, as well as increased commercial infrastructure and increased legal fees incurred related to the Company's lawsuit against CMS in 2024. The increase was also attributable to increases in headcount and related personnel costs, including an increase in stock-based compensation expense totaling $17.8 million and $2.4 million in 2024 and 2023, respectively.

Interest Expense

Interest expense represents the interest associated with our loan agreements.

The increase in interest expense in 2024 and 2023 was due to a higher loan balance resulting from the term loan draws in each respective year: $50.0 million for the Term D Loan in October 2024, $50.0 million for the Term C Loan in March 2024, and $22.5 million for the Term B Loan in October 2023.

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. Non-cash interest expense is impacted by the outstanding balance of the deferred royalty obligation, which increases from milestone payments received from HCR under the sale of future royalties agreement and imputed interest accrued on the outstanding deferred royalty obligation, and decreases as royalties received from Kyowa Kirin related to the sale of tenapanor for cardiorenal indications in Japan are subsequently remitted to HCR. Refer to *Note 8. Deferred Royalty Obligation Related To The Sale Of Future Royalties* for further detail.

The increase in non-cash interest expense related to the sale of future royalties in 2024 and 2023 was due to the increasing outstanding balance of the deferred royalty obligation attributed to the upfront milestones received from HCR, including the $10.0 million upfront payment received in June 2022 and the $5.0 million milestone payment received in October 2023 as a result of Kyowa Kirin's receipt of regulatory approval to market tenapanor for hyperphosphatemia in Japan in February 2024 and imputed interest accrued on the outstanding balance. In 2024, we began to receive royalties from Kyowa Kirin which were remitted to HCR, thereby reducing the outstanding deferred royalty obligation.

Other Income, Net

Other income, net consists of interest income earned on our cash, cash equivalents and short-term investments, the periodic revaluation of the exit fees related to our loan agreements, as well as currency exchange gains and losses.

The increase in other income, net in 2024 and 2023 primarily reflected higher income on our investments, resulting from both higher interest rates and larger investment balances throughout the periods.

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 tax balances reflect the effects of temporary differences between the carrying amounts of assets and liabilities and their income tax bases, as well as from net operating loss and tax credit carryforwards. Our deferred tax assets continue to be fully offset by a valuation allowance, including deferred tax assets related to our net operating loss and tax credit carryforwards, which may be subject to annual limitations as a result of ownership changes that may have occurred or could occur in the future.

Refer to *Note 2. Summary Of Significant Accounting Policies* for further discussion of our significant accounting policies.

LIQUIDITY AND CAPITAL RESOURCES

Below is a summary of our cash, cash equivalents and short-term investments:

	December 31,		Change 2024 vs. 2023	
($ in thousands)	**2024**	**2023**	**$**	**%**
Cash and cash equivalents	$ 64,932	$ 21,470	$ 43,462	202 %
Short-term investments	185,168	162,829	22,339	14 %
Total liquid funds	$ 250,100	$ 184,299	$ 65,801	36 %

We regularly assess our cash position and our working capital needs to execute our strategy. Our primary uses of cash to date have been to fund research and development expenditures related to our development of tenapanor and to support the commercialization of our marketed products. We have funded our operations primarily from the sale of common stock, product sales, funds from our collaboration partnerships, funds from our loan agreements with SLR, as well as sales of future royalties to HCR. We expect that we will increasingly rely on cash generated from operations to fund our operating plan while maintaining financial flexibility from our ability to source cash from future equity sales and debt financing.

Under a registration statement filed in 2020, we had the ability to sell up to $150.0 million of our common stock through Jefferies, as our sales agent. As of March 2023, we had received the maximum gross proceeds of $150.0 million at a weighted average share price of approximately $1.57.

In January 2023, we filed a registration statement on Form S-3, which became effective in January 2023, 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. As of December 31, 2024, we have completed sales pursuant to the 2023 Open Market Sales Agreement resulting in the issuance of 16.8 million shares of our common stock and receipt of gross proceeds of $70.0 million at a weighted average sales price of approximately $4.17.

We have a loan and security agreement (as amended, the 2022 Loan Agreement) with SLR. The 2022 Loan Agreement provides a total of $200.0 million, of which $150.0 million has been drawn as of December 31, 2024 to support our ongoing operations and the commercial launches of IBSRELA and XPHOZAH. The borrowings under the 2022 Loan Agreement bear interest at SOFR plus a spread based on our public debt rating. We classify outstanding borrowings under the 2022 Loan Agreement as long-term based on the maturity date of the loan. All the term loans mature on July 1, 2028. See *Note 9. Borrowing* for further discussion.

We believe our available cash, cash equivalents and short-term investments as of December 31, 2024 will be sufficient to fund our planned operations for at least a period of one year from the issuance of these financial statements. We have based this estimate on assumptions that may prove to be wrong and we could utilize our available capital resources sooner than we currently expect. In particular, our operating plan may change and we may require significant additional capital to fund our operations. There are no assurances that our efforts to meet our operating cash flow requirements will be successful. If our current cash, cash equivalents 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 following the issuance of these financial statements, our liquidity, financial condition and business prospects will be materially affected.

Our future funding requirements will depend on many factors as described in Part I, Item 1A, “Risk Factors,” of this Annual Report on Form 10-K.

CASH FLOW ACTIVITIES

The following table summarizes our cash flows activities:

	Year Ended December 31,			Change 2024 vs. 2023		Change 2023 vs. 2022	
($ in thousands)	**2024**	**2023**	**2022**	**$**	**%**	**$**	**%**
Net cash used in operating activities	$ (44,809)	$ (89,717)	$ (70,044)	$ 44,908	(50)%	$ (19,673)	28 %
Net cash (used in) provided by investing activities	(18,318)	(131,248)	18,415	112,930	(86)%	(149,663)	(813)%
Net cash provided by financing activities	106,589	146,295	75,341	(39,706)	(27)%	70,954	94 %
Net increase (decrease) in cash and cash equivalents	$ 43,462	$ (74,670)	$ 23,712	$ 118,132	(158)%	$ (98,382)	(415)%

Cash Flows from Operating Activities

Net cash used in operating activities decreased in 2024 compared to 2023, primarily due to cash generated from higher product sales, net, partially offset by working capital cash uses to support our commercial growth. Net working capital cash outflows were driven primarily by increases in customer credit and inventory purchases, which were partially offset by increases in accounts payable and accruals.

Net cash used in operating activities increased in 2023 compared to 2022, primarily due to working capital cash uses to support our commercial launches, partially offset by cash generated from higher product sales, net from such launches. Net working capital cash outflows were driven primarily by increases in customer credit, upfront payments to CMOs for the commercial manufacturing of IBSRELA and XPHOZAH and increased prepaid selling and marketing spending.

Cash Flows from Investing Activities

Net cash used in investing activities for 2024 and 2023 was primarily impacted by the timing of our investment maturities and purchases. In 2023, net investment purchases were significantly higher when compared to other reported periods. To a lesser extent, the 2024 cash used for investing activities included property, plant and equipment purchases associated with our new leased facility and build outs of existing facilities.

Cash Flows from Financing Activities

Net cash provided by financing activities decreased in 2024 compared to 2023, primarily due to $99.5 million net proceeds from the Term C Loan and Term D Loan and proceeds from the issuance of common stock under our equity incentive and stock purchase plans in 2024 which were less than $119.2 million received in 2023 from the issuance of common stock pursuant to at the market offerings. We have not received any proceeds under the 2021 Open Market Sales Agreement in 2024.

Net cash provided by financing activities increased in 2023 compared to 2022, primarily due to higher net proceeds from issuance of our common stock pursuant to the at the market offerings of $47.6 million, as well as net proceeds received of $22.4 million from drawing the Term B Loan as compared to net expenditure of $6.1 million in 2022 in conjunction with entering into the 2022 Loan Agreement and repaying the principal outstanding under the 2018 Loan. This increase was partially offset by lower net proceeds from the sale of future royalties to HCR of $5.0 million.

SMALLER REPORTING COMPANY AND LARGE ACCELERATED FILER STATUS

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 for the year ended December 31, 2022. On June 30, 2023, our public float exceeded $700.0 million and therefore since January 1, 2024, we are considered a large accelerated filer. This Annual Report on Form 10-K includes an opinion of Ernst & Young LLP, our independent auditors with respect to our internal control over financial reporting as of December 31, 2024.

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. 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, 2024, we had cash, cash equivalents and short-term investments of $250.1 million, which consisted of bank deposits and money market funds, as well as high quality fixed income instruments including commercial paper, U.S. government-sponsored agency bonds, U.S. treasury securities, corporate bonds, Yankee bonds and asset-backed securities. 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 2022 Loan Agreement, which bear interest at SOFR plus a spread based on our public debt rating. A hypothetical increase in one-month CME Term SOFR of 100 basis points above the current one-month CME Term SOFR rate would have increased our interest expense by approximately $1.0 million for the year ended December 31, 2024. As of December 31, 2024, we had an aggregate principal amount of $150.0 million outstanding pursuant to our 2022 Loan Agreement.

Foreign Currency 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, Japanese yen 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, non-cash royalty revenue related to the sale of future royalties, 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, 2024, we had no open forward foreign currency exchange contracts.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

ARDELYX, INC.
INDEX TO FINANCIAL STATEMENTS

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. (the "Company") as of December 31, 2024 and 2023, 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, 2024, 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, 2024 and 2023, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 20, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit 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.

Description of the Matter

Estimates of Reserves for Variable Consideration Impacted by Estimated Payor Mix

As described in Notes 2 and 6 to the financial statements, the transaction price for product sales, net is reduced for estimates of variable consideration related to gross-to-net ("GTN") adjustments for discounts and chargebacks, rebates, wholesaler and group purchasing organization ("GPO") fees, copay assistance and returns. Except for certain wholesaler and GPO fees and discounts, which are based on contracts, these adjustments involve estimation and judgment. The GTN adjustments for rebates, copay assistance and chargebacks are impacted by our estimate of payor mix, which requires significant judgment. The Company's total estimate of reserves for variable consideration was $27.3 million as of December 31, 2024. During 2024, the Company recorded $109.9 million in total reductions to gross product sales for variable consideration.

Auditing the Company's estimates of reserves for variable consideration relating to rebates, copay assistance and chargebacks was especially challenging as it involved evaluation of management's subjective judgments with respect to payor mix that considers various data sources. The Company has a limited history upon which to base its assumptions, and changes in these assumptions could have a material impact on the reserves recorded for variable consideration.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of internal controls over the Company's process to determine the reserves for variable consideration that are impacted by the payor mix. For example, we tested controls over management's review of the completeness and accuracy of the data used to determine the estimate.

To test the Company's estimates of reserves for variable consideration relating to rebates, copay assistance and chargebacks, 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 payor mix analysis and the related reserves. We compared the assumptions used by management to third-party industry data and evaluated trends in the data. We also 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 payor mix assumptions on the reserves recorded for variable consideration impacted by the payor mix. 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.

Boston, MA

February 20, 2025

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

	December 31,	
	2024	**2023**
Assets		
Current assets		
Cash and cash equivalents	$ 64,932	$ 21,470
Short-term investments	185,168	162,829
Accounts receivable	57,705	22,031
Inventory	21,173	12,448
Prepaid commercial manufacturing	16,378	18,925
Prepaid expenses and other current assets	11,096	8,408
Total current assets	356,452	246,111
Property and equipment, net	1,495	1,009
Inventory, non-current	70,011	37,039
Prepaid commercial manufacturing, non-current	—	4,235
Right-of-use assets	2,380	5,589
Other assets	5,416	3,596
Total assets	$ 435,754	$ 297,579
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	$ 16,000	$ 11,138
Accrued compensation and benefits	14,940	12,597
Current portion of operating lease liability	1,562	4,435
Deferred revenue	10,686	7,182
Accrued expenses and other current liabilities	34,642	15,041
Total current liabilities	77,830	50,393
Operating lease liability, net of current portion	1,023	1,725
Long-term debt	150,853	49,822
Deferred revenue, non-current	7,232	8,644
Deferred royalty obligation related to the sale of future royalties	25,527	20,179
Total liabilities	262,465	130,763
Commitments and contingencies (Note 19)		
Stockholders' equity		
Common stock, $ 0.0001 par value; 500,000,000 shares authorized; 238,015,825 and 232,453,190 shares issued and outstanding as of December 31, 2024 and December 31, 2023, respectively.	24	23
Additional paid-in capital	1,058,548	1,012,773
Accumulated deficit	(885,340)	(846,204)
Accumulated other comprehensive income	57	224
Total stockholders' equity	173,289	166,816
Total liabilities and stockholders' equity	$ 435,754	$ 297,579

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,		
	2024	**2023**	**2022**
Revenues			
Product sales, net	$ 319,196	$ 82,526	$ 15,600
Product supply revenue	11,649	6,121	1,527
Licensing revenue	78	35,809	35,031
Non-cash royalty revenue related to the sale of future royalties	2,692	—	—
Total revenues	333,615	124,456	52,158
Cost of goods sold			
Cost of product sales	6,851	2,323	566
Other cost of revenue	43,705	15,472	3,551
Total cost of goods sold	50,556	17,795	4,117
Operating expenses			
Research and development	52,317	35,536	35,201
Selling, general and administrative	258,692	134,401	76,599
Total operating expenses	311,009	169,937	111,800
Loss from operations	(27,950)	(63,276)	(63,759)
Interest expense	(13,006)	(4,950)	(3,400)
Non-cash interest expense related to the sale of future royalties	(7,088)	(3,924)	(1,673)
Other income, net	9,174	6,630	1,633
Loss before provision for income taxes	(38,870)	(65,520)	(67,199)
Provision for income taxes	266	547	8
Net loss	$ (39,136)	$ (66,067)	$ (67,207)
Net loss per share of common stock - basic and diluted	$ (0.17)	$ (0.30)	$ (0.42)
Shares used in computing net loss per share - basic and diluted	235,232,927	219,331,253	158,690,083
Comprehensive loss			
Net loss	$ (39,136)	$ (66,067)	$ (67,207)
Unrealized (losses) gains on available-for-sale securities	(167)	278	(48)
Comprehensive loss	$ (39,303)	$ (65,789)	$ (67,255)

