ARDELYX, INC.
Form 10-K
March 06, 2019
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2018

OR

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

FOR THE TRANSITION PERIOD FROM TO

COMMISSION FILE NUMBER 001-36485

ARDELYX, INC.

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

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

34175 ARDENWOOD BLVD., SUITE 200, FREMONT, CALIFORNIA 94555

(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:	Name of Each Exchange on Which Registered:

Common Stock, par value $0.0001 per share	The Nasdaq Global Market

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

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 definition of "large accelerated filer", "accelerated filer", "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Small reporting company
	Emerging growth company

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

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

The aggregate market value of the Registrant's common stock held by non-affiliates of the Registrant as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2018, based on the last reported sales price of the Registrant's common stock of $3.70 per share was $171,401,057.

The number of shares of Registrant's Common Stock outstanding as of March 1, 2019, was 62,599,673.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the Registrant's Definitive Proxy Statement for its 2019 Annual Meeting of Stockholders, which will be filed with the Commission within 120 days of December 31, 2018, the close of the Registrant's 2018 fiscal year, are incorporated by reference into Part III of this Report.

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ARDELYX, INC.

FORM 10 K FOR THE FISCAL YEAR ENDED DECEMBER 31, 2018

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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,” “positioned,” “seek,” “should,” “target,” “will,” “would,” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- our expectation regarding the timing of receipt of results from the PHREEDOM trial, our second Phase 3 clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in patients with end-stage renal disease, or ESRD, on dialysis;
- our expectation regarding the timing of receipt of results from the AMPLIFY trial, our Phase 3 clinical trial evaluating tenapanor in combination with phosphate binders for the treatment of hyperphosphatemia in patients with end-stage renal disease, or ESRD, on dialysis;
- our expectations regarding our plans for and our participation in the commercialization of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, including our expectations regarding our plans to build our own sales and marketing organization to market and sell tenapanor for such indication;
- our plans to seek one or more collaboration partners to commercialize tenapanor for IBS-C;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates;
- our plans with respect to our pre-clinical programs;
- our ability to identify and validate targets and novel drug candidates using our proprietary drug discovery and design platform including the Ardelyx Primary Enterocyte and Colonocyte Culture System, or APECCS, or any other proprietary drug discovery and design platform we develop for the identification, screening, testing, design and development of new product candidates for the treatment of renal diseases;
- the implementation of our business model and strategic plans for our business, product candidates and technology;
- estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
- our financial performance; and
- developments and projections relating to our competitors and our industry.

Factors that could cause actual results or conditions to differ from those anticipated by these and other forward-looking statements include those more fully described in the “ITEM 1A. RISK FACTORS” section and elsewhere in this Annual Report on Form 10 K. Except as required by law, we assume no obligation to update any forward-looking statement publicly, or to revise any forward-looking statement to reflect events or developments occurring after the date of this Annual Report on Form 10 K, even if new information becomes available in the future. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in any such forward-looking statement.

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ITEM 1. BUSINESS

Company overview

We are a biopharmaceutical company focused on developing first-in-class medicines to improve treatment choices for people with cardiorenal diseases. This includes patients with end-stage renal disease, or ESRD, suffering from elevated serum phosphorus, or hyperphosphatemia; and patients with chronic kidney disease, or CKD, and/or heart failure patients with elevated serum potassium, or hyperkalemia.

Our portfolio is led by the development of tenapanor, a first-in-class inhibitor of NHE3. In our cardiorenal pipeline, tenapanor is being evaluated in a second Phase 3 clinical trial, the PHREEDOM trial, for the treatment of hyperphosphatemia in patients with ESRD who are on dialysis, with topline results expected in the fourth quarter of 2019. This trial follows a successful first Phase 3 clinical trial completed in 2017, which achieved statistical significance for the primary endpoint. Tenapanor, if successfully developed and approved, would be the first therapy for phosphate management that is not a phosphate binder. Tenapanor is a novel, potent, small molecule dosed twice daily in milligram quantities. This results in significantly reduced pill burden when compared to the multi-gram quantities of phosphate binders that patients are required to take. We believe tenapanor's reduced pill burden and twice daily dosing could greatly improve patient adherence and compliance, freeing patients from having to take pills before every meal.

We are also evaluating tenapanor in combination with phosphate binders in a Phase 3 clinical trial, the AMPLIFY trial, from which results are currently expected in the second half of 2019. If our AMPLIFY trial is successful, tenapanor would, if approved, be the first and only phosphate lowering therapy to be indicated as adjunctive therapy for use in combination with binders.

We are also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia. Hyperkalemia is a common problem in patients with heart and kidney disease, particularly in patients taking common blood pressure medications known as RAAS inhibitors, which inhibit the renin-angiotensin-aldosterone system. Similar to what we are doing with tenapanor, RDX013 is designed to lower elevated potassium with a much lower pill burden than potassium binders and we believe may provide significant advantages as a stand-alone agent or also in combination with potassium binders.

In addition to the development of tenapanor in our cardiorenal portfolio, we have developed tenapanor for the treatment of patients with irritable bowel syndrome with constipation, or IBS-C. On September 12, 2018, we submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for the treatment of patients with IBS-C and have been granted a target action date under the Prescription Drug User Fee Act, or PDUFA, of September 12, 2019. The NDA submission was supported by a clinical package encompassing more than 3,100 patients and healthy volunteers who have participated in Ardelyx clinical trials and extensive clinical and preclinical data supporting the favorable safety profile. The data include results from the completed IBS-C registration T3MPO program, which consisted of two Phase 3 trials, T3MPO-1 and T3MPO-2, and a long-term safety extension trial, T3MPO-3. Both the T3MPO-1 and T3MPO-2 trials achieved statistical significance for their primary endpoint and demonstrated that tenapanor had a durable effect on reducing constipation and abdominal pain that patients with IBS-C experience. The favorable safety profile of tenapanor, which has been shown across all clinical trials, was further supported by the completed T3MPO-3 study.

Our Commercial Strategy

We aim to build a multi-product company that commercializes its cardiorenal products in the United States. Our strategy is to leverage ex-U.S. collaborations with established industry leaders to efficiently bring our cardiorenal medicines to patients outside the United States. Additionally, our goal is to bring tenapanor for IBS-C to market by leveraging domestic and ex-U.S. collaborations.

In November 2017, we entered into a license agreement that provides Kyowa Hakko Kirin Co., Ltd., or KHK, with exclusive rights to develop and commercialize tenapanor for the treatment of cardiorenal diseases, including hyperphosphatemia, in Japan. Under the terms of the license agreement, we received a $30.0 million upfront payment

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and are eligible to receive up to $55.0 million in total development milestones. Additionally, under the license agreement, Ardelyx is eligible to receive up to 8.5 billion yen in total commercialization milestones, worth up to $77.5 million at the currency exchange rate on December 31, 2018, as well as high-teen royalties on net sales throughout the term of the agreement. In February 2019, KHK announced initiation of a Phase 2 clinical study of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis. As a result of this development milestone, we received a $5.0 million milestone payment in February 2019.

In December 2017, we entered into a license agreement with Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd., or Fosun Pharma, providing Fosun Pharma with the exclusive rights to develop and commercialize tenapanor in China for the treatment of patients with hyperphosphatemia related to CKD and patients with IBS-C. Under the terms of the agreement, we received an upfront payment of $12.0 million and are eligible to receive additional milestones of up to $113.0 million, as well as tiered royalties on net sales ranging from the mid-teens to 20%.

In March 2018, we entered into a license agreement with Knight Therapeutics, Inc., or Knight, that provides Knight with exclusive rights to commercialize tenapanor in Canada. Under the terms of the agreement, Ardelyx is eligible to receive up to CAD 25 million in total payments including an upfront payment and development and sales milestones, as well as tiered royalties on net sales ranging from mid-single digits to the low twenties. Knight has made significant commercial progress with tenapanor in Canada including the submission to Heath Canada in February of a New Drug Submission, or NDS, for the treatment of IBS-C.

OUR PROPRIETARY DRUG DISCOVERY AND DESIGN PLATFORM

In line with our overall strategy and transition to focus solely on our cardiorenal pipeline, we have shifted our research focus to support our preclinical and clinical stage cardiorenal candidates including tenapanor and RDX013, as well as other potential cardiorenal opportunities. We successfully developed and continue to employ our Ardelyx Primary Enterocyte and Colonocyte System, or APECCS, stem cell platform to emulate, in a miniaturized format, the function and structure of cells of specific segments of the intestine, and we are now developing a similar system with kidney cells. We intend to continue to utilize our unique discovery and design platform to help elucidate first-in-class mechanisms of action, as with tenapanor, and to inform preclinical experiments to help advance our product candidates.

OUR PRODUCT PIPELINE

Tenapanor: A New Approach for Treating Hyperphosphatemia in ESRD Patients on Dialysis

The lead product candidate in our cardiorenal portfolio is tenapanor for the treatment of hyperphosphatemia, or high levels of blood phosphorus, in ESRD patients on dialysis. Hyperphosphatemia is an independent predictor of morbidity and mortality in patients with ESRD and is a significant problem among dialysis patients worldwide.

CKD is the progressive deterioration of renal function that can occur over several months or years. The symptoms of worsening kidney function are nonspecific, and can include having less energy, reduced appetite, dry itchy skin, swollen feet and ankles or generally just not feeling well. If the deterioration continues and is not halted by changes in lifestyle or with the assistance of pharmacological intervention, the disease will likely cause significant cardiovascular morbidity, and can progress to ESRD, the final stage of CKD, where kidney function will be lost entirely.

Current management of ESRD includes hemodialysis and peritoneal dialysis as a means to filter toxins from the blood once kidneys have failed. Unless this intervention occurs, kidney failure results in the accumulation of waste products that may ultimately cause death. Hemodialysis, the most common form of dialysis, generally requires a patient to visit

a dialysis center at least three times per week for a minimum three-hour session, significantly reducing quality of life.

Phosphorus, a vital element required for most cellular processes, is present in almost every food in the Western diet, and, in individuals with normal kidney function, any excess dietary phosphorus is efficiently removed by the kidneys and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.5 to 4.5 mg/dL.

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With kidney failure, elevated phosphorus becomes harmful and is typically diagnosed as hyperphosphatemia when serum phosphorus levels are greater than 4.5 mg/dL, according to guidelines published by KDIGO, the global nonprofit foundation dedicated to improving the care and outcomes of kidney disease patients worldwide. Although patients with ESRD rely on dialysis to eliminate harmful agents, phosphorus is not readily removed by the procedure and other means of managing phosphorus levels must be employed. Studies have shown that 95% of ESRD patients need phosphate control.

In ESRD patients, excess levels of phosphorus have been shown to lead to an increase in cardiovascular disease risk, as well as increases in serum FGF 23, an important regulator of phosphate and vitamin D metabolism. Highly elevated levels of FGF23 is an independent risk factor for adverse cardiac clinical outcomes as well as the development of secondary hyperparathyroidism, or SHPT, marked by elevated parathyroid hormone. SHPT is associated with renal osteodystrophy, a condition of abnormal bone growth characterized by brittle bones.

Since dialysis is unable to efficiently eliminate excess phosphorus, ESRD patients are put on restrictive, low phosphorus diets and are currently prescribed medications called phosphate binders, the only interventions available for the treatment of hyperphosphatemia. Phosphate binders, which commonly need to be taken with meals and snacks, act by binding dietary phosphorus and limiting its absorption. Phosphate binders have multiple limitations, including:

- systemic excess absorption of calcium, iron or lanthanum, resulting in side effects and other unintended consequences for ESRD patients;
- significant challenges with patient compliance because of the large quantity and/or mass of the binders that must be taken each day; and
- significant gastrointestinal, or GI, tolerability issues making frequent dosing difficult for patients

Safety and tolerability have also been significant concerns with many approved phosphate binders, with side effects that include long-term vascular calcification with calcium-based binders and iron-overload with iron-based binders. Common side effects of many approved phosphate binders include GI-related adverse events such as nausea, vomiting, diarrhea, constipation, and dyspepsia as well as hypercalcemia for calcium-based binders and discolored feces for iron-based binders.