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	Accumulated	Accumulated Other Comprehensive	Total Stockholder'
	Shares	Amount	Paid-In Capital	Deficit	(Loss) Income	Equity
Balance as of December 31, 2021	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)
Balance as of December 31, 2022	198,575,016	$ 20	$ 878,500	$ (780,137)	$ (54)	$ 98,329
Issuance of common stock under employee stock purchase plan	435,708	—	808	—	—	808
Issuance of common stock for services	86,095	—	337	—	—	337
Issuance of common stock upon exercise of options	225,988	—	365	—	—	365
Issuance of common stock upon vesting of restricted stock units	855,642	—	—	—	—	—
Issuance of common stock in at-the-market offering	32,274,741	3	119,233	—	—	119,236
Stock-based compensation	—	—	13,530	—	—	13,530
Unrealized gains on available-for-sale securities	—	—	—	—	278	278
Net loss	—	—	—	(66,067)	—	(66,067)
Balance as of December 31, 2023	232,453,190	$ 23	$ 1,012,773	$ (846,204)	$ 224	$ 166,816
Issuance of common stock under employee stock purchase plan	479,609	—	2,227	—	—	2,227
Issuance of common stock for services	40,549	—	257	—	—	257
Issuance of common stock upon exercise of options	2,654,370	1	5,910	—	—	5,911
Issuance of common stock upon vesting of restricted stock units	2,388,107	—	—	—	—	—
Stock-based compensation	—	—	37,381	—	—	37,381
Unrealized losses on available-for-sale securities	—	—	—	—	(167)	(167)
Net loss	—	—	—	(39,136)	—	(39,136)
Balance as of December 31, 2024	238,015,825	$ 24	$ 1,058,548	$ (885,340)	$ 57	$ 173,289

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

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

	Year Ended December 31,		
	2024	**2023**	**2022**
Operating activities			
Net loss	$ (39,136)	$ (66,067)	$ (67,207)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization expense	2,063	1,292	1,144
Non-cash lease expense	4,008	3,624	3,457
Stock-based compensation	37,381	13,530	10,750
Non-cash interest expense	7,400	4,220	1,962
Non-cash royalty revenue related to the sale of future royalties	(2,692)	—	—
Gain on sale of equipment	—	—	(1,260)
Other, net	(4,664)	(2,930)	685
Changes in operating assets and liabilities			
Accounts receivable	(35,674)	(14,298)	(7,231)
Inventory	(41,697)	(21,141)	(28,346)
Prepaid commercial manufacturing	6,782	(9,593)	(4,161)
Prepaid expenses and other assets	(4,543)	(6,035)	2,299
Accounts payable	4,862	279	6,582
Accrued compensation and benefits	2,343	5,049	2,126
Operating lease liabilities	(4,588)	(3,928)	(3,491)
Accrued and other liabilities	21,254	3,691	4,138
Deferred revenue	2,092	2,590	8,509
Net cash used in operating activities	(44,809)	(89,717)	(70,044)
Investing activities			
Proceeds from maturities and redemptions of investments	177,854	84,321	67,000
Purchases of investments	(195,161)	(215,225)	(50,328)
Proceeds from sale of property and equipment	—	—	1,798
Purchases of property and equipment	(1,011)	(344)	(55)
Net cash (used in) provided by investing activities	(18,318)	(131,248)	18,415
Financing activities			
Proceeds from issuance of common stock in at the market offering, net of issuance costs	—	119,236	71,625
Proceeds from 2022 Loan Agreement, net of issuance costs	99,451	22,386	26,971
Proceeds from the sale of future royalties, net of issuance costs	—	5,000	9,581
Proceeds from issuance of common stock under equity incentive and stock purchase plans	8,138	1,173	202
Payment of the exit fees	(1,000)	(1,500)	—
Payments for the 2018 Loan, net of costs	—	—	(33,038)
Net cash provided by financing activities	106,589	146,295	75,341
Net increase (decrease) in cash and cash equivalents	43,462	(74,670)	23,712
Cash and cash equivalents at beginning of period	21,470	96,140	72,428
Cash and cash equivalents at end of period	$ 64,932	$ 21,470	$ 96,140
Supplementary disclosure of cash flow information			
Cash paid for interest	$ 11,408	$ 4,240	$ 2,901
Cash paid for income taxes	$ 266	$ 51	$ 6
Supplementary disclosure of non-cash activities			
Right-of-use assets obtained in exchange for lease obligations	$ 1,010	$ 339	$ —
Issuance of common stock for services	$ 257	$ 337	$ 390
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

NOTE 1. NATURE OF OPERATIONS

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 minimally absorbed, first-in-class, oral, small molecule therapy. Tenapanor, branded as IBSRELA®, is approved in the U.S. for the treatment of adults with IBS-C. Tenapanor, branded as XPHOZAH®, is approved in the U.S. to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

We operate in one business segment, which is the development and commercialization of biopharmaceutical products. Refer to *Note 17. Segment Reporting* for further segment reporting information.

NOTE 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). Certain prior year amounts have been reclassified to conform to the current year presentation.

Refer to the *Summary of Abbreviated Terms* at the end of this Annual Report on Form 10-K for definitions of terms used throughout the document.

Use of Estimates

The preparation of financial statements requires management to make estimates, judgments and assumptions. The most significant assumptions are estimates used in our revenue gross-to-net accruals and other assumptions. 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.

Cash and Cash Equivalents

Cash and cash equivalents consist of highly liquid investments purchased with an original maturity date of 90 days or less and are recognized at cost, which approximates fair value.

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 or other observable market data. Unrealized (losses) gains on available-for-sale securities are included in accumulated other comprehensive income on our balance sheets. The cost of available-for-sale securities sold is based on the specific-identification method.

Marketable debt securities are reviewed for impairment by determining whether the decline in their market value below carrying value is other-than-temporary. This assessment considers the intent and ability to retain the investment for a period of time sufficient for an anticipated recovery in market value, the duration and extent that the market value has been below cost, and the investee's financial condition. Other-than-temporary impairments and credit losses are recorded in the statements of operations and comprehensive loss.

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 our balance sheets. Cash, cash equivalents and short-term investments are invested through banks and other financial institutions in the U.S.

Foreign Currency

Our business is conducted 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. Foreign currency transactions are translated into the functional currency using exchange rates prevailing at the dates of the transactions. At the end of each reporting period, monetary assets and liabilities that are denominated in foreign currencies are translated at the rates prevailing at that date. All gains and losses on these foreign currency transactions are recorded in other income, net in our statements of operations and comprehensive loss.

Property and Equipment

Expenditures for property and equipment are capitalized at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets, ranging from three to five years for laboratory equipment and office equipment and furniture. 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 values 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.

Income Taxes

The asset and liability method of accounting is used for income taxes. Deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax basis 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 a portion or all of a deferred tax asset will not be realized.

Accounts Receivable

Accounts receivable are stated at amortized cost less allowance for credit losses. The allowance for credit losses reflects our best estimate of future losses over the contractual life of outstanding accounts receivable and is determined on the basis of historical experience, specific allowances for known troubled accounts, other currently available information including customer financial condition and both current and forecasted economic conditions. To date, we have determined that an allowance for doubtful accounts is not required. As of December 31, 2024, our accounts receivable balance was comprised of $ 56.7 million from commercial customers and $ 1.0 million from our collaboration partners. As of December 31, 2023, our accounts receivable balance was comprised of $ 17.1 million from commercial customers and $ 4.9 million from our collaboration partners.

Inventory

Inventory costs incurred are capitalized after regulatory approval, or if based on management's judgment, future commercialization is considered probable and future economic benefit is expected to be realized. 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 launch of IBSRELA. We began to capitalize inventory costs associated with XPHOZAH during the fourth quarter of 2023, following approval by the U.S. FDA to market XPHOZAH in the U.S. Inventory costs incurred prior to regulatory approval were expensed as research and development.

Inventories are stated at the lower of cost or estimated net realizable value with cost determined under the specific identification method. 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 assets on our balance sheets.

Revenue Recognition

The application of ASC 606 *Revenue from Contracts with Customers* substantially impacts our reported results, particularly product sales, net, which requires certain estimates in determining the transaction price. Total revenues are recognized following a five-step model: (i) identify the customer contract; (ii) identify the contract's performance obligations; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations; and (v) recognize revenue when or as a performance obligation is satisfied.

Product Sales, Net Recognition

The transaction price for product sales, net is reduced for estimates of variable consideration related to GTN adjustments for discounts and chargebacks, rebates, wholesaler and GPO fees, copay assistance and returns. Except for certain wholesaler and GPO fees and discounts, which are based on contracts, these adjustments involve estimation and judgment. The GTN adjustments for rebates, copay assistance and chargebacks are impacted by our estimate of payor mix, which requires significant judgment. We consider legal interpretations of applicable laws and regulations, historical experience, current contract prices under applicable programs, unbilled claims, processing time lags and inventory levels in the distribution channel in determining our estimates.

Estimates are assessed each period and adjusted as required to revise information or actual experience. Changes in estimates recorded through December 31, 2024 have not been material.

Licensing Revenue Recognition

Licensing revenue and product supply revenue result from our collaboration and licensing agreements as discussed in *Note 7. Collaboration And Licensing Agreements.* Goods and services in these agreements may include the grant of licenses for use of our intellectual property and manufacturing services. Significant judgment is required to determine whether promised goods and services represent distinct performance obligations, which are identified and separated when the other party can benefit from the rights, goods or services either on their own or together with other readily available resources and when the rights, goods or services are not highly interdependent or interrelated.

Transaction prices for these arrangements may include non-refundable, up-front license fees; research, development, regulatory and commercial milestone payments; payments for manufacturing supply services; and future royalties on net sales of licensed products. Variable consideration is included in the transaction price only to the extent significant reversal of cumulative revenue recognized is not probable of occurring when the uncertainty associated with the variable consideration is subsequently resolved. Significant judgment is required in estimating variable consideration for each performance obligation identified in the contract. This judgment involves assessing factors outside of our influence, including market conditions, development timelines, likelihood of regulatory success, reimbursement rates for personnel costs, forecasted revenues, potential limitations on the selling price of the product, discount rates, lack of relevant past experience and a large number and broad range of possible amounts. The most likely amount method is used to estimate contingent development, regulatory and sales-based milestones because the ultimate outcomes are binary in nature. The expected value method is used to estimate royalties because a broad range of potential outcomes exists, except in instances where the royalties relate to a license. For arrangements with multiple separable performance obligations, the transaction price assigned to each distinct performance obligation is reflective on the relative stand-along selling price and recognized at a point in time upon the transfer of control.

Collaboration agreements typically include: (i) licensing intellectual property to a third party with no further performance obligations and (ii) arrangements that include both a license and an additional performance obligation to supply product upon the request of the third party. Out-licensing arrangements that contain a single performance obligation are satisfied upon execution of the agreement, when development and commercialization rights are transferred to a third party. Upfront fees are immediately recognized as licensing revenue. Contingent development and regulatory milestones are assessed each period for likelihood of achievement, however, they are typically constrained and recognized when uncertainty is subsequently resolved for the full amount of the milestone and included in licensing revenue. Licensing revenue also includes sales-based milestones and royalties, which are recognized when the milestone is achieved or when the subsequent sales occur.

Certain collaboration agreements also include contingent performance obligations to supply commercial product to the third party upon its request. The license and supply obligations are accounted for as separate distinct performance obligations as the third party can benefit from the license either on its own or together with the other supply resources readily available to it and the other obligations in the contract. Consideration for the supply obligation is based upon stipulated cost-plus margin contractual terms which represent a standalone selling price. The supply consideration is recognized as product supply revenue at a point in time upon transfer of control of the product to the third party. After considering the stand-alone selling price of these supply arrangements, the upfront fees, contingent development, regulatory and sales-based milestones and royalties are allocated to the license.

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. Contract modifications due to the addition of distinct promised goods or services with price increases consistent with stand-alone selling prices are accounted for as a separate contract. Contract modifications that are not considered a separate contract and containing remaining goods or services distinct from the goods or services transferred on or before the date of the contract modification are accounted for as a termination of the existing contract and the subsequent creation of a new contract. Contract modifications not considered a

separate contract and containing remaining goods or services not distinct are accounted for as an add-on to the existing contract and as an adjustment to revenue on a cumulative catch-up basis.

Accrued Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses, which 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 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.

Service fee accruals are estimated based on the period over which each component of service will be performed, with vendor input if appropriate. 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 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.

Retirement Savings Plan

We offer retirement saving plans through our 401(k) plan, which is available to all full-time employees. In June 2023, we expanded the benefit with the inclusion of a company matching contribution.We contribute to tax-qualified retirement plans for the benefit of employees who meet certain eligibility requirements and choose to participate in the plans. Participating employees specify the percentage of salary they wish to contribute from their compensation, and we make matching contributions. We recognized compensation costs from our contributions of $ 1.1 million and $ 0.2 million in 2024 and 2023, respectively.

Stock-Based Compensation

Stock-based compensation expense is recognized for all stock-based payment awards made to employees, non-employees and directors based on estimated fair values. The grant date fair value of the awards is determined using the Black-Scholes option-pricing model. Stock-based compensation expense is recognized on a straight-line basis over the requisite service period and is reduced for estimated forfeitures at the date of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Non-cash Interest Expense on Deferred Royalty Obligation

Non-cash interest expense related to the sale of future royalties represents imputed interest expense on our deferred royalty obligation related to the sale of future royalties using the effective interest method.

Leases

Operating leases are included in right-of-use assets, current portion of operating lease liability, and operating lease liability, net of current portion on 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 information available at the lease commencement date. 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 a lease when it is reasonably certain that we will exercise any such option. 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 account for these as a single lease component.

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 because the effects of potentially dilutive securities are antidilutive due to net loses recognized for each period presented.

Recent Accounting Pronouncements

New Accounting Pronouncements - Recently Adopted

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting* (Topic 280) - *Improvements to Reportable Segment Disclosures*. This Update requires publicly traded entities to provide enhanced disclosures about significant segment expenses regularly reviewed by the chief operating decision maker, including publicly traded entities with a single reportable segment. The amendments in this update were effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024. We adopted the ASU in the fourth quarter of 2024 and determined that its adoption did not have a material impact on our financial statements. Refer to *Note 17. Segment Reporting* for additional information.

Recent Accounting Pronouncements Not Yet Adopted

In December 2023, the FASB issued ASU No. 2023-09, Income Taxes (Topic 740) - *Improvements to Income Tax Disclosures*, an amendment which modifies the measurement and recognition of credit losses for most financial assets and certain other instruments. The amendments in this Update provide more transparency about income tax information through improvements to income tax disclosures primarily related to the rate reconciliation and income taxes paid information. For public business entities, the amendments in this Update are effective for annual periods beginning after December 15, 2024. Early adoption is permitted on a prospective basis for annual financial statements that have not yet been issued or made available for issuance. Management is currently assessing the impact of this standard on our financial statements.

In November 2024, the FASB issued ASU No. 2024-03, Income Statement (Topic 220) - *Reporting Comprehensive Income - Expense Disaggregation Disclosures, Disaggregation of Income Statement Expenses*, which requires public companies to disclose, in interim and reporting periods, additional information about certain expenses in the financial statements. ASU No. 2024-03 is effective for annual periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption is permitted and is effective on either a prospective basis or retrospective basis. Management is currently assessing the impact of this standard on our financial statements.

NOTE 3. CASH, CASH EQUIVALENTS AND SHORT-TERM INVESTMENTS

Securities classified as cash, cash equivalents and short-term investments as of December 31, 2024 and 2023 were as follows:

	December 31, 2024			
		Gross Unrealized		
(in thousands)	Amortized Cost	Gains	Losses	Fair Value
Cash and cash equivalents				
Cash	$ 16,282	$ —	$ —	$ 16,282
Money market funds	48,650	—	—	48,650
Total cash and cash equivalents	64,932	—	—	64,932
Short-term investments				
U.S. treasury securities	$ 79,720	$ 58	$ (5)	$ 79,773
U.S. government-sponsored agency bonds	45,960	29	(27)	45,962
Commercial paper	37,061	19	(15)	37,065
Corporate bonds	17,415	4	(6)	17,413
Asset-backed securities	2,983	2	—	2,985
Yankee bonds	1,972	—	(2)	1,970
Total short-term investments	185,111	112	(55)	185,168
Total cash, cash equivalents and investments	$ 250,043	$ 112	$ (55)	$ 250,100

	December 31, 2023			
		Gross Unrealized		
(in thousands)	Amortized Cost	Gains	Losses	Fair Value
Cash and cash equivalents				
Cash	$ 2,829	$ —	$ —	$ 2,829
Money market funds	18,641	—	—	18,641
Total cash and cash equivalents	21,470	—	—	21,470
Short-term investments				
U.S. government-sponsored agency bonds	$ 101,892	$ 235	$ (34)	$ 102,093
Commercial paper	49,630	41	(17)	49,654
Asset-backed securities	8,628	2	(5)	8,625
U.S. treasury securities	2,455	2	—	2,457
Total short-term investments	162,605	280	(56)	162,829
Total cash, cash equivalents and investments	$ 184,075	$ 280	$ (56)	$ 184,299

Realized gains or losses have not been significant and are included in other income, net, in our statements of operations and comprehensive loss.

Unrealized losses in 2024 and 2023 were not material. We determined that none of our available-for-sale securities were other-than-temporarily impaired as of December 31, 2024 and 2023, and no investment was in a continuous unrealized loss position for more than one year. Therefore, we believe that it is more likely than not that the investments will be held until maturity or a forecasted recovery of fair value.

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 as of December 31, 2024 and 2023.

NOTE 4. FAIR VALUE MEASUREMENTS

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 by 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:

	December 31, 2024				December 31, 2023			
(in thousands)	Total Fair Value	Level 1	Level 2	Level 3	Total Fair Value	Level 1	Level 2	Level 3
Assets								
Money market funds	$ 48,650	$ 48,650	$ —	$ —	$ 18,641	$ 18,641	$ —	$ —
U.S. government-sponsored agency bonds	45,962	—	45,962	—	102,093	—	102,093	—
U.S. treasury securities	79,773	—	79,773	—	2,457	—	2,457	—
Commercial paper	37,065	—	37,065	—	49,654	—	49,654	—
Corporate bonds	17,413	—	17,413	—	—	—	—	—
Asset-backed securities	2,985	—	2,985	—	8,625	—	8,625	—
Yankee bonds	1,970	—	1,970	—	—	—	—	—
Total	$ 233,818	$ 48,650	$ 185,168	$ —	$ 181,470	$ 18,641	$ 162,829	$ —
Liabilities								
Derivative liabilities for exit fee	$ —	$ —	$ —	$ —	$ 675	$ —	$ —	$ 675
Total	$ —	$ —	$ —	$ —	$ 675	$ —	$ —	$ 675

The 2022 Exit Fee valuation as of December 31, 2023 as defined and discussed in *Note 10. Derivative Liabilities*, was classified as Level 3. During 2024, the conditions for payment of the 2022 Exit Fee were met and the $ 1.0 million contract amount was fully valued and settled accordingly.

Fair Value of Debt

The principal outstanding under our term loan is subject to a variable interest rate and therefore, we believe the carrying amount of the term loan approximates fair value. See *Note 9. Borrowing* 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, 2024 and is based on our current estimate of future royalties and commercialization milestones expected to be paid to us by Kyowa Kirin 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.

NOTE 5. INVENTORY

Inventory consisted of the following:

	December 31,	
(in thousands)	2024	2023
Raw materials	$ 30,792	$ 22,920
Work in process	58,685	24,582
Finished goods	1,707	1,985
Total	$ 91,184	$ 49,487
Reported as		
Inventory	$ 21,173	$ 12,448
Inventory, non-current	70,011	37,039
Total	$ 91,184	$ 49,487

Prepaid commercial manufacturing with third-party CMOs not included in inventory was $ 16.4 million and $ 23.2 million at December 31, 2024 and 2023, respectively. There were no prepayments expected to be converted into inventory after 12 months at December 31, 2024, compared to $ 4.2 million at December 31, 2023.

NOTE 6. REVENUE

Disaggregation of total revenues by nature is as follows:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Product sales, net	$ 319,196	$ 82,526	$ 15,600
Product supply revenue	11,649	6,121	1,527
Licensing revenue	78	35,809	35,031
Non-cash royalty revenue related to the sale of future royalties	2,692	—	—
Total revenues	$ 333,615	$ 124,456	$ 52,158

Product Sales, Net

Total product sales, net was as follows:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Product sales, net			
IBSRELA	$ 158,286	$ 80,062	$ 15,600
XPHOZAH	160,910	2,464	—
Total product sales, net	$ 319,196	$ 82,526	$ 15,600

Product sales, net approximated 95.7 %, 66.3 % and 29.9 % of total revenues in 2024, 2023 and 2022, respectively. Products are primarily sold to wholesalers, GPOs and specialty pharmacies, and to a lesser extent, directly to retailers, hospitals, clinics and government agencies. Customer orders are generally fulfilled within a few days from receipt. Contractual performance obligations are fulfilled once control of product is transferred to our customer, which occurs when our customer receives the product and obtains legal title. At this point, our customers are able to direct the use of and obtain substantially all of the remaining benefits of the product.

GTN Adjustments

Wholesalers, GPOs and specialty pharmacies are initially invoiced at contract list prices. Wholesalers and GPOs may also receive prompt pay discounts for payment within a specified period, generally approximating two percent of the invoiced sales price. Our payment terms are generally 30 to 60 days. At the time of recognition, revenue is reduced from contract list price for estimates of variable consideration related to GTN adjustments for chargebacks and cash discounts, rebates, wholesaler and GPO fees, and copay assistance and returns. These GTN adjustments are attributed to governmental programs such as Medicare, Medicaid and the 340B program, which involve various pricing implications, including mandatory discounts and discounts when Medicare Part D beneficiaries are in the coverage gap. Chargebacks and specialty pharmacies fees are reflected as reductions to receivables and are typically settled within contractual terms through credits to our customers. All other GTN adjustments are reflected as a liability and settled through cash payments to our customer or government payor program, typically over various time periods that may span for multiple quarters. Significant judgment is required to estimate certain of our GTN adjustments, considering factors such as legal interpretations of applicable laws and regulations, historical experience, payor mix (e.g., Medicare or Medicaid), current contract prices under applicable programs, unbilled claims, processing time lags and inventory levels in the distribution channel.

The activities and ending reserve balances for each significant category of GTN adjustments on product sales, net, which constitute variable consideration, were as follows:

(in thousands)	Discounts and chargebacks	Rebates, wholesaler and GPO fees	Copay assistance and returns	Total
Balance as of December 31, 2022	$ 142	$ 1,444	$ 1,258	$ 2,844
Provisions	5,341	15,365	10,629	31,335
Credits/payments	(5,005)	(12,575)	(7,971)	(25,551)
Balance as of December 31, 2023	478	4,234	3,916	8,628
Provisions	15,099	65,833	28,925	109,857
Credits/payments	(13,934)	(55,592)	(21,671)	(91,197)
Balance as of December 31, 2024	$ 1,643	$ 14,475	$ 11,170	$ 27,288

Adjustments to prior period provisions recorded in the current period were not material.

Geographic Information and Concentrations

Revenues are attributed to geographical areas based on the location at which we earned revenue for product sales of IBSRELA and XPHOZAH or the domicile of our collaboration partners. A summary of our revenues by geographic area is as follows:

	Year Ended December 31,		
(in thousands)	2024	2023	2022
United States[1]	$ 319,196	$ 83,276	$ 15,600
International			
Asia Pacific[2]	14,341	41,121	36,527
North America[3]	78	59	31
Total revenues	$ 333,615	$ 124,456	$ 52,158

(1) Revenues from the United States are primarily comprised of amounts earned from sales of IBSRELA and XPHOZAH, as well as the upfront license fee from the METiS Agreement.

(2) Revenues from Asia Pacific are primarily comprised of amounts earned in accordance with the Kyowa Kirin Agreement and the Fosun Agreement.

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

Gross product sales from Customers and revenues from collaboration partners, each accounting for more than 10% of total revenues, were as follows:

	Year Ended December 31,		
	2024	2023	2022
Customers			
BioRidge Pharma, LLC	75.4 %	24.0 %	3.2 %
Cencora	16.4 %	19.1 %	11.1 %
Cardinal Health	14.5 %	19.8 %	9.6 %
McKesson Corporation	14.1 %	15.7 %	8.9 %
Collaboration partners			
Kyowa Kirin	4.3 %	29.0 %	70.0 %

NOTE 7. COLLABORATION AND LICENSING AGREEMENTS

We out-licensed to external partners the development of tenapanor and commercialization of tenapanor through agreements with Kyowa Kirin in Japan, Fosun Pharma in China and Knight in Canada for the development and commercialization of tenapanor for certain indications in their respective territories. We recognize revenue from such arrangements as licensing revenue, product supply revenue or non-cash royalty revenue related to the sale of future royalties. Our significant accounting policies for such revenue streams are as follows:

Licensing revenue includes:

- upfront license fees, as well as developmental, regulatory and commercialization milestone payments. We assess upfront and milestone payments using the most likely amount method, including variable payments only when it is probable that no significant revenue reversal will occur. Upfront license fees are recognized upon receipt. Milestones tied to external factors, such as regulatory approvals, are considered probable when those accomplishments are achieved.
- sales-based royalties, other than non-cash royalty revenue related to the sale of future royalties as discussed below, are recognized when sales occur or when related performance obligations are met.

Product supply revenue includes drug substance or drug supply revenue received from our out-licensing agreements. Product supply revenue is recognized when control of goods is transferred upon delivery. Advanced payments from partners for drug substance are recognized as deferred revenue until delivery.

Non-cash royalty revenue related to the sale of future royalties includes royalties earned and received under the Kyowa Kirin Agreement, which are remitted to HCR upon receipt, pursuant to the HCR Agreement as discussed in *Note 8. Deferred Royalty Obligation Related To The Sale Of Future Royalties*.

The following table summarizes total revenue by collaboration partner:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Licensing revenue			
Kyowa Kirin	$ —	$ 30,000	$ 35,000
Fosun Pharma	—	5,000	—
METiS	—	750	—
Knight	78	59	31
Total licensing revenue	$ 78	$ 35,809	$ 35,031
Product supply revenue			
Kyowa Kirin	11,649	6,092	1,518
Fosun Pharma	—	29	9
Total supply revenue	$ 11,649	$ 6,121	$ 1,527
Non-cash royalty revenue related to the sale of future royalties			
Kyowa Kirin	$ 2,692	$ —	$ —

Kyowa Kirin

We granted Kyowa Kirin an exclusive license (Kyowa Kirin Agreement) to develop and commercialize certain NHE3 inhibitors including tenapanor in Japan for the treatment of cardiorenal diseases and conditions, excluding cancer, in exchange for future royalties defined below, an upfront license fee of $ 30.0 million, and potential future development and regulatory milestones up to $ 55.0 million, of which $ 35.0 million has been received and recognized as revenue to date, as well as approximately ¥ 8.5 billion for commercialization milestones, or approximately $ 54.0 million at the currency exchange rate on December 31, 2024. In addition, we are eligible to receive royalties on net sales of tenapanor in Japan throughout the term of the agreement. Under a Commercial Supply Agreement, we supply tenapanor drug substance that will be used to satisfy Kyowa Kirin's commercial needs which includes advanced payments for reimbursement of costs plus a reasonable overhead for the supply of product. In February 2024, Kyowa Kirin announced the launch of tenapanor, marketed as PHOZEVEL®, for patients with CKD with hyperphosphatemia in Japan.