ESRD patients, who generally are severely restricted in their fluid intake, are prescribed as many as 12 or more phosphate binder pills per day, among other medications. The amount of phosphorus a binder can remove is limited by its binding capacity, and therefore, increasing the dose, and hence the pill burden, of the binder is the only way to increase the amount of phosphorus being bound and excreted. As a result of pill burden and mass, as well as a number of side effects, on average one out of two patients is not compliant with their prescribed treatment and two out of three patients at any point in time are not at target serum phosphorus levels.

We are developing tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, as we believe it has the potential to address certain of the key limitations of current treatments and offer a completely new mechanism of action. If approved, tenapanor would be the first small molecule/non-binder approach to treating hyperphosphatemia, with a unique mechanism of action that acts by inhibiting, or blocking, the NHE3 transporter in the GI tract. Our scientists, in collaboration with global academic experts, discovered that phosphate absorption in humans occurs primarily through a dynamically regulated paracellular pathway. Tenapanor inhibits the NHE3 transport, and this results in a transient increase in the intracellular proton concentration in cells lining the gastrointestinal lumen, which induces a conformational change in tight junction proteins, thereby decreasing permeability to paracellular phosphate transport. This pathway of phosphate flux that is inhibited by tenapanor appears largely specific for phosphate, whereas the overall absorption of other ions and large molecules appear not to be affected. Notably, in clinical trials, tenapanor has not affected the absorption of other ions (except sodium) or nutrients. A consequence of intestinal NHE3 inhibition is that systemic sodium absorption is reduced leading to an increase in stool sodium and water content, loosening stool consistency and increasing bowel movement

frequency. Tenapanor's unique mechanism of action inhibiting paracellular phosphate absorption was published in the peer-reviewed journal Science Translational Medicine.

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This unique mechanism of action allows tenapanor to be active in many patients at a dose of 10 mg to 30 mg twice daily as opposed to the multiple gram quantities per day required of the phosphate binders. Over the course of a week, the amount of tenapanor required would be less than 500 mg, or a total of 14 small pills, whereas the amount of phosphate binder required, based on package inserts, would be 10 to 30 grams, or up to 63 large pills, depending on the phosphate binder. We believe this significant pill burden advantage will result in better adherence and compliance which could lead to more consistent efficacy in ESRD patients on dialysis.

Tenapanor has been specifically designed to work exclusively within the GI tract, thereby significantly reducing the amount of drug that is absorbed into the bloodstream and the potential side effects that could occur. In human studies of orally-administered tenapanor, the drug was detected in the blood in less than 1% in thousands of collected serum samples, and even in those, at very low levels (< 1.5 ng/mL). We have evaluated tenapanor across 20 clinical studies in over 3,100 individuals to date.

Clinical data supporting tenapanor in hyperphosphatemia

In October 2018, we reported preclinical data from animal models in which sevelamer, a phosphate binder and today's standard-of-care for the treatment of hyperphosphatemia, was administered at three dose levels, with either tenapanor or placebo, twice daily for 11 days. Two additional groups received either tenapanor or placebo alone. Results from this preclinical study showed that the combination of tenapanor and sevelamer resulted in greater reductions in intestinal phosphate absorption than when either agent was administered alone, with a synergistic effect between the two treatments. These data support our evaluation of tenapanor in combination with phosphate binders in an ongoing Phase 3 clinical trial.

In February 2017, we announced data from our first Phase 3 clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis. The Phase 3 trial was an eight-week, double-blind, randomized trial, with a four-week placebo-controlled randomized withdrawal period. We enrolled a total of 219 ESRD patients with hyperphosphatemia who are on dialysis. Enrolled patients were randomized evenly into three arms, in which all groups received tenapanor for eight weeks.

Tenapanor was administered at fixed doses of 3 mg or 10 mg twice-daily and in a dose-titration arm starting at 30 mg twice-daily with the option to down-titrate once a week during the first four weeks to 20, 15, 10 and 3 mg twice-daily, based on GI tolerability. After the end of the eight-week treatment period, patients were re-randomized 1:1 to either remain on their current tenapanor dose or switch to placebo for a four-week, placebo-controlled, randomized withdrawal period.

The primary endpoint of the trial was the difference in change in serum phosphorus between the pooled tenapanor-treated patients and placebo-treated patients from the end of the eight-week treatment period to the end of the four-week randomized withdrawal period, in the responder population. The responder population, which was reviewed by the FDA, is defined as patients who demonstrate a greater than or equal to 1.2 mg/dL decrease in serum phosphorus from baseline during the initial eight-week treatment period.

The study demonstrated a statistically significant difference in serum phosphorus levels from the end of the eight-week treatment period to the end of the four-week randomized withdrawal period between the tenapanor-treated group and the placebo-treated group in the responder patient population (mean -1.01 mg/dL, median of -1.3 mg/dL) and met its primary endpoint (95% confidence interval, -1.44, -0.21, LSmean -0.82 mg/dL, p=0.01). The responder population (n=80 out of 164) had a mean reduction in serum phosphorus from baseline to the end of the eight-week treatment period of 2.56 mg/dL, with a reduction of up to 5.7 mg/dL. Notably, in this group, 33% of patients had a

reduction in serum phosphorus of greater than 3 mg/dL.

Tenapanor was well-tolerated in the trial. In the eight-week treatment period, the only adverse event that affected more than five percent of patients treated with tenapanor was diarrhea (39%), a patient-reported side effect of loosened stool or increased frequency in bowel movements regardless of magnitude. In the four-week randomized withdrawal period, there was a diarrhea rate of 1.2% for patients treated with tenapanor compared with 2.4% on placebo.

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Treatment discontinuations due to diarrhea for patients on tenapanor was 7.8% (n=17). There were no discontinuations due to diarrhea in the randomized withdrawal period.