The Kyowa Kirin Agreement was amended to reduce the royalty rate Kyowa Kirin would pay on tenapanor sales in Japan from 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 (2022 Amendment). As consideration for reduction in the royalty rate, Kyowa Kirin agreed to pay us up to an additional $ 40.0 million payable in two tranches, with the first payment due following Kyowa Kirin's filing with the Japanese MHLW of its application for marketing approval for tenapanor and the second payment due following Kyowa Kirin's receipt of regulatory approval to market tenapanor for hyperphosphatemia in Japan, both of which occurred as of September 30, 2023. As discussed in *Note 8. Deferred Royalty Obligation Related To The Sale Of Future Royalties* , future royalties and commercial milestone payments we may receive under the license, as amended, will be remitted to HCR pursuant to the HCR Agreement.

The following table presents changes in our current and non-current deferred revenue balances, which are all attributable to Kyowa Kirin:

	2024		2023	
(in thousands)	Current	Non-Current	Current	Non-Current
Balance at January 1,	$ 7,182	$ 8,644	$ 4,211	$ 9,025
Prepaid product supply	3,716	8,212	1,547	5,629
Product supply delivered	(9,836)	—	(4,586)	—
Reclassify amounts to be recognized in the next twelve months	9,624	(9,624)	6,010	(6,010)
Balance at December 31,	$ 10,686	$ 7,232	$ 7,182	$ 8,644

Fosun Pharma

We have 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. The Fosun Agreement granted exclusive license rights to Fosun Pharma in exchange for an upfront license fee of $ 12.0 million, recognized upon execution of the agreement, and potential regulatory milestone payments up to $ 113.0 million, of which $ 8.0 million has been received and recognized to date. In addition, we are eligible to receive 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 %.

Knight

We have an exclusive license agreement with Knight (Knight Agreement) for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. The Knight Agreement granted exclusive license rights to Knight in exchange for an upfront license fee of $ 2.3 million, recognized upon execution, and potential regulatory and commercialization milestones up to CAD 22.2 million, or approximately $ 15.4 million at the currency exchange rate on December 31, 2024, of which $ 0.7 million has been received and recognized to date. In addition, we are 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 supply services.

METiS

We have an exclusive license agreement with METiS Therapeutics Inc., (METiS Agreement) for the development and commercialization of a portfolio of TGR5 agonist compounds that we discovered and developed for all therapeutic areas in exchange for an upfront license fee of $ 0.8 million, recognized upon execution in 2023. In addition, we may be eligible to receive development and commercialization milestone payments worth up to $ 243.0 million. We are also eligible to receive royalties ranging within the mid-single digits throughout the term of the agreement.

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 other NHE3 products, up to a maximum of $ 75.0 million in aggregate for (i) and (ii). Royalty expense recognized under this agreement as other cost of revenue on our statements of operations and comprehensive loss was $ 34.7 million, $ 12.4 million and $ 3.6 million in 2024, 2023 and 2022, respectively. As of December 31, 2024, we have recognized $ 62.3 million of the total $ 75.0 million outstanding royalty obligation.

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

In June 2022, we and HCR entered into the HCR Agreement in which HCR agreed to pay up to $ 20.0 million in exchange for royalty payments and commercial milestone payments that we may receive under our Kyowa Kirin License Agreement. See *Note 7. Collaboration And Licensing Agreements* for further detail. The $ 20.0 million is payable as follows:

- $ 10.0 million upfront upon agreement execution, received in June 2022;
- $ 5.0 million upon Kyowa Kirin's receipt of regulatory approval to market tenapanor for hyperphosphatemia in Japan, received in October 2023; and

- $ 5.0 million in the event net sales by Kyowa Kirin 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.

Payments received from HCR are recorded as a deferred royalty obligation on our balance sheets. Due to our ongoing manufacturing obligations under the Kyowa Kirin Agreement, we account for the proceeds as imputed debt and therefore recognize royalties earned under the Kyowa Kirin Agreement as non-cash royalty revenue. In conjunction with the HCR Agreement, we incurred approximately $ 0.4 million in transaction costs, which, along with the deferred royalty obligation, are being amortized as non-cash interest expense over the estimated life of the HCR Agreement using the effective interest method, which is based on the imputed interest rate derived from estimated amounts and timing of future royalty payments to be received from Kyowa Kirin. The deferred royalty obligation will be effectively repaid over the life of the HCR Agreement as we remit royalties paid to us from Kyowa Kirin, recorded as non-cash royalty revenue related to the sale of future royalties, to HCR. We periodically assess the estimated royalty payments from Kyowa Kirin 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.

A summary of financial information related to the HCR Agreement is as follows:

	Year Ended December 31,		
($ in thousands)	**2024**	**2023**	**2022**
Non-cash interest expense related to the sale of future royalties	$ (7,088)	$ (3,924)	$ (1,673)
Effective interest rate	31.0 %	34.7 %	34.4 %

(in thousands)	**2024**	**2023**	**2022**
Beginning deferred royalty obligation	$ 20,179	$ 11,254	$ —
Upfront payment, net of transaction costs	—	—	9,581
Regulatory approval milestone	—	5,000	—
Non-cash interest expense related to sale of future royalties	7,088	3,924	1,673
Royalty distributed to HCR	(1,740)	—	—
Other	—	1	—
Ending deferred royalty obligation	$ 25,527	$ 20,179	$ 11,254

NOTE 9. BORROWING

Long-term borrowing was as follows:

	December 31,		
(in thousands)	**2024**	**2023**	**Interest rate**
Principal			
Term A Loan	$ 27,500	$ 27,500	7.95 % + 0.022 % + SOFR (subject to a floor of 1.0 %)
Term B Loan	22,500	22,500	7.95 % + 0.022 % + SOFR (subject to a floor of 1.0 %)
Term C Loan	50,000	—	4.25 % + 0.022 % + SOFR (subject to a floor of 4.7 %)
Term D Loan	50,000	—	4.00 % + 0.022 % + SOFR (subject to a floor of 4.7 %)
Total principal	$ 150,000	$ 50,000	
Adjustments to principal value			
Unamortized discount and debt issuance costs	(1,136)	(912)	
Accreted value of final fee	1,989	734	
Total long-term debt	150,853	49,822	
Less: Current portion of long-term debt	—	—	
Long-term debt, net of current portion	$ 150,853	$ 49,822	

On February 23, 2022 (Closing Date), we entered into a loan and security agreement with SLR (2022 Loan Agreement) as collateral agent (Agent) and the lenders listed in the 2022 Loan Agreement (collectively, the 2022 Lenders), which was subsequently amended in August 2022 (the First Amendment) and February 2023 (the Second Amendment). The 2022 Loan Agreement, as amended, provided for a senior secured loan facility (the Term A Loan) funded on the Closing Date and Term B Loan borrowable on or prior to December 20, 2023; provided that (i) we received approval by the U.S. FDA for our NDA for

XPHOZAH by November 30, 2023, and (ii) we achieved certain product revenue milestone targets described in the 2022 Loan Agreement. We met the requirements to borrow Term B Loan and subsequently drew it in October 2023.

In October 2023, we entered into a Third Amendment (the Third Amendment) with the 2022 Lenders. The Third Amendment provided us with the option to draw the Term C Loan by March 15, 2024, contingent upon having drawn the Term B Loan; and provided us with the option to draw the Term D Loan of uncommitted capital by December 31, 2026, subject to approval by the Agent's investment committee. We provided the Agent with notice of our decision to draw the Term C Loan in February 2024 and received the proceeds in March 2024.

In October 2024, we entered into a Fourth Amendment (the Fourth Amendment) with the 2022 Lenders. The Fourth Amendment, among other things, provided for the immediate draw of the Term D Loan on the closing date of the Fourth Amendment and provides us with the option to draw an additional $ 50.0 million of committed capital by June 30, 2025 (the Term E Loan and together with the Term A, B, C and D Loans, the Five Loans). The interest rate for the Term E Loan will be 4.00 % plus a SOFR value equal to 0.022 % plus the 1-month CME Term SOFR reference rate as published by the CME Term SOFR Administrator on the CME Term SOFR Administrator's Website, subject to a SOFR floor of 4.7 %. We drew the Term D Loan in October 2024.

Under the Fourth Amendment, the maturity date for the Five Loans was extended to July 1, 2028 (the Maturity Date) and the period under which we are permitted to make interest-only payments on the Five Loans was extended to the Maturity Date.

We paid fees of $ 0.2 million, $ 0.1 million, $ 0.3 million and $ 0.3 million on each funding date of the Term A, Term B, Term C and Term D Loans, respectively. In addition, we will be obligated to pay 0.5 % of the aggregate original principal amount of the Term E Loan commitment, which shall be due on the earliest of (1) the funding of the Term E Loan, (2) June 30, 2025, or (3) the prepayment, refinancing, substitution or replacement of any of the Five Loans on or prior to the date immediately preceding June 30, 2025.

We are obligated to pay a final fee equal to 4.95 % of the aggregate original principal amount of the Five Loans, to the extent such loans are funded, upon the earliest to occur of the maturity date, the acceleration of the Five Loans, and the prepayment, refinancing, substitution, or replacement of the Five Loans. The total unaccreted final fee was $ 5.4 million and $ 1.7 million at December 31, 2024 and December 31, 2023, respectively.

We may voluntarily prepay all amounts outstanding under the Five Loans, subject to a prepayment premium of 2 % of the outstanding principal amount of the Five Loans if prepaid through and including October 17, 2025 or 1 % of the outstanding principal amount of the Five Loans if prepaid after October 17, 2025 and prior to the maturity date. The Five Loans are secured by substantially all of our assets, except for our intellectual property and certain other customary exclusions. Additionally, as discussed in *Note 10. Derivative Liabilities*, in connection with the Term A and Term B Loans (Original Loans), we paid an exit fee in the amount of $ 1.0 million in October 2024.

The 2022 Loan Agreement, as amended, contains customary representations and warranties that place restrictions on disposition of assets, granting liens, occurring additional debt and other matters, as well as customary events of default. We have agreed to not allow our cash, cash equivalents and available-for-sale investments to be less than the eighty percent (80 %) of the outstanding balance of the Five Loans 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 balance of the Five Loans. We have concluded that the provisions that could cause acceleration of the principal repayment are remote as of December 31, 2024.

As of December 31, 2024, our total future payment obligation related to the outstanding balance of the Five Loans, excluding interest payments, was $ 157.4 million, which is due on July 1, 2028.

NOTE 10. DERIVATIVE LIABILITIES

2018 Exit Fee

In October 2023, we received approval from the U.S. FDA for XPHOZAH to reduce serum phosphorus in adults with CKD on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy. In connection with a previous loan agreement (2018 Loan), we became obligated to pay an exit fee of $ 1.5 million, which was paid in 2023.

2022 Exit Fee

The 2022 Loan Agreement obligated us to pay an exit fee in the amount of 2 % of the Original Loans 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. The 2022 Exit Fee was accounted for as a freestanding derivative and recorded at fair value. The estimated fair value of the 2022 Exit Fee of $ 0.7 million was recorded as a derivative liability and included in accrued expenses and other current liabilities at December 31, 2023. The Revenue Milestone was achieved in the second quarter of 2024, resulting in a $ 1.0 million payment in October 2024 to settle the obligation. The Term C and Term D Loans do not contain an exit fee obligation.

The fair value of the derivative liability was determined using a discounted cash flow analysis and was classified as a Level 3 measurement within the fair value hierarchy since our valuation utilized significant unobservable inputs prior to June 30, 2024. Specifically, the key assumptions included in the calculation of the estimated fair value of the 2022 Exit Fee derivative liability included: (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 was dependent upon (a) approval by the U.S. FDA for our NDA for the control of serum phosphorus in adult patients with CKD on dialysis by November 30, 2023, and (b) achievement of certain product revenue milestone targets. As of December 31, 2023, uncertainty around all of the noted valuation estimates had been removed, as the Term B Loan had been funded, the U.S. FDA had approved our NDA for the control of serum phosphorus in adult patients with CKD on dialysis prior to November 30, 2023, and we had achieved the Revenue Milestone.

Changes in the fair value of recurring measurements are presented as other income, net in our statements of operations and comprehensive loss and were as follows:

(in thousands)	**2024**	**2023**
January 1,	$ 675	$ 1,656
Changes in estimated fair value		
2018 Exit Fee	—	292
2022 Exit Fee	325	227
2018 Exit Fee payment	—	(1,500)
2022 Exit Fee payment	(1,000)	—
Fair value of exit fee derivative liabilities at December 31,	$ —	$ 675

NOTE 11. LEASES

Our lease obligation is comprised of operating leases for our offices and research facilities with remaining lease terms ranging from two months to four years and each containing customary rent escalation clauses. Our leases contain one renewal, at our option, which is generally for a five-year period. We have not included these renewal periods in the calculation of the right-of-use asset and lease liability since it is uncertain whether we will exercise the renewal option.

Our leased offices and research facilities in Fremont, California expired on February 10, 2025 and our sub-lease agreement for office space at that facility, entered into with Chronus Health in 2023 expired on February 1, 2025.

The following table provides additional details of our facility leases presented in our balance sheets:

($ in thousands)	December 31,	
Facilities	**2024**	**2023**
Right-of-use assets	$ 2,380	$ 5,589
Current portion of lease liabilities	1,562	4,435
Operating lease liability, net of current portion	1,023	1,725
Total lease liabilities	$ 2,585	$ 6,160
Weighted-average remaining term (in years)	1.8	1.6
Weighted-average discount rate	6.5 %	6.8 %

The lease costs, which are included in operating expenses in our statements of operations and comprehensive loss, were as follows:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Operating lease expense	$ 4,699	$ 3,857	$ 4,257
Cash paid for operating leases	$ 4,931	$ 4,481	$ 4,292

The following table summarizes our undiscounted cash payment obligations for our operating lease liabilities as of December 31, 2024:

(in thousands)	**Operating Leases**
2025	$ 1,660
2026	702
2027	238
2028	124
Thereafter	21
Total undiscounted operating lease payments	2,745
Imputed interest expenses	(160)
Total operating lease liabilities	2,585
Less: Current portion of operating lease liability	(1,562)
Operating lease liability, net of current portion	$ 1,023

NOTE 12. STOCKHOLDERS' EQUITY

Under a registration statement filed in 2020, we had the ability to sell up to $ 150.0 million of our common stock through Jefferies, as our sales agent. As of March 2023, we had received the maximum gross proceeds of $ 150.0 million at a weighted average share price of approximately $ 1.57 .