In order to fully assess GI tolerability, patients used an eDiary to record the frequency of daily bowel habits, as well as stool form using the Bristol Stool Form Scale, or BSFS. During the eight-week treatment period, there was an average 0.4 per day increase in bowel movement frequency from baseline, and during the four-week randomized withdrawal period, there was an average 0.29 per day increase as compared to placebo. Average bowel movement frequency was within the normal range in all groups. During the eight-week treatment period, there was an average 0.87 point increase in BSFS from a baseline score of 4.2, out of a maximum of seven, where seven is liquid stool. During the four-week randomized withdrawal period, there was an average 0.7 point difference in BSFS between placebo (4.4) and tenapanor treatment (5.1).

The PHREEDOM Trial, our second Phase 3 clinical trial of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, is currently underway. The study's design, shown in Figure 1 below, includes a 26 week open-label treatment period, with a 12-week randomized withdrawal period followed by an additional 14 week open-label safety extension. Topline results from this trial are expected in the fourth quarter of 2019. We currently intend to build our own sales and marketing organization to market and sell tenapanor for hyperphosphatemia in the United States.

Figure 1. PHREEDOM Clinical Trial Design

The AMPLIFY clinical trial, shown in Figure 2, is a randomized, double-blind, placebo-controlled study evaluating tenapanor in combination with phosphate binders as adjunctive therapy for the treatment of hyperphosphatemia in patients with ESRD on dialysis. Approximately 215 patients on a stable phosphate binder regimen with a serum phosphorus greater than or equal to 5.5 mg/dL and less than or equal to 10 mg/dL at screening, and after an up to 3-week run-in period will be randomized into the clinical trial 1:1 to receive tenapanor or placebo twice daily. Patients will be allowed to titrate their dose of tenapanor (or placebo) from a starting dose of 30 mg to 20 mg or 10 mg and then back up to 30 mg twice daily, based on GI tolerability and serum phosphorus levels. The primary endpoint will be the difference in change between tenapanor and placebo of serum phosphate levels from randomization to end of the 4-week treatment period. Results from the AMPLIFY clinical trial are currently expected in the second half of 2019. If our AMPLIFY trial is successful, tenapanor would, if approved, be the first and only phosphate lowering therapy to be indicated as adjunctive therapy for use in combination with binders.

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Figure 2. AMPLIFY Clinical Trial Design

The hyperphosphatemia market

Phosphate binders are the only drugs marketed for the treatment of hyperphosphatemia in ESRD patients. The various types of phosphate binders commercialized in the United States include the following:

•Calcium carbonate (many over-the-counter brands including Tums and Caltrate)

•Calcium acetate (several prescription brands including PhosLo and Phoslyra)

•Lanthanum carbonate (Fosrenol)

•Sevelamer hydrochloride (Renagel)

•Sevelamer carbonate (Renvela)

•Sucroferric oxyhydroxide (Velphoro)

•Ferric citrate (Auryxia)

The hydrochloride form of sevelamer, Renagel, was launched in the United States by Genzyme Corporation in 1998 prior to its acquisition by Sanofi, and the carbonate form, Renvela, was launched in 2008. Sanofi reported €802 million ($980 million) in worldwide sales of sevelamer during 2017 and €411 million ($470 million) in 2018. Generic sevelamer carbonate has been approved in certain jurisdictions in Europe since 2015 and in the U.S. market since June 2017.

In addition to the currently marketed phosphate binders, we are aware of at least two other binders in development, including fermagate (Alpharen), an iron-based binder in Phase 3 studies being developed by Opko Health, Inc., and PT20, an iron-based binder in Phase 3 being developed by Shield Therapeutics.

According to the most recent data available from the U.S. Renal Data System, in 2016 there were 457,957 patients on hemodialysis in the United States. Additionally, according to the European ERA-EDTA Registry 2016 Annual Report and a study in 2016 by the Japanese Society for Dialysis Therapy, there were approximately 327,000 patients on hemodialysis in Europe and about 329,000 in Japan. We estimate, based on phosphate binder utilization, the only approved therapies for hyperphosphatemia, that there are approximately 320,000, 260,000 and 289,000 ESRD

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patients with hyperphosphatemia in the United States, countries in Europe and Japan, respectively, resulting in approximately 869,000 ESRD patients with hyperphosphatemia in such countries.

Because many ESRD patients with hyperphosphatemia are unable to lower serum phosphorus levels to below 5.5 mg/dL with currently marketed phosphate binders, we believe there is a significant medical need for new agents with new mechanisms, demonstrated efficacy, a strong safety profile, and significantly lower pill burden. We believe that tenapanor, if approved, has the potential to have the lowest pill burden and mass among any currently marketed hyperphosphatemia products, with milligram rather than gram quantities. In addition, we are evaluating whether tenapanor has the potential to be used in combination with phosphate binders for those patients who cannot achieve adequate phosphate control with a single agent.

Our intention is to build a United States-focused, highly efficient, specialized sales and marketing organization focused on nephrology. The nephrology market is a concentrated market strongly influenced by key opinion leaders. There were 10,798 nephrologists in the United States in 2017 and 7,281 dialysis facilities in the United States that offer in-center dialysis. Based on the experience of our management team, we believe that a specialty salesforce is appropriate for this marketplace. We believe that tenapanor for the treatment of hyperphosphatemia could represent a market opportunity of between $500 million and $700 million in the United States.

With its significantly reduced pill burden and well-tolerated safety profile, tenapanor, if approved, could address the significant pill burden challenges and intolerability that patients experience with today’s binder treatments. After we obtain results from our PHREEDOM and AMPLIFY clinical trials, if successful, we intend to submit a New Drug Application to the FDA in 2020 for tenapanor, both as a monotherapy and, as a first in this therapeutic class, in combination with binders as an adjunctive therapy, for the treatment of hyperphosphatemia in patients with ESRD on dialysis.

To bring tenapanor to patients outside the United States, we intend to establish strategic collaborations with industry leading pharmaceutical companies with established commercial infrastructures. We currently have three collaboration partnerships: with KHK for commercialization of tenapanor for the treatment of cardiorenal diseases, including hyperphosphatemia, in Japan; with Fosun for the commercialization of tenapanor for the treatment of IBS-C and hyperphosphatemia in China; and with Knight for commercialization of tenapanor in Canada.