In January 2023, we filed a registration statement on Form S-3, which became effective in January 2023, 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. As of December 31, 2024, we have completed sales pursuant to the 2023 Open Market Sales Agreement resulting in the issuance of 16.8 million shares of our common stock and receipt of gross proceeds of $ 70.0 million at a weighted average sales price of approximately $ 4.17 .

NOTE 13. EQUITY INCENTIVE PLANS

2008 Plan

The 2008 Stock Incentive Plan (2008 Plan), which governed the granting of stock options, stock purchase rights and other equity awards, was terminated in June 2014 for future awards. When the 2014 Equity Incentive Award Plan (2014 Plan) was approved by the board of directors and stockholders on June 18, 2014, all remaining shares available for future award under the 2008 Plan were transferred to the 2014 Plan, as discussed below.

2014 Plan

The 2014 Equity Incentive Plan (2014 Plan), effective on June 18, 2014, provided for the stock-based compensation awards, including stock options, stock appreciation rights, restricted stock, service-based RSUs, performance-based RSUs, deferred stock, deferred stock units, dividend equivalents, stock payments and performance awards. The 2014 Plan initially reserved 1.5 million shares, including the 35 thousand shares remaining for future awards under the 2008 Plan, with up to 1.2 million additional shares which could be added from forfeited or lapsed awards from the 2008 Plan. The 2014 Plan allowed for an annual increase in the number of shares available for issuance on the first day of each year through 2024, equal to the lesser of four percent (4.0 %) of our outstanding common stock on the last day of the immediately preceding year or a smaller amount determined by the board of directors (2014 Plan evergreen provision).

On June 14, 2024, stockholders approved the Amended and Restated 2014 Equity Incentive Award Plan (2014 A&R Plan). The key provisions pursuant to the 2014 A&R Plan include: (1) 19.0 million shares were added to the total existing share reserve; (2) the 2014 Plan evergreen provision was removed such that any increase to the total number of shares that may be issued must be approved by our stockholders; and (3) the limit of shares that may be issued upon exercise of incentive stock options was increased from 10.7 million to 58.5 million shares. In addition to increases resulting from repurchases, forfeitures, expirations and cancellations of awards under the 2008 Plan, shares reserved for issuance under the 2014 A&R Plan will be increased by the number of shares subject to awards granted under the Inducement Plan, as discussed below, that are repurchased, forfeited, expire or are cancelled on or after June 14, 2024. As a result, no new awards will be made under the Inducement Plan after June 14, 2024. As of December 31, 2024, approximately 18.1 million shares of our common stock were available for future issuance under the 2014 A&R Plan.

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, December 2022 and January 2024, 0.5 million, 2.0 million, 3.0 million and 5.8 million shares, respectively, were added to the Inducement Plan. As of December 31, 2024, 8.8 million shares of our common stock were subject to inducement grants that were issued pursuant to the Inducement Plan. As of December 31, 2024, approximately 3.9 million shares of our common stock were available for future issuance under the 2016 Plan.

Stock Options

A summary of our stock option activity and related information during the year ended December 31, 2024 is as follows:

	Options Issued and Outstanding		Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
	Number of Shares (in thousands)	Weighted-Average Exercise Price per Share		
Balance at December 31, 2023	22,168	$ 4.20		
Options granted	9,674	$ 7.95		
Options exercised	(2,654)	$ 2.24		
Options canceled	(1,103)	$ 5.35		
Balance at December 31, 2024	28,085	$ 5.63	7.1	$ 31,830
Vested and expected to vest at December 31, 2024	28,085	$ 5.63	7.1	$ 31,830
Exercisable at December 31, 2024	14,968	$ 5.52	5.7	$ 19,161

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, 2024, based on our common stock closing price of $ 5.07 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, 2024, 2023 and 2022 was $ 19.6 million, $ 1.1 million and $ 30 thousand, respectively. The total fair value of options vested during the years ended December 31, 2024, 2023 and 2022 was $ 61.0 million, $ 24.9 million and $ 7.0 million, respectively.

The weighted-average grant-date estimated fair value of options granted during the years ended December 31, 2024, 2023 and 2022 was $ 6.22 , $ 2.36 and $ 0.63 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,		
	2024	2023	2022
Expected term (in years)	5.4	5.1	4.9
Expected volatility	100.8 %	97.6 %	92.1 %
Risk-free interest rate	4.0 %	3.8 %	2.2 %
Dividend yield	— %	— %	— %

Expected Term—We estimate the expected term of our options based upon historical exercises and post-vesting termination behavior.

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 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 do 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 year ended December 31, 2024 is as follows:

	Number of RSUs (in thousands)	Weighted-Average Grant Date Fair Value Per Share
Non-vested restricted stock units at December 31, 2023	3,646	$ 3.09
Granted	7,382	$ 7.94
Vested	(2,430)	$ 5.65
Forfeited	(585)	$ 5.68
Non-vested restricted stock units at December 31, 2024	8,013	$ 6.59

The total estimated fair value of RSUs vested during the years ended December 31, 2024, 2023 and 2022 was $ 16.4 million, $ 3.5 million and $ 2.6 million, respectively.

Issuance of Common Stock for Services

During the years ended December 31, 2024, 2023 and 2022, we issued approximately 41 thousand, 0.1 million and 0.7 million 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, 2024, 2023 and 2022 were valued at $ 0.3 million, $ 0.3 million and $ 0.4 million, respectively, based on the fair value of the common stock on the date of grant.

Employee Stock Purchase Plan

The 2014 ESPP, effective on June 18, 2014, initially reserved approximately 0.2 million shares of common stock for our eligible employees to purchase shares of our common stock at a discount. If approved by the administrator of the ESPP, on the first day of each calendar year through 2024, the number of shares in the reserve increased 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 (2014 ESPP evergreen provision); provided, however, no more than 2.2 million shares of our common stock could be issued under the ESPP.

On June 14, 2024, stockholders approved the Amended and Restated 2014 ESPP (A&R ESPP). The key provisions pursuant to the A&R ESPP include: (1) 3.0 million shares were added to the total existing share reserve and (2) the 2014 ESPP evergreen provision was eliminated and no evergreen increases will be made after June 14, 2024.

During the years ended December 31, 2024, 2023 and 2022, we issued approximately 0.5 million, 0.4 million and 0.3 million shares, respectively, at an average share price of $ 4.64 , $ 1.85 and $ 0.63 , respectively, pursuant to the ESPP. As of December 31, 2024, approximately 3.7 million shares of our common stock were available for future issuance under the A&R ESPP.

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,		
	2024	2023	2022
Expected term (in years)	0.5	0.5	0.5
Expected volatility	82.8 %	86.0 %	97.2 %
Risk-free interest rate	5.0 %	5.3 %	1.9 %
Dividend yield	— %	— %	— %

Stock-based Compensation Expense

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

	Year Ended December 31,		
(in thousands)	2024	2023	2022
Selling, general and administrative	$ 27,791	$ 9,952	$ 7,525
Research and development	9,590	3,578	3,225
Total	$ 37,381	$ 13,530	$ 10,750

A summary of our total unrecognized stock-based compensation expense, net of estimated forfeitures, as of December 31, 2024 is as follows:

	December 31, 2024	
	Unrecognized Compensation Expense (in thousands)	Average Remaining Vesting Period (in years)
Stock option grants	$ 55,610	2.71
RSU grants	$ 49,930	2.96
ESPP	$ 162	0.1

NOTE 14. PROPERTY AND EQUIPMENT, NET

Property and equipment consisted of the following:

	December 31,	
(in thousands)	2024	2023
Laboratory equipment	$ 46	$ 46
Office equipment and furniture	2,923	2,433
Leasehold improvements	9,144	8,731
Property and equipment, gross	12,113	11,210
Less: Accumulated depreciation	(10,618)	(10,201)
Total property and equipment, net	$ 1,495	$ 1,009

We recognized depreciation expense in the amount of $ 0.5 million, $ 0.6 million and $ 0.7 million in 2024, 2023 and 2022, respectively.

NOTE 15. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consisted of the following:

	December 31,	
(in thousands)	**2024**	**2023**
Accrued payments due to AstraZeneca	$ 12,077	$ 3,680
Accrued gross to net revenue liabilities	10,112	3,258
Accrued sales and marketing expenses	3,696	3,223
Other	8,757	4,880
Total accrued expenses and other current liabilities	$ 34,642	$ 15,041

NOTE 16. INCOME TAXES

The components of our provision for income taxes were as follows:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Current			
State	$ 266	$ 47	$ 8
Foreign	—	500	—
Total current	266	547	8
Deferred			
Federal	—	—	—
Total deferred	—	—	—
Provision for income taxes	$ 266	$ 547	$ 8

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

	Year Ended December 31,		
	2024	**2023**	**2022**
Income tax at the federal statutory rate	21.0 %	21.0 %	21.0 %
State taxes, net of federal benefit	4.0	3.4	1.9
Tax credits	0.6	1.7	1.5
Stock based compensation	5.2	0.1	(2.3)
Foreign withholding tax	—	(0.8)	—
Executive compensation disallowed under IRC Sec 162(m)	(5.8)	(1.9)	(1.6)
Other	(0.6)	—	(0.8)
Change in valuation allowance	(25.0)	(24.3)	(19.7)
Effective tax rate	(0.6)%	(0.8)%	— %

Deferred income tax balances reflect the effects of temporary differences between the carrying amounts of assets and liabilities and their income tax bases, as well as from net operating loss and tax credit carryforwards. Significant components of our deferred tax assets were as follows:

	December 31,	
(in thousands)	**2024**	**2023**
Deferred tax assets		
Amortization and depreciation	$ 64,237	$ 64,919
Net operating loss carryforwards	103,643	98,702
Tax credits	15,529	15,375
Stock-based compensation	11,226	6,946
Deferred royalty obligation	6,409	4,907
Other	8,122	6,707
Deferred tax assets	209,166	197,556
Valuation allowance	(208,568)	(196,197)
Deferred tax assets net of valuation allowance	598	1,359
Deferred tax liabilities		
Right-of-use asset	(598)	(1,359)
Deferred tax liabilities	(598)	(1,359)
Net deferred taxes	$ —	$ —

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, 2024. 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, 2024, 2023 and 2022, a full valuation allowance has been recorded against our deferred tax assets. The valuation allowance increased by $ 12.4 million in 2024 primarily attributable to net operating loss carryforwards and stock-based compensation. The amount of the deferred tax assets considered realizable could be adjusted if estimates of future taxable income during the carryforward period are reduced or increased, or if objective negative evidence, such as cumulative losses, are no longer present. In such cases, additional weight may be given to subjective evidence, such as our projections for growth.

As of December 31, 2024, we had net operating loss carryforwards for federal income tax purposes of approximately $ 495.0 million, of which approximately $ 344.8 million can be carried forward indefinitely and the remaining net operating losses begin to expire in 2030, if not utilized. We had approximately $ 17.8 million of federal research and development tax credit carryforwards and approximately $ 1.7 million of foreign tax credit carryforwards that begin to expire in 2027, if not utilized.

In addition, we had net operating loss carryforwards for California income tax purposes of approximately $ 94.7 million that begin to expire in 2030, if not utilized, and state research and development tax credit carryforwards of approximately $ 9.2 million that do not expire. We had approximately $ 0.1 million of minimum tax credit carryovers for California income tax purposes that do not expire. We had other state net operating losses of approximately $ 64.0 million that begin to expire in 2031.

The future utilization of net operating loss and tax credit carryforwards 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.

Effective January 1, 2022, research and development expenses are required to be capitalized and amortized for U.S. tax purposes. 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:

	December 31,		
(in thousands)	**2024**	**2023**	**2022**
Balance at beginning of year	$ 23,625	$ 24,075	$ 24,426
Additions based on tax positions related to current year	105	262	460
Additions based on tax positions related to prior year	—	99	—
Subtractions based on tax positions related to prior year	(811)	(811)	(811)
Balance at end of year	$ 22,919	$ 23,625	$ 24,075

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, 2024, 2023 and 2022, 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.

NOTE 17. SEGMENT REPORTING

We operate in a single reportable segment with a mission to discover, develop and commercialize innovative, first-in-class medicines that meet significant unmet medical needs. A centralized research and development organization, supply chain organization and commercial organization are all responsible for the discovery, development, manufacturing, supply and sale of our products. Our business is also supported by centralized corporate functions. We currently operate primarily in the U.S. and earn revenues from sales of IBSRELA and XPHOZAH, both branded products derived from tenapanor, a molecule developed from our unique and innovative platform. Licensing agreements with international partners are utilized for development and commercialization activities outside the U.S. Currently, we maintain such agreements for certain indications of tenapanor in Japan (Kyowa Kirin), China (Fosun Pharma) and Canada (Knight). Refer to *Note 7. Collaboration And Licensing Agreements* for further detail. We recognize other revenue in the form of product supply revenue and licensing revenue under the Kyowa Kirin and Knight agreements. Revenue streams associated with the Kyowa Kirin Agreement are subject to a separate agreement where such future royalties and commercial milestones were sold to a third-party. Refer to *Note 8. Deferred Royalty Obligation Related To The Sale Of Future Royalties* for further information.

Our Chief Executive Officer (CEO) is our Chief Operating Decision Maker (CODM), responsible for allocating resources and assessing Company performance using aggregated financial information. Utilizing aggregated financial information enables the CODM to determine the most appropriate resource allocation across the commercial organization, research and development projects or other initiatives consistent with our long-term corporate wide strategic goals. The CODM primarily uses aggregated net loss as reported on the statements of operations and comprehensive loss to measure segment loss, supplemented by certain additional significant expense details reflected in the table below.