License agreement with KHK

In November 2017, we entered into a license agreement, the KHK License Agreement, with KHK under which we granted KHK an exclusive license to develop and commercialize tenapanor in Japan for the treatment of cardiorenal diseases and conditions, excluding cancer, the KHK Field. We retained the rights to tenapanor outside of Japan, and also retained the rights to tenapanor in Japan for indications other than those in the KHK Field. Pursuant to the KHK License Agreement, KHK is responsible for all of the development and commercialization costs for tenapanor in the KHK Field in Japan.

Under the KHK License Agreement, we are responsible for supplying the tenapanor drug product for KHK’s use in development and during commercialization until KHK has assumed such responsibility. Additionally, we are responsible for supplying the tenapanor drug substance for KHK’s use in development and commercialization throughout the term of the KHK License Agreement, provided that KHK may exercise an option to manufacture the tenapanor drug substance under certain conditions.

Under the terms of the KHK license agreement, we have received a $30.0 million upfront payment and are eligible to receive up to $55.0 million in total development milestones, of which $5.0 million has been recognized to date. Additionally, under the KHK License Agreement we are eligible to receive up to 8.5 billion yen in commercialization milestones, worth up to $77.5 million at the exchange rate on December 31, 2018, and royalties based on aggregate annual net sales of the licensed products at a high teens percentage, subject to certain single digit reductions under certain circumstances described in the KHK License Agreement.

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The KHK License Agreement will continue until all of KHK's applicable payment obligations under the KHK License Agreement have been performed or have expired, or the agreement is earlier terminated. Under the terms of the KHK License Agreement, we and KHK each have the right to terminate the agreement for material breach by the other party. In addition, KHK may terminate the agreement for convenience; for certain safety reasons or if certain primary endpoints under an applicable development plan are not met despite KHK's commercially reasonable efforts and KHK reasonably determines that it cannot obtain regulatory approval. KHK may also terminate the agreement if certain pivotal clinical trials conducted by us do not meet their primary endpoints. We may terminate the KHK License Agreement if KHK challenges any patents licensed to KHK under the agreement.

License agreement with Fosun

In December 2017, we entered into a license agreement, the Fosun License Agreement, with Fosun Pharma under which we granted Fosun Pharma an exclusive license to develop and commercialize tenapanor in China for the treatment, diagnosis or prevention of irritable bowel syndrome with constipation and chronic idiopathic constipation, hyperphosphatemia related to chronic kidney disease, and other diseases or conditions for which we obtain marketing approval in either the US or China, collectively, the Fosun Field. The Fosun Field excludes the treatment of cancer. We retained the rights to tenapanor outside of China, and also retained the rights to tenapanor in China for indications other than those in the Fosun Field. Pursuant to the terms of the Fosun License Agreement, Fosun Pharma is responsible for all of the development and commercialization costs for tenapanor in the Fosun Field in China.

Under the terms of the Fosun License Agreement, we are responsible for supplying the tenapanor drug product for Fosun Pharma's use in development and during commercialization until Fosun Pharma has assumed such responsibility. Additionally, we are responsible for supplying the tenapanor drug substance for Fosun Pharma's use in development and commercialization throughout the term of the Fosun License Agreement.

Under the terms of the Fosun License Agreement, we received an upfront payment of $12.0 million and are eligible to receive additional milestones of up to $113.0 million in the aggregate, as well as tiered royalty payments on aggregate net sales ranging from the mid-teens percent to twenty percent, subject to certain reductions under certain circumstances, as described in the Fosun License Agreement.

The Fosun License Agreement will continue until all of Fosun Pharma's applicable payment obligations under the License Agreement have been performed or have expired, or the agreement is earlier terminated. Under the terms of the Fosun License Agreement, we and Fosun Pharma each have the right to terminate the agreement for material breach by the other party or in the event of insolvency by the other party. In addition, Fosun Pharma may terminate the agreement for convenience and we may terminate the agreement if Fosun Pharma challenges any patents licensed to it under the agreement.

License agreement with Knight Therapeutics

In March 2018, we entered into a license agreement with Knight that provides Knight with exclusive rights to commercialize tenapanor in Canada. Under the terms of the agreement, Ardelyx is eligible to receive up to CAD 25 million in total payments including an upfront payment and development and sales milestones, as well as tiered royalties on net sales ranging from the mid-single digits to the low twenties. Knight will have the exclusive rights to market and sell tenapanor in Canada.

RDX013 Program: Small Molecule for Treating Hyperkalemia

RDX013 is our novel, small molecule program for the potential treatment of hyperkalemia. Our RDX013 approach works by leveraging the GI tract's natural ability to secrete potassium into the lumen of the gut to reduce serum

potassium levels. This mechanism differs significantly from the potassium binders currently on or approaching the market. For a potassium binder to work, it must be present when dietary potassium is ingested so that the agent can bind the potassium and prevent its absorption in the gut. This results in the need for large quantities of binder in order to bind the large amounts of potassium in the diets of most individuals. In contrast, we observed in our preclinical models that a small amount of RDX013 could cause potassium to be secreted into the lumen of the gut. In this way, we believe

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that RDX013 may have the potential to lower serum potassium whether or not potassium is present in the diet and could result in a very low pill burden, potentially allowing better patient compliance, longer-term use and potentially better efficacy than potassium binders. As described below, certain medications commonly administered to patients with CKD and/or heart failure can also cause hyperkalemia. With the successful development of an effective potassium secretagogue to treat hyperkalemia in a small, convenient pill format, we believe our RDX013 approach may provide nephrologists and cardiologists with an opportunity to treat hyperkalemia chronically without reducing the dose of these medications.

Hyperkalemia is generally defined as the presence of blood potassium levels greater than 5.0 mEq/L. Normal levels are 3.5 to 5.0 mEq/L. When hyperkalemia is severe, above 7.0 mEq/L, there is a significantly increased risk of death because of the potential for heart conductance problems.