Detailed information regarding our single operating segment's significant revenues, expenses and operating loss are as follows:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Revenues			
Product sales, net	$ 319,196	$ 82,526	$ 15,600
Other revenues[1]	14,419	41,930	36,558
Total revenues	333,615	124,456	52,158
Less:			
Cost of product sales	6,851	2,323	566
Other cost of revenue	43,705	15,472	3,551
Total cost of goods sold	50,556	17,795	4,117
Research and development[2]	39,480	29,231	28,777
Selling expenses[2]	162,957	80,028	10,750
General and administrative expenses[2]	52,916	34,020	34,895
Stock-based compensation	37,381	13,530	25,144
Other segment expenses[3]	18,275	13,128	12,234
Total operating expenses	311,009	169,937	111,800
Segment and consolidated loss from operations	(27,950)	(63,276)	(63,759)
Other reconciliation items[4]	(11,186)	(2,791)	(3,448)
Segment and consolidated net loss	$ (39,136)	$ (66,067)	$ (67,207)

(1) *"Other revenues"* includes revenues from our collaboration partnerships, including license fees, milestone payments, product supply revenue and non-cash royalty revenue related to the sale of future royalties.

(2) Research and development, selling and general administrative expenses herein do not include certain allocated items, such as stock-based compensation expenses.

(3) *"Other segment expenses"* primarily consists of allocated facilities, information technology, and employee costs of approximately $ 16.9 million,$ 12.3 million and $ 11.4 million in 2024, 2023 and 2022, respectively.

(4) *"Other reconciliation items"* includes interest expense, non-cash interest expense related to the sale of future royalties, provision for income taxes and other income, net.

NOTE 18. 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 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, 2024, 2023 and 2022, all potential common shares were determined to be anti-dilutive.

The following table sets forth the computation of net loss per common share:

	Year Ended December 31,		
(in thousands, except per share amounts)	**2024**	**2023**	**2022**
Numerator:			
Net loss	$ (39,136)	$ (66,067)	$ (67,207)
Denominator:			
Weighted average common shares outstanding - basic and diluted	235,233	219,331	158,690
Net loss per share of common stock - basic and diluted	$ (0.17)	$ (0.30)	$ (0.42)

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:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**2022**
Options to purchase common stock	27,800	20,877	13,522
Restricted stock units	7,883	3,086	2,694
ESPP shares issuable	230	249	166
Total	35,913	24,212	16,382

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, 2024, 2023 and 2022, was approximately 9.2 million, 6.3 million and 0.6 million, respectively.

NOTE 19. 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 (the Exchange Act), as amended, and Rule 10b-5 thereunder, by making false and misleading statements and omissions of material fact related to tenapanor. 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 a second amended complaint under which the plaintiffs seek to represent all persons who purchased or otherwise acquired Ardelyx securities between March 6, 2020 and July 19, 2021. Defendants filed a motion to dismiss the amended complaint on June 2, 2023. On March 22, 2024, the court granted defendants' motion to dismiss. The court provided plaintiffs a third opportunity to amend and plaintiffs filed a third amended complaint on April 19, 2024. Defendants filed a motion to dismiss the third amended complaint on June 3, 2024. The case was dismissed with prejudice on September 12, 2024. On October 9, 2024, plaintiff appealed the District Court's dismissal of the case to the Ninth Circuit. We believe the plaintiffs' claims are without merit.

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. The consolidated case remains stayed pending resolution of the appeal in the Securities Class Action. We believe the plaintiffs' claims are without merit.

On July 17, 2024, in partnership with the AAKP and the NMQF, we filed a lawsuit in the U.S. District Court for the District of Columbia against the CMS, claiming that CMS has violated its statutory and regulatory authority under the MIPPA, which established the ESRD PPS bundled payment system for dialysis services in 2008. Specifically, the lawsuit claims that CMS's plan to move XPHOZAH, along with all oral-only drugs, into the ESRD PPS is inconsistent with MIPPA's statutory provision, and contradicts CMS's own regulations. XPHOZAH and other oral-only drugs, which are currently available to patients under Medicare Part D, are not administered by dialysis providers and cannot be taken during the delivery of maintenance dialysis. The Company, AAKP and NMQF are seeking relief under the Administrative Procedure Act to enjoin CMS from proceeding with its plan to include XPHOZAH in the ESRD PPS and eliminate coverage under Medicare Part D beginning on January 1, 2025. On November 8, 2024, the U.S. District Court for the District of Columbia granted defendants' Motion to Dismiss and denied plaintiffs Motion for Preliminary Injunction, or in the Alternative, for Expedited Summary Judgment. Following the District Court's denial of plaintiffs' Motion to Alter or Amend the Judgment, or in the Alternative, for an Injunction Pending Appeal, plaintiffs filed an Emergency Motion for an Administrative Stay and Injunction Pending Appeal, which was denied by the United States Court of Appeals for the District of Columbia Circuit. Appellants filed a brief in the appeal on February 4, 2025, and Appellee's brief is due March 6, 2025. Final briefs in the appeal are currently expected to be filed on April 10, 2025.

On August 16, 2024, a complaint was filed against us in the U.S. District Court of Massachusetts, captioned Yarborough v. Ardelyx, Inc., et al., No. 24-cv-12119 (D. Mass.). The complaint names the Company, Mike Raab, and Justin Renz as defendants and alleges violations of Sections 10(b) and 20(a) the Exchange Act and Rule 10b-5 promulgated thereunder, related to the our announcement on July 2, 2024 that it had chosen not to file an application for Transitional Drug Add-on Payment Adjustment for XPHOZAH (the "Yarborough Action"). The plaintiffs seek damages and interest, and an award of costs, including attorneys' fees. Two shareholders filed motions to be appointed lead plaintiff in the Yarborough Action on October 15, 2024. The Court appointed Tate Wood as lead plaintiff on October 30, 2024. Lead Plaintiff filed an amended complaint on January 13, 2025, alleging violations of Sections 10(b) and 20(a) of the Exchange Act and Rule 10b-5 promulgated thereunder related to our announcement on July 2, 2024 regarding TDAPA. Lead Plaintiff purports to bring claims on behalf of all those who acquired Ardelyx common stock between February 23, 2024 and July 1, 2024. Defendants' motion to dismiss the amended complaint is due March 14, 2025. We believe the plaintiff's claims are without merit.

On September 6 and 13, 2024, certain Ardelyx shareholders filed two verified derivative complaints purportedly on behalf of the Company in the United States District Court for the District of Massachusetts alleging violations of Sections 10(b) and/or 14(a) of the Exchange Act, breaches of fiduciary duty, unjust enrichment, waste, and aiding and abetting breaches of fiduciary duty against certain members of our board of directors and management based on substantially the same factual allegations in the Yarborough Action. The complaints seek unspecified damages and corporate governance reforms, as well as costs and attorneys' fees. On September 25, 2024, the Court consolidated the two derivative actions into the case In re Ardelyx, Inc. Stockholder Derivative Litigation, Case No. 1:24-cv-12302-LTS (D. Mass.). On November 7, 2024, the Court stayed the consolidated derivative action pending resolution of any and all motion(s) to dismiss in the Yarborough Action. We believe the plaintiffs' claims are without merit.

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. As of December 31, 2024, there is no litigation pending that would reasonably be expected to have a material adverse effect on our results of operations and financial condition.

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, 2024, management, with the participation of our 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, 2024, 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 CFOO, 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, 2024, 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, 2024, 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, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Attestation Report of Independent Registered Public Accounting Firm

Our independent registered public accounting firm, Ernst & Young LLP, has audited our Financial Statements included in Item 8 of this Annual Report on Form 10-K and have issued a report on our internal control over financial reporting as of December 31, 2024. Their report on the audit of internal control over financial reporting appears below.

Report of Independent Registered Public Accounting Firm

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

Opinion on Internal Control Over Financial Reporting

We have audited Ardelyx, Inc.'s internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Ardelyx, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the balance sheets of Ardelyx, Inc. as of December 31, 2024 and 2023, 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, 2024, and the related notes, and our report dated February 20, 2025 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are

required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Boston, Massachusetts

February 20, 2025

ITEM 9B. OTHER INFORMATION

Trading Plans

During the three months ended December 31, 2024, our Section 16 officers and directors adopted or terminated contracts, instructions or written plans for the purchase or sale of our securities as noted below:

Name and Title of Director or Officer	Action	Date	Trading Arrangement		Total Shares Available to be Sold	Expiration Date
			Rule 10b5-1*	Non-Rule 10b5-1**		
Robert Blanks , Chief Regulatory Officer	Termination	December 20, 2024	X		339,500	June 21, 2024
* Intended to satisfy the affirmative defense conditions of Rule 10b5-1(c)						
** Not intended to satisfy the affirmative defense conditions of Rule 10b5-1(c)						

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not Applicable.

PART III

Items 10, 11, 12, 13, 14.

As described below, we incorporate by reference in this Annual Report on Form 10-K certain information appearing in the Proxy Statement that we will furnish to our stockholders for our 2025 Annual Meeting of Stockholders.

	Incorporated by reference to our Proxy Statement
Item 10. Directors, Executive Officers, and Corporate Governance.	"Executive Officers," "Election of Directors," "Corporate Governance," and " Section 16(a) Beneficial Ownership Reporting Compliance" sections. We have included information regarding our Code Business Conduct and Ethics and our Insider Trading Policy below.
Item 11. Executive Compensation.	"Executive Compensation" section.
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.	"Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" sections.
Item 13. Certain Relationships and Related Transactions, and Director Independence.	"Certain Relationships and Related Party Transactions" and "Election of Directors" sections.
Item 14. Principal Accountant Fees and Services.	"Principal Accountant Fees and Services" section.

Code of Business Conduct and Ethics

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. 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. 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.

Insider Trading Policy and Procedures

We have an insider trading compliance policy and procedures governing the purchase, sale and other dispositions of our securities that applies to all of our personnel, including directors, officers, employees and other covered persons. We believe that our insider trading compliance policy and procedures are reasonably designed to promote compliance with insider trading laws, rules and regulations, and listing standards applicable to us. A copy of our Trading Policy is filed as Exhibit 19.1 to this Form 10-K.

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	Amended and Restated Certificate of Incorporation	8-K	6/24/2014	3.1	
3.2	Certificate of Amendment to Amended and Restated Certificate of Incorporation	8-K	6/20/2023	3.1	
3.3	Amended and Restated Bylaws	8-K	6/24/2014	3.2	
4.1	Reference is made to Exhibits 3.1 and 3.2				
4.2	Form of Common Stock Certificate	S-1/A	6/18/2014	4.2	
4.3	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934	10-K	3/8/2021	4.4	
10.1(a)	Termination Agreement, dated June 2, 2015, by and between AstraZeneca AB and Ardelyx, Inc.	10-Q	8/12/2015	10.1	
10.1(b)	Amendment No. 1 to Termination Agreement and to Manufacturing and Supply Agreement, dated November 2, 2015 by and between AstraZeneca AB and Ardelyx, Inc.	10-K	3/4/2016	10.1(d)	
10.2(a)	Lease, dated August 8, 2008, by and between 34175 Ardenwood Venture, LLC and Ardelyx, Inc.	S-1	5/19/2014	10.4(a)	
10.2(b)	First Amendment to Lease, dated December 20, 2012, by and between 34175 Ardenwood Venture, LLC and Ardelyx, Inc.	S-1	5/19/2014	10.4(b)	
10.2(c)	Second Amendment to Lease, dated September 5, 2014, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC	8-K	9/9/2014	10.1	
10.2(d)	Third Amendment to Lease, dated April 28, 2016, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC	10-Q	8/8/2016	10.3	
10.2(e)	Fourth Amendment to Lease, dated May 25, 2021, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC	10-K	3/2/2023	10.2(e)	
10.2(f)	Fifth Amendment to Lease, dated May 25, 2021, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC	8-K	6/1/2021	10.1	
10.2(g)	Sixth Amendment to Lease, dated May 25, 2021, by and between Ardelyx, Inc. and 34175 Ardenwood Venture, LLC.	8-K	10/9/2024	10.2	
10.3(a)	Lease Agreement, dated December 30, 2020, by and between Ardelyx, Inc. and Prospect Fifth Ave, LLC.	10-K	3/8/2021	10.31	
10.3(b)	Amendment Number 2 to Lease Agreement by and between Ardelyx, Inc, and Prospect Fifth Avenue, LLC.	10-Q	5/2/2024	10.3(b)	
10.3(c)	Amendment Number 3 to Lease Agreement by and between Ardelyx, Inc, and Prospect Fifth Avenue, LLC.	10-Q	5/2/2024	10.3(c)	
10.4	Lease Agreement, dated October 3, 2024, by and between Ardelyx, Inc. and BMR-Pacific Research Center LP.	8-K	10/9/2024	10.1	
10.5#	Ardelyx, Inc. Amended and Restated 2014 Equity Incentive Award Plan.	10-Q	8/1/2024	10.1	
10.6#	Ardelyx, Inc. Amended and Restated 2014 Employee Stock Purchase Plan.	10-Q	8/1/2024	10.2	
10.7(a)#	Ardelyx, Inc. 2008 Stock Incentive Plan, as amended	S-1	5/19/2014	10.5(a)	
10.7(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2008 Stock Incentive Plan, as amended	S-1	5/19/2014	10.5(b)	
10.7(c)#	Form of Restricted Stock Purchase Grant Notice and Restricted Stock Purchase Agreement under the 2008 Stock Incentive Plan, as amended	S-1	5/19/2014	10.5(c)	
10.8(a)#	Ardelyx, Inc. Amended and Restated 2014 Equity Incentive Award Plan	10-Q	8/1/2024	10.1	
10.8(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan	S-1/A	6/9/2014	10.6(b)	
10.8(c)#	Form of Restricted Stock Award Agreement and Restricted Stock Unit Award Grant Notice under the 2014 Equity Incentive Award Plan	S-1/A	6/9/2014	10.6(c)	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.9#	Ardelyx, Inc. Amended and Restated 2014 Employee Stock Purchase Plan	10-Q	8/1/2024	10.2	
10.10(a)#	Ardelyx, Inc. 2016 Employment Commencement Incentive Plan	10-K	2/22/2024	10.7(a)	
10.10(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2016 Employment Commencement Incentive Plan	S-8	11/10/2016	99.2	
10.10(c)#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2016 Employment Commencement Incentive Plan	S-8	11/10/2016	99.3	
10.10(d)#	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2016 Employment Commencement Incentive Plan	S-8	11/10/2016	99.4	
10.11	Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated June 2, 2015	S-3	7/13/2015	99.1	
10.12	Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated July 14, 2016	10-Q	8/8/2016	10.2	
10.13#	Form of Indemnification Agreement for directors and officers	S-1/A	6/9/2014	10.7	
10.14#	Amended and Restated Executive Employment Agreement, dated June 6, 2014, by and between Ardelyx, Inc. and Michael Raab	S-1/A	6/9/2014	10.8	
10.15#	Offer Letter, dated December 28, 2009, by and between Ardelyx, Inc. and David Rosenbaum, Ph.D.	S-1/A	6/9/2014	10.13	
10.16(a)#	Second Amended and Restated Change in Control and Severance Agreement by and between Ardelyx, Inc. and David P. Rosenbaum, Ph.D.	10-Q	5/8/2018	10.1	
10.16(b)#	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	10-K	2/28/2022	10.20	
10.17#	Offer Letter, dated November 21, 2012, by and between Ardelyx, Inc. and Elizabeth Grammer, Esq.	S-1/A	6/9/2014	10.14	
10.18#	Second Amended and Restated Change in Control and Severance Agreement by and between Ardelyx, Inc. and Elizabeth Grammer.	10-Q	5/8/2018	10.0	
10.19#	Offer Letter, dated April 27, 2020, by and between Ardelyx, Inc. and Susan Rodriguez	10-Q	8/6/2020	10.1	
10.20#	Change in Control Severance Agreement dated June 2, 2020, by and between Ardelyx, Inc. and Susan Rodriguez	10-Q	8/6/2020	10.2	
10.21#	Offer Letter, dated June 2, 2020, by and between Ardelyx, Inc. and Justin Renz	10-Q	8/6/2020	10.3	
10.22#	Change in Control Severance Agreement, dated June 8, 2020, by and between Ardelyx, Inc. and Justin Renz	10-Q	8/6/2020	10.4	
10.23(a)#	Second Amended and Restated Non-Employee Director Compensation Program	10-Q	8/4/2022	10.3	
10.23(b)#	Third Amended and Restated Non-Employee Director Compensation Program	10-K	2/22/2024	10.20(b)	
10.24#	Offer Letter, dated February 13, 2024 by and between Ardelyx, Inc. and Michael Kelliher.	10-Q	5/2/2024	10.29	
10.25#	Offer Letter, dated July 25, 2024 by and between Ardelyx, Inc. and Eric Foster.	10-Q	10/31/2024	10.6	
10.26†	Commercial Supply Agreement, dated August 7, 2024 and effective as of July 23, 2024, by and between Ardelyx, Inc. and Catalent.	8-K	8/12/2024	10.1	
10.27†	Commercial Supply Agreement, dated October 25, 2024, by and among Ardelyx, Inc., Hovione Farmaciência, S.A. and Hovione, LLC.	10-Q	10/31/2024	10.2	