Hyperkalemia can be caused by a variety of issues. Kidney disease can result in the elevation of potassium in the blood, and certain drugs such as the common hypertension medications known as RAAS inhibitors, which inhibit the renin-angiotensin-aldosterone system, can cause hyperkalemia. As a result, the dosage of RAAS inhibitors must often be significantly reduced in patients whose potassium levels are elevated, such as in those with CKD and heart failure. Because of the risk of hyperkalemia, several published guidelines have suggested that physicians should reduce and possibly discontinue RAAS inhibitors in order to manage the risk of hyperkalemia in CKD and heart failure patients. The alternative medications used to control hypertension, including diuretics and calcium channel blockers, are less effective than RAAS inhibitors, particularly in patients with failing kidneys and severe hypertension. According to the 2015 publication Market Dynamix: Hyperkalemia, released by Spherix Global Insights, U.S. cardiologists reported that of the patients who would benefit from RAAS inhibition, up to 38% of patients with heart failure and up to 55% of patients with both heart failure and CKD are being administered a sub-optimal dose or none at all. Nephrologists reported that at least one-third of patients who would benefit from RAAS inhibition receive a sub-optimal dose or none at all. We believe there is clearly a strong medical need for new medications that control hyperkalemia in order to allow for optimal use of RAAS inhibitors to control hypertension in these patient populations.

The hyperkalemia market

Of the people with CKD and/or heart failure in the United States, we estimate that there are approximately 2.1 million people who also have occurrences of hyperkalemia. According to a retrospective study conducted in 2005 of a national cohort of 246,000 patients cared for in the Veterans Health Administration, about 21% and 42% of patients with CKD Stage 3b and Stage 4, respectively, had a hyperkalemic event during a 12-month period, suggesting that hyperkalemia affects about 900,000 individuals with CKD Stage 3b or Stage 4 in the United States. According to the United States Renal Data System 2014 Atlas of CKD & ESRD, over 50% of CKD Stage 3b and Stage 4 patients are prescribed RAAS inhibitors to control hypertension and to slow the course of CKD.

Additionally, the number of adults in the U.S. living with heart failure is about 6.5 million, based on data collected in the National Health and Nutrition Examination Survey, which is taken in stages over multiple years. Our proprietary research suggests that up to 16%, or approximately 1.0 million, of these patients had hyperkalemia during a 12-month period. Over half of heart failure patients are prescribed RAAS inhibitors. Our proprietary research also suggests that up to 200,000 patients with ESRD in the U.S. could benefit from an agent that treats hyperkalemia.

We are aware of at least two drugs on the market for the treatment of hyperkalemia. Veltassa (patiromer FOS), an oral, polymer-based potassium binder, was approved for marketing by the FDA in October 2015 and was commercially launched by Relypsa, which was acquired by Galenica AG for $1.5 billion in September 2016. Additionally, Lokelma (sodium zirconium cyclosilicate), an oral, potassium binder developed by ZS Pharma (acquired by AstraZeneca in December 2015 for $2.7 billion) was approved in May 2018 and launched by

AstraZeneca.

We believe that, unlike these agents which require large amounts of drug for the desired effect, RDX013 may have the potential to lower serum potassium whether or not potassium is present in the diet and could result in very low pill burden, allowing better compliance, longer-term use and potentially better efficacy than potassium binders.

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If we are successful in developing RDX013 and obtaining marketing authorization from the FDA, we would expect to leverage the renal sales and marketing organization that we intend to build to support commercialization in the United States of tenapanor for treating hyperphosphatemia in dialysis patients.

Tenapanor: NHE3 Inhibitor for Treating IBS-C

In addition to its development for hyperphosphatemia, we have completed development of tenapanor for the treatment of IBS-C and are pursuing strategic collaborations to bring it to market in this indication. We completed two Phase 3 clinical trials in patients with IBS-C, T3MPO-1 and T3MPO-2, along with a long-term safety study, T3MPO-3, and submitted an NDA to the FDA in September 2018. We have been granted a target action date under PDUFA of September 12, 2019.

IBS-C is a GI disorder in which abdominal pain or discomfort is associated with constipation, and which significantly impacts the health and quality of life of affected patients. Tenapanor is a minimally-systemic small molecule that acts locally in the GI tract to inhibit the sodium transporter NHE3 and reduce sodium uptake from the gut. Part of its mechanism to treat constipation caused by IBS-C is an osmotic effect in the intestines – water follows salt and stool is gently loosened by the body's own fluids. In addition to this mechanism, data from nonclinical studies, which were presented in November 2017 at the American Society of Nephrology Annual Meeting, suggest that tenapanor reduced abdominal pain caused by IBS-C through the inhibition of TRPV-1 dependent signaling. TRPV-1, better known as the "hot chili pepper receptor," is a well-established pain target known for transmitting painful stimuli from a variety of sources including heat, protons and inflammatory molecules. Using an established rodent model of IBS-like colonic hypersensitivity, preclinical data showed that tenapanor treatment reduced visceral hypersensitivity (pain in the internal organs) and normalized colonic sensory neuronal excitability and TRPV-1 currents. Treatment with tenapanor also increased stool excretion and stool water content. In these nonclinical studies, tenapanor had a superior effect on visceral hypersensitivity than placebo or polyethylene glycol, a well-known laxative not known to have an analgesic effect.

Phase 3 clinical data supporting tenapanor in IBS-C

At the end of 2017, we completed our Phase 3 program, the T3MPO program, for tenapanor for the treatment of IBS-C. This included two Phase 3 studies, T3MPO-1 and T3MPO-2, and a long-term safety extension study, T3MPO-3. In the discussion below, statistical significance is denoted by p-values. The p-value is the probability that the reported result was achieved purely by chance (e.g., a p-value <0.001 means that there is a less than a 0.1% probability that the observed change was purely due to chance). Generally, a p-value less than 0.05 is considered statistically significant.

In May 2017, we reported data from the first Phase 3 study, T3MPO-1. T3MPO-1 was a 12-week, double-blind, placebo-controlled, multi-center, randomized trial with a four-week, randomized withdrawal period conducted in a total of 610 patients meeting the ROME III criteria for the diagnosis of IBS-C. Patients were randomized one to one to receive either 50 mg of tenapanor or placebo twice-daily. The trial included a two-week screening period, during which patients with active disease, based on bowel movement frequency and abdominal pain score recorded in a daily phone diary, were randomized into the trial.

The study achieved statistical significance for the primary endpoint and seven of eight secondary endpoints. The primary endpoint, the combined responder rate for six of 12 weeks, showed that a greater proportion of tenapanor-treated patients compared to placebo-treated patients (27.0% vs 18.7%, p=0.02) had at least a 30% reduction in abdominal pain and an increase of one or more complete spontaneous bowel movements, or CSBM, in the same week for at least six of the 12 weeks of the treatment period. The CSBM responder rate in the six of 12 weeks (defined as having an increase of at least one CSBM from baseline during a week for six of 12 weeks) did not

reach statistical significance (33.9% vs. 29.4%, p=0.27); however, the abdominal pain responder rate in the six of 12 weeks (defined as having at least a 30% decrease in abdominal pain from baseline during a week for six of 12 weeks) did achieve statistical significance (44.0% vs. 33.1%, p=0.008). In the nine of 12 treatment weeks, the study achieved statistical significance for the combined responder rate (13.7% vs. 3.3%, p<0.001), in which patients must have had an increase of at least one CSBM from baseline and at least three CSBMs during a week for nine of 12 weeks as well as a 30% or greater reduction in abdominal pain for nine of the 12 weeks. In addition, for the nine of 12 weeks, the study achieved statistical

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significance for the individual CSBM responder rate (16.9% vs. 5%, p<0.001) and the abdominal pain responder rate (30.3% vs. 19.4%, p=0.003).

Tenapanor was well-tolerated in the study. The only adverse events observed in more than 2% of patients treated with tenapanor, as compared with placebo, were diarrhea (14.6% vs 1.7%) and nausea (2.6% vs 1.7%). The placebo adjusted discontinuation rate due to diarrhea was 5.3%.

In October 2017, we reported results from the second Phase 3 study of tenapanor for the treatment of IBS-C, T3MPO-2, a 26-week, double-blind, placebo-controlled, multi-center, randomized trial in 593 patients. Patients were randomized one to one to receive either 50 mg of tenapanor or placebo twice-daily. The trial included a two-week screening period, during which patients with active disease, based on bowel movement frequency and abdominal pain score recorded in a daily phone diary, were randomized into the trial.

The study achieved statistical significance for the primary endpoint and all secondary endpoints evaluated for the topline results and demonstrated the ability to normalize bowel movements. The primary endpoint, the combined responder rate for six of 12 weeks, showed that a greater proportion of tenapanor-treated patients compared to placebo-treated patients (36.5% vs. 23.7%, p<0.001) had at least a 30% reduction in abdominal pain and an increase of one or more CSBMs in the same week for at least six of the 12 weeks of the treatment period. The study achieved statistical significance for the CSBM and abdominal pain responder rates in the six of 12 weeks (47.4% vs. 33.3%, p<0.001; 49.8% vs. 38.3%, p=0.004). In the nine of 12 treatment weeks, the study achieved statistical significance for the combined responder rate (18.4% vs. 5.3%, p<0.001), in which patients must have had an increase of at least one bowel movement from baseline and at least three per week and a 30% reduction in abdominal pain for nine of the 12 weeks. In addition, for the nine of 12 weeks, the study achieved statistical significant for the individual CSBM responder rate (22.2% vs. 6.0%, p<0.001) and the abdominal pain responder rate (35.8% vs. 26.7%, p=0.015). The study also achieved statistical significance for all three durable responder endpoints, the combined responder rate (18.1% vs. 5.0%, p<0.001), CSBM responder rate (21.2% vs. 5.7%, p<0.001) and abdominal pain responder rate (34.8% vs. 26.7%, p=0.028), which are identical to the nine of 12-week responder endpoints, except the response must also occur in three of the last four treatment period weeks.

Tenapanor was well-tolerated in the T3MPO-2 study. The only adverse events observed in more than 2% of patients in the tenapanor-treated group that were also greater than placebo were diarrhea (16.0% vs. 3.7%), flatulence (3.1% vs. 1.0%), nasopharyngitis (4.4% vs. 3.7%) and abdominal distension (3.4% vs. 0.3%). The placebo adjusted discontinuation rate due to diarrhea was 5.8%.

Patients who completed T3MPO-1 and T3MPO-2 were eligible to enter T3MPO-3, our open-label, long-term safety trial where patients could continue to receive tenapanor for up to one year. In October 2018, data from the T3MPO-3 trial was presented at the American College of Gastroenterology (ACG) 2018 Annual Meeting in a poster (P0338), entitled “An Open Label Long-Term Safety Trial (T3MPO-3) of Tenapanor in Patients with Irritable Bowel Syndrome with Constipation (IBS-C).”

The T3MPO-3 trial enrolled a total of 240 patients who completed either the T3MPO-1 or T3MPO-2 Phase 3 trials. All participants in T3MPO-3 received 50 mg of tenapanor twice-daily for up to 55 weeks. Results from T3MPO-3 showed a mean compliance rate with tenapanor of approximately 98%. Overall, tenapanor was well-tolerated, with the most common adverse event being diarrhea (9.2%). There were limited discontinuations (2.1%), with only 1.7% of patients discontinuing due to diarrhea.

The IBS-C market

Numerous treatments exist for the constipation component of IBS-C, many of which are over-the-counter. There are three prescription products marketed for IBS-C: Linzess (linaclotide); Amitiza (lubiprostone); and Trulance (plecanatide).

We believe that tenapanor may offer a significant benefit over currently marketed drugs like Amitiza, Linzess and Trulance in part because of the profile demonstrated in our Phase 3 program, which showed best-in-class efficacy

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results for the 9-of-12 week combined responder rates. Within the United States, there are approximately 11 million patients that suffer that suffer from IBS-C. There is significant unmet need for prescription medications, where, according a 2015 American Gastroenterological Association report, only one in four treated patients are very satisfied with the current FDA approved treatments in IBS-C.