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.28(a)††	License Agreement, dated November 27, 2017, by and between Kyowa Hakko Kirin Co., Ltd. and Ardelyx, Inc.	10-K	3/14/2018	10.35	
10.28(b)	Amendment Number 1 to License Agreement, dated as of November 27, 2017, by and among Ardelyx, Inc., and Kyowa Kirin Co., Ltd.	10-K	3/2/2023	10.21(b)	
10.28(c)††	Amendment Number 2 to License Agreement, dated as of April 11, 2022, by and among Ardelyx, Inc., and Kyowa Kirin Co., Ltd.	8-K	4/11/2022	99.1	
10.29††	License Agreement, dated December 11, 2017, by and between Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. and Ardelyx, Inc.	10-K	3/14/2018	10.36	
10.30††	Royalty and Sales Milestone Interest Acquisition Agreement dated June 29, 2022, by and between Ardelyx, Inc. and Healthcare Royalty Partners IV, L.P.	10-Q	8/4/2022	10.1	
10.31(a)	Loan and Security Agreement dated February 23, 2022, by and between Ardelyx, Inc. and SLR Investment Corp.	10-Q	5/5/2022	10.1	
10.31(b)	First Amendment to the Loan and Security Agreement dated August 1, 2022, by and between Ardelyx, Inc. and SLR Investment Corp.	10-Q	8/4/2022	10.2	
10.31(c)	Second Amendment to the Loan and Security Agreement dated February 9, 2023, by and between Ardelyx, Inc. and SLR Investment Corp.	10-K	3/2/2023	10.24(c)	
10.31(d)	Third Amendment to the Loan and Security Agreement dated October 17, 2023, by and between Ardelyx, Inc. and SLR Investment Corp.	8-K	10/18/2023	10.1	
10.31(e)	Fourth Amendment to the Loan and Security Agreement dated October 29, 2024, by and between Ardelyx, Inc. and SLR Investment Corp.	10-Q	10/31/2024	10.5	
10.32	Exit Fee Agreement dated February 23, 2022, by and between Ardelyx, Inc. and SLR Investment Corp.	10-Q	5/5/2022	10.2	
10.33	Exit Fee Agreement, dated May 16, 2018, by and between the Company and Solar Capital Ltd. and Western Alliance Bank	10-Q	8/7/2018	10.2	
10.34(a)††	Manufacturing Services Agreement, dated May 18, 2020, between Ardelyx, Inc. and Patheon Pharmaceuticals Inc.	10-Q	8/6/2020	10.5	
10.34(b)††	First Amendment to the Manufacturing Services Agreement dated February 27, 2023, between Ardelyx, Inc. and Patheon Pharmaceuticals Inc.	10-K	3/2/2023	10.27(b)	
10.35	Open Market Sales Agreement, dated January 18, 2023 between Ardelyx, Inc. and Jefferies LLC.	S-3	1/19/2023	1.2	
19.1	Ardelyx, Inc. Insider Trading Compliance Policy and Procedures			—	X
23.1	Consent of Independent Registered Public Accounting Firm			—	X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended			—	X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended			—	X
32.1	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C §1350			—	X
97.1	Policy for Recovery of Erroneously Awarded Compensation	10-K	2/22/2024	97.1	
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

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
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: February 20, 2025

By: /s/ Joseph Reilly

Joseph Reilly
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 Joseph Reilly, 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.

Signature	Title	Date
/s/ Michael Raab Michael Raab	President, Chief Executive Officer and Director *(Principal Executive Officer)*	February 20, 2025
/s/ Justin Renz Justin Renz	Chief Financial and Operations Officer *(Principal Financial Officer)*	February 20, 2025
/s/ Joseph Reilly Joseph Reilly	Chief Accounting Officer *(Principal Accounting Officer)*	February 20, 2025
/s/ David Mott David Mott	Chairman of the Board of Directors	February 20, 2025
/s/ Robert Bazemore Robert Bazemore	Director	February 20, 2025
/s/ William Bertrand, Jr. William Bertrand, Jr., J.D.	Director	February 20, 2025
/s/ Muna Bhanji Muna Bhanji, R.Ph	Director	February 20, 2025
/s/ Onaiza Cadoret-Manier Onaiza Cadoret-Manier	Director	February 20, 2025
/s/ Richard Rodgers Richard Rodgers	Director	February 20, 2025

SUMMARY OF ABBREVIATED TERMS

Throughout this 2024 Form 10-K, we have used terms which are defined below:

340B Program	Public Health Service's 340B Drug Pricing Program	HCR Agreement	Royalty and Sales Milestone Interest Acquisition Agreement
AAKP	American Association of Kidney Patients	HHS	Department of Health and Human Services
ACA	Affordable Care Act	HIPAA	Health Insurance Portability and Accountability Act of 1996, as amended, and regulations promulgated thereunder
AI Technologies	Artificial intelligence, machine learning and certain automated decision-making technologies	HRSA	Health Resources and Services Administration
AMP	average manufacturer price	IBS-C	irritable bowel syndrome with constipation
ANDA	abbreviated New Drug Application	IND	Investigational New Drug
API	active pharmaceutical ingredient	IRA	Inflation Reduction Act of 2022
AstraZeneca	AstraZeneca AB	IRB	institutional review board
ASU	Accounting Standards Update	Jefferies	Jefferies, LLC
CCPA	California Consumer Privacy Act, as amended by the California Privacy Rights Act	Kyowa Kirin	Kyowa Kirin Co., Ltd.
cGMP	current Good Manufacturing Practice	Knight	Knight Therapeutics, Inc.
CKD	chronic kidney disease	MDRP	Medicaid Drug Rebate Program
CME	Chicago Mercantile Exchange	METiS	METiS Therapeutics, Inc.
CMO	contract manufacturing organization	MHLW	Ministry of Health, Labour and Welfare
CMS	Centers for Medicare & Medicaid Services	MIPPA	Medicare Improvements for Patients and Providers Act
CRO	contract research organization	OLC	Oxylanthanum Carbonate
Customers	collectively, major wholesalers, specialty pharmacies and GPOs (IBSRELA) and specialty wholesaler (XPHOZAH)	NCE	new chemical entity
DPF	EU-US Data Privacy Framework	NDA	New Drug Application
EEA	European Economic Area	NH3	sodium hydrogen exchange 3
ESPP	Employee Stock Purchase Plan	NMPA	National Medical Products Administration
ESRD	End-Stage Renal Disease	NOL	net operating loss
ESRD PPS	End-Stage Renal Disease Prospective Payment System	NMQF	National Minority Quality Forum
EU Patent Package	European Patent Package	Non-FAMP	Non-Federal Average Manufacturer Price
FASB	Financial Accounting Standards Board	R&D	research and development
FDA	Food and Drug Administration	REMS	Risk Evaluation and Mitigation Strategy
FFDCA	Federal Food, Drug, and Cosmetic Act	RSU	restricted stock units
Fosun Pharma	Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd.	SLR	SLR Investment Corp.
FSS	Federal Supply Schedule	SEC	Securities and Exchange Commission
FTC	Federal Trade Commission	SOFR	Secured Overnight Financing Rate
GCP	Good Clinical Practice	TDAPA	Transitional Drug Add-on Payment Adjustment
GDPR	European Union General Data Protection Regulation	UPC	European Unified Patent Court
GLP	Good Laboratory Practice	U.S.	United States
GPO	group purchasing organization	USPTO	U.S. Patent and Trademark Office
GTN	gross-to-net	VA	Department of Veterans Affairs
HCR	HealthCare Royalty Partners IV, L.P.		

Exhibit 19.1

ARDELYX, INC.
INSIDER TRADING COMPLIANCE POLICY AND PROCEDURES

(As amended on February 18, 2025)

I. SUMMARY

Preventing insider trading is necessary to comply with securities laws and to preserve the reputation and integrity of Ardelyx, Inc. (the "Company") as well as that of all persons affiliated with the Company. "Insider trading" occurs when any person purchases or sells a security (e.g., stock) while in possession of "inside information" relating to the security. "Inside information" is information that is both "material" and "non-public." Insider trading violates several laws, including civil and criminal laws. This Insider Trading Compliance Policy (this "Policy") is designed to facilitate compliance with those laws. The penalties for violating insider trading laws include imprisonment, disgorgement of profits, civil fines, and criminal fines. Insider trading is also prohibited by this Policy, and violation of this Policy may result in Company-imposed sanctions, including removal or dismissal for cause. The Company reserves the right to take disciplinary or other measure(s) it determines in its sole discretion to be appropriate in any particular situation, including disclosure of wrongdoing to governmental authorities.

II. PERSONS COVERED AND ADMINISTRATION OF POLICY

This Policy applies to all officers, directors and employees of the Company and extends to all activities within and outside an individual's duties at the Company. For purposes of this Policy, "officers" refer to those individuals who meet the definition of "officer" under Section 16 of the Securities Exchange Act of 1934 (as amended, the "Exchange Act"). Individuals subject to this Policy are responsible for ensuring that members of their household comply with this Policy. This Policy also applies to any entities controlled by individuals subject to this Policy, including any corporations, limited liability companies, partnerships or trusts, and transactions by these entities should be treated for the purposes of this Policy as if they were for the individual's own account. The Company may determine that this Policy applies to additional persons with access to material nonpublic information, such as contractors or consultants, listed under "Applicable

Contractors and Consultants" (if any) on Schedule A or any other consultant otherwise designated as such by written notice from the Company's Chief Legal Officer, together with members of their households and any other person designated as being subject to this Policy by the Company's Chief Legal Officer are referred to collectively as "Covered Persons.".

Questions regarding this Policy should be directed to the Company's Chief Legal Officer, who is responsible for the administration of this Policy.

III. POLICY STATEMENT

Unless otherwise permitted by this Policy, no Covered Person shall:

- purchase, sell, gift, or otherwise transfer any type of security of the Company while in possession of material nonpublic information about the Company;
- purchase, sell, gift, or otherwise transfer any security of any other company, including a customer, supplier, business partner, or an economically-linked company, such as a competitor or peer company, while in possession of material nonpublic information obtained in connection with your employment by or service to the Company (to the extent there is a reasonable likelihood that such information would be considered important to an investor in making an investment decision in such other company);
- directly or indirectly communicate (or "tip") material nonpublic information to anyone outside the Company unless in accordance with Company policy regarding confidential information; or
- directly or indirectly communicate material nonpublic information to anyone within the Company except on a need-to-know basis.

For this purpose:

"Securities" includes stocks, bonds, notes, debentures, options, warrants, equity and other convertible securities, as well as derivative instruments.

"Purchase" and *"sale"* are defined broadly under the federal securities law. *"Purchase"* includes not only the actual purchase of a security, but also any contract to purchase or otherwise acquire a security. *"Sale"* includes not only the actual sale of a security, but also any contract to sell or otherwise dispose of a security. These definitions extend to a broad range of transactions, including conventional cash-for-stock transactions, conversions, the exercise of stock options or warrants, puts, calls, pledging and margin loans, or other derivative securities.

The laws and regulations concerning insider trading are complex, and Covered Persons are encouraged to seek guidance from the Chief Legal Officer prior to considering a transaction in Company securities.

IV. BLACKOUT PERIODS

Quarterly Blackout Periods

The Chief Legal Officer will designate a list of persons on Schedule B, as it may be revised by the Securities Director (as defined in Section V below) or the Chief Legal Officer in each of his or her reasonable discretion (together with their controlled entities and household members) must not purchase, sell, gift or otherwise transfer any security of the Company during any blackout period, except as otherwise permitted by this Policy.