INTELLECTUAL PROPERTY

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

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of our issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the U.S. Patent and Trademark Office, or 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 United States, the patent term is generally 20 years from the earliest date of filing a non-provisional patent application in the applicable country. In the United States, 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 United States, 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.

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NHE3 patents

Our NHE3 patent portfolio is wholly owned by us. This portfolio includes four issued U.S. patents, two issued Japanese patents, two issued patents in each of Korea, Hong Kong, Israel and Mexico and one issued patent in each of the following territories: Australia, China, and the European Union. These issued patents cover the composition and methods of using tenapanor and are predicted, without extension or adjustment, to expire in December 2029. We have related national patent applications pending in Europe, China, India, Israel and a number of other countries. Any patents issuing from these patent applications are also predicted without extension or adjustment to expire in December 2029.

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

Other program patents

We have patent applications pending in the United States and internationally that cover the compositions and methods of using our TGR5 agonists, our FXR agonists and compounds in our RDX013 program.

MANUFACTURING

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

GOVERNMENT REGULATION/FDA

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

The process required by the FDA before a drug may be marketed in the United States generally involves:

· completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies, some performed in accordance with the FDA's current Good Laboratory Practice, or GLP, regulations;

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- submission to the FDA of an Investigational New Drug, or IND, application which must become effective before human clinical trials in the United States may begin;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice, or GCP, regulations to establish the safety and efficacy of the drug candidate for each proposed indication;
- submission to the FDA of a new drug application, or NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current Good Manufacturing Practice, or cGMP, regulations;
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the NDA prior to any commercial marketing, sale or commercial shipment of the drug.

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

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

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

All clinical research performed in the United States in support of an NDA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA so long as the clinical trial is conducted in compliance with GCP and if the FDA is able to validate the data from the study through an onsite inspection, if necessary. GCP includes review and approval by an independent ethics committee, such as an IRB, and obtaining and documenting the freely given informed consent of the subject before study initiation. If the applicant seeks approval of an NDA solely on the basis of foreign data, the FDA will only accept such data if they are applicable to the U.S. population and U.S. medical practice, the studies have been performed

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by clinical investigators of recognized competence, and the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or through other appropriate means.

Clinical trials

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

- Phase 1: Clinical trials are initially conducted in a limited population of subjects to test the drug candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.
- Phase 2: Clinical trials are generally conducted in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific targeted indications in patients with the disease or condition under study.
- Phase 3: Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as "pivotal" studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. Phase 3 clinical trials are generally undertaken with large numbers of patients, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population at multiple, geographically-dispersed clinical trial sites.
- Phase 4: In some cases, the FDA may condition approval of an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after NDA approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the drug. Such post approval trials are typically referred to as Phase 4 clinical trials.

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

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

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

New drug applications

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the drug, are submitted to the FDA in the

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form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use.

Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs of 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, but this timeframe is often extended by FDA requests for additional information or clarification. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an application, the FDA will inspect the facility or the facilities at which the finished drug product, and sometimes the active pharmaceutical ingredient, or API, is manufactured, and will not approve the drug unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance, and will not approve the drug unless compliance with cGCP requirements is satisfactory.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities where the drug product and/or its API will be produced, 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 pivotal Phase 3 clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA could also approve the NDA with a Risk Evaluation and Mitigation Strategy, or REMS, to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. The FDA has the authority to prevent or limit further marketing of a drug based on the results of these post-marketing programs. Once the FDA approves an NDA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the drug reaches the market.

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

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

Other regulatory requirements

Any drugs manufactured or distributed by us or our collaboration partners pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences

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

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

Hatch-Waxman Act

Section 505 of the FFDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application. Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product. ANDAs are termed "abbreviated" because they are generally not required to include nonclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's drug or a method of using the drug. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA or 505(b)(2) NDA.

Upon submission of an ANDA or a 505(b)(2) NDA, an applicant must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the

manufacture, use or sale of the drug product for which the application is submitted. Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use,

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the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired.

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

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

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

Fraud and abuse laws

In the United States, the research, manufacturing, distribution, sale and promotion of drug products and medical devices are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, or 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. Violations of this law are punishable by up to five years in prison, criminal fines, administrative civil money penalties, and exclusion from participation in federal healthcare programs. In addition, 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. Moreover, the Affordable Care Act provides that the

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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 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 future 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. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their off-label promotion of drugs. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $11,181 and $22,363 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. 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 and certain states have enacted laws modeled after the federal False Claims Act.

In addition to the laws described above, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively known as the Affordable Care Act, also imposed new reporting requirements on drug manufacturers for payments made to physicians 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 civil monetary penalties of up to an aggregate of $165,786 per year (or up to an aggregate of $1.105 million per year 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.

Because we intend to commercialize products that could be reimbursed under a federal healthcare program and other governmental healthcare programs, we plan to develop a comprehensive compliance program that establishes internal controls to facilitate adherence to the rules and program requirements to which we will or may become subject. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Due to the breadth of these laws, the absence of guidance in the form of regulations or court decisions, and the potential for additional legal or regulatory change in this area, it is possible that our future sales and marketing practices and/or our future relationships with physicians and other healthcare providers might be challenged under such laws. 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.

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

In addition, in July 2010, CMS released its final rule to implement a bundled prospective payment system for the treatment of ESRD patients as required by the Medicare Improvements for Patients and Providers Act, or MIPPA. The bundled payment includes all renal dialysis services furnished for outpatient maintenance dialysis, including ESRD-related drugs and biologicals. The final rule delayed the inclusion of oral medications without intravenous equivalents in the bundled payment until January 1, 2014 and in April 2014, due to subsequent legislative amendments, CMS provided that such inclusion will remain delayed until January 1, 2025. Unless additional Congressional action is taken, beginning in 2025 ESRD-related drugs will be included in the bundle and separate Medicare reimbursement will no longer be available for such drugs, as it is today under Medicare Part D. While it is too early to project the full impact that bundling may have on drugs for the treatment of hyperphosphatemia, the impact could potentially cause dramatic price reductions for tenapanor, if approved.

Healthcare reform

In March 2010, Congress passed and President Obama signed into law, the Patient Protection and Affordable Care