The quarterly blackout period:

- begins on the tenth (10th) calendar day before the end of any fiscal quarter of the Company and
- ends one full trading day after the public release of earnings data for such fiscal quarter.

For the purposes of this Policy, a "trading day" is a day on which U.S. national stock exchanges are open for trading. If, for example, the Company were to make an announcement on Monday prior to 9:30 a.m. Eastern Time, then the blackout period would terminate after the close of trading on Monday. If an announcement were made on Monday after 9:30 a.m. Eastern Time, then the blackout period would terminate after the close of trading on Tuesday. If you have any question as to whether information is publicly available, please direct an inquiry to the Chief Legal Officer.

Additional Blackout Periods

From time to time, the Chief Legal Officer may determine that an additional blackout period is appropriate. Persons subject to an additional blackout period must not purchase, sell, gift or otherwise transfer any security of the Company, except as otherwise permitted by this Policy, and must not disclose to others that an additional blackout period is in effect.

V. PRECLEARANCE OF TRADES

All transactions in the Company's securities (including without limitation, acquisitions and dispositions of Company stock, the "cashless exercise" of stock options and the sale of Company stock issued upon exercise of stock options) by all directors and officers and those employees and consultants (if any) listed on Schedule C, as it may be revised by the Securities Director (as defined below) or the Chief Legal Officer in each of his or her reasonable discretion (together with their controlled entities and household members, each, a "Preclearance Person") must be precleared by the Senior Director of Corporate Securities and Governance ("Securities Director") by emailing him at erabinowitz@ardelyx.com and, if the Securities Director is not available, the Chief Legal Officer.

A request for pre-clearance must be in writing, should be made at least two business days in advance of the proposed transaction, and should include the identity of the Preclearance Person, a description of the proposed transaction, the proposed date of the transaction, and the number of shares or other securities involved. In addition, the Preclearance Person must confirm

in writing that he or she is not aware of material nonpublic information about the Company. The Securities Director, or the Chief Legal Officer, Officer, shall have sole discretion to decide whether to clear any contemplated transaction. Notwithstanding receipt of preclearance, if the Preclearance Person becomes aware of material nonpublic information, or becomes subject to a blackout period before the transaction is effected, the transaction may not be completed.

Preclearance should not be understood to represent legal advice by the Company that a proposed transaction complies with the law and preclearance does not relieve anyone of their responsibility under SEC rules. None of the Company, the Securities Director, Chief Legal Officer, or the Company's other employees will have any liability for any delay in reviewing, or refusal of, a request for preclearance.

VI. EXEMPT TRANSACTIONS

The prohibitions set forth in Section IV and Section V do not apply to:

- purchases of the Company's securities from the Company or sales of the Company's securities to the Company, or the surrender to or withholding by the Company of the Company's securities (*e.g.*, to cover withholding obligations upon the vesting or settlement of equity-based awards);
- exercises of stock options or other equity awards or vesting of equity-based awards that do not involve a market sale of the Company's securities (note that the "cashless exercise" of a Company stock option or other equity award through a broker does involve a market sale of the Company's securities, and therefore would not qualify under this exception);
- initial elections to participate in the Company's Employee Stock Purchase Plan ("ESPP"), subsequent elections to change the contribution amount under the ESPP, or purchases made pursuant to and in accordance with the ESPP;
- gift transactions for family or estate planning purposes, where securities are gifted to a person or entity subject to this Policy, except that gift transactions involving Company securities are subject to pre-clearance;
- "sell-to-cover" transactions pursuant to a non-discretionary policy adopted by the Company that is intended to facilitate the payment of withholding taxes associated with vesting of equity awards (other than stock options; or
- purchases or sales of the Company's securities made pursuant to a plan adopted to comply with Exchange Act Rule 10b5-1 ("Rule 10b5-1") and which plan (i) was precleared in advance pursuant to this Policy and (ii) has not been amended or modified in any respect after such initial preclearance without such amendment or modification being precleared in advance pursuant to this Policy. For more information about Rule 10b5-1 trading plans, see Section IX below.

Exceptions to the blackout period policy may be approved by the Chief Legal Officer or, in the case of exceptions for directors, the Audit Committee of the Board of Directors.

VII. MATERIAL NON-PUBLIC INFORMATION

The materiality of a fact depends upon the circumstances. A fact is considered "material" if there is a substantial likelihood that a reasonable investor would consider it important in making a decision to buy, sell or hold a security, or if the fact is likely to have a significant effect on the market price of the security. Material information can be positive or negative and can relate to virtually any aspect of a company's business or to any type of security, debt or equity. Also, information that something is likely to happen in the future—or even just that it may happen—could be deemed material.

Examples of material information may include (but are not limited to) information about:

- corporate earnings or earnings forecasts;
- communications sent to or received from the U.S. Food and Drug Administration;
- possible mergers, acquisitions, tender offers or dispositions;
- major new products or product developments;
- important business developments such as developments regarding strategic collaborations;
- management or control changes;
- significant borrowing or financing developments including pending public sales or offerings of debt or equity securities;
- defaults on borrowings;
- bankruptcies;
- cybersecurity or data security incidents; and
- significant litigation or regulatory actions.

Information is "non-public" if it is not available to the general public. In order for information to be considered public, it must be widely disseminated in a manner making it generally available to investors in a Regulation FD-compliant method, such as through a press release, a filing with the Securities and Exchange Commission ("SEC") or a Regulation FD-compliant conference call. The Chief Legal Officer shall have sole discretion to decide whether information is public for purposes of this Policy.

The circulation of rumors, even if accurate and reported in the media, does not constitute public dissemination. In addition, even after a public announcement, a reasonable period of time may need to lapse in order for the market to react to the information. Generally, one should allow one full trading day following release of information to the public, as a reasonable waiting period before such information is deemed to be public.

VIII. POST-TERMINATION AND PROHIBITED TRANSACTIONS

A. Post-Termination Transactions

If an individual is in possession of material non-public information when his or her service terminates, that individual may not trade in the Company's securities until that information has become public or is no longer material.

B. Prohibited Transactions

The Company has determined that there is a heightened legal risk and/or the appearance of improper or inappropriate conduct if the persons subject to this Policy engage in certain types of transactions. Therefore, Covered Persons shall comply with the following policies with respect to certain transactions in the Company's securities:

1. Short Sales

Short sales of the Company's securities are prohibited by this Policy. Short sales are sales of shares that the insider does not own at the time of sale, or sales of shares against which the insider does not deliver the shares within 20 days after the sale, evidence an expectation on the part of the seller that the securities will decline in value, and therefore signal to the market that the seller has no confidence in the Company or its short-term prospects. In addition, Section 16(c) of the Exchange Act prohibits Section 16 reporting persons (i.e., directors, officers, and the Company's 10% stockholders) from making short sales of the Company's equity securities.

2. Options

Transactions in puts, calls, or other derivative securities involving covered equity securities, on an exchange, on an over-the-counter market, or in any other organized market, are prohibited by this Policy. A transaction in options is, in effect, a bet on the short-term movement of the Company's stock and, therefore, creates the appearance that a Covered Person is trading based on material non-public information. Transactions in options, whether traded on an exchange, on an over-the-counter market, or any other organized market, also may focus a Covered Person's attention on short-term performance at the expense of the Company's long-term objectives.

3. Hedging Transactions

Hedging transactions involving covered securities, such as prepaid variable forward contracts, equity swaps, collars and exchange funds, or other transactions that hedge or offset, or are designed to hedge or offset, any decrease in the market value of the Company's equity securities, are prohibited by this Policy. Such transactions allow the Covered Person to continue to own the covered securities, but without the full risks and rewards of ownership. When that occurs, the Covered Person may no longer have the same objectives as the Company's other stockholders.

4. Margin Accounts and Pledging

Individuals are prohibited from pledging covered securities as collateral for a loan, purchasing covered securities on margin (i.e., borrowing money to purchase the securities), or placing covered securities in a margin account. This prohibition does not apply to cashless

exercises of stock options under the Company's equity plans, nor to situations approved in advance by the Company's Chief Legal Officer.

IX. RULE 10b5-1 TRADING PLANS

The trading restrictions set forth in this Policy, other than those transactions described under "Prohibited Transactions", do not apply to transactions under a previously established contract, plan or instruction to trade in the Company's securities entered into in accordance with the terms of Rule 10b5-1 and all applicable state laws (a "Trading Plan") that:

- has been submitted to and pre-approved by the Company's Chief Legal Officer or Chief Financial Officer, or such other person as the Company's Board of Directors may designate from time to time at least 30 days before the commencement of any transactions under the Trading Plan;
- includes a "Cooling Off Period" for:
    - Section 16 reporting persons that extends to the later of 90 days after adoption or modification of a Trading Plan or two business days after filing the Form 10-K or Form 10-Q covering the fiscal quarter in which the Trading Plan was adopted, up to a maximum of 120 days; and
    - employees and any other persons, other than the Company, that extends 30 days after adoption or modification of a Trading Plan;
- for Section 16 reporting persons, includes a representation in the Trading Plan that the Section 16 reporting person is (i) not aware of any material non-public information about the Company or its securities; and (ii) adopting the Trading Plan in good faith and not as part of a plan or scheme to evade Rule 10b-5;
- has been entered into in good faith at a time when the individual was not in possession of material non-public information about the Company and not otherwise in a blackout period, and the person who entered into the Trading Plan has acted in good faith with respect to the Trading Plan;
- either (i) specifies the amounts, prices, and dates of all transactions under the Trading Plan, (ii) provides a written formula, algorithm, or computer program for determining the amount, price, and date of the transactions, or (iii) prohibits the individual from exercising any subsequent influence over the transactions; and
- complies with all other applicable requirements of Rule 10b5-1.

The Chief Legal Officer may impose such other conditions on the implementation and operation of the Trading Plan as the Chief Legal Officer deems necessary or advisable. Individuals may not adopt more than one Trading Plan at a time except under the limited circumstances permitted by Rule 10b5-1 and subject to preapproval by the Chief Legal Officer.

An individual may only modify a Trading Plan outside of a blackout period and, in any event, when the individual does not possess material non-public information. Modifications to and terminations of a Trading Plan are subject to preapproval by the Chief Legal Officer and

modifications of a Trading Plan that change the amount, price, or timing of the purchase or sale of the securities underlying a Trading Plan will trigger a new Cooling-Off Period.

The Company reserves the right to publicly disclose, announce, or respond to inquiries from the media regarding the adoption, modification, or termination of a Trading Plan and non-Rule 10b5-1 trading arrangements, or the execution of transactions made under a Trading Plan. The Company also reserves the right from time to time to suspend, discontinue, or otherwise prohibit transactions under a Trading Plan if the Chief Legal Officer or the Board of Directors, in its discretion, determines that such suspension, discontinuation, or other prohibition is in the best interests of the Company.

Compliance of a Trading Plan with the terms of Rule 10b5-1 and the execution of transactions pursuant to the Trading Plan are the sole responsibility of the person initiating the Trading Plan, and none of the Company, the Chief Legal Officer, or the Company's other employees assumes any liability for any delay in reviewing and/or refusing to approve a Trading Plan submitted for approval, nor the legality or consequences relating to a person entering into, informing the Company of, or trading under, a Trading Plan.

X. INTERPRETATION, AMENDMENT, AND IMPLEMENTATION OF THIS POLICY

The Chief Legal Officer shall have the authority to interpret and update this Policy and all related policies and procedures. In particular, such interpretations and updates of this Policy, as authorized by the Chief Legal Officer, may include amendments to or departures from the terms of this Policy to the extent consistent with the general purpose of this Policy and applicable securities laws.

Actions taken by the Company, the Chief Legal Officer, or any other Company personnel do not constitute legal advice, nor do they insulate you from the consequences of noncompliance with this Policy or with securities laws.

XI. REVIEW AND ACKNOWLEDGMENT OF THIS POLICY

Each Covered Person that is employed by the Company is required to review this Policy and acknowledge such review and understanding of this Policy through ComplianceWire upon commencement of their employment with the Company and annually thereafter.

SCHEDULE A

APPLICABLE CONTRACTORS AND CONSULTANTS

[intentionally omitted]

SCHEDULE B

INDIVIDUALS SUBJECT TO QUARTERLY BLACKOUT PERIODS

[intentionally omitted]

SCHEDULE C

INDIVIDUALS SUBJECT TO PRECLEARANCE REQUIREMENT

[intentionally omitted]

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement 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 Statement 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 Statements on Form S-8 (Nos. 333-254187 and 333-270314) 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 (No. 333-263145) pertaining to the 2014 Equity Incentive Award Plan and the 2016 Employment Commencement Incentive Plan of Ardelyx, Inc.,
8. Registration Statement on Form S-8 (No. 333-270314) pertaining to the 2014 Equity Incentive Award Plan and the 2014 Employee Stock Purchase Plan of Ardelyx, Inc., and
9. Registration Statement on Form S-8 (Nos. 333-283006) pertaining to the Amended and Restated 2014 Equity Incentive Award Plan and the Amended and Restated 2014 Employee Stock Purchase Plan of Ardelyx, Inc.;

of our reports dated February 20, 2025, with respect to the financial statements of Ardelyx, Inc. and the effectiveness of internal control over financial reporting of Ardelyx, Inc. included in this Annual Report (Form 10-K) of Ardelyx, Inc. for the year ended December 31, 2024.

/s/ Ernst & Young LLP
Boston, Massachusetts
February 20, 2025

Exhibit 31.1

CERTIFICATION

I, Michael Raab, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ardelyx, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 20, 2025

By: /s/ Michael Raab

Michael Raab
President, Chief Executive Officer and Director
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

I, Justin Renz, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ardelyx, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 20, 2025

By: /s/ Justin Renz

Justin Renz
Chief Financial & Operations Officer
(Principal Financial Officer)

Exhibit 32.1

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, 2024, 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: February 20, 2025 By: /s/ Michael Raab

Michael Raab
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: February 20, 2025 By: /s/ Justin Renz

Justin Renz
Chief Financial & Operations Officer
(Principal Financial Officer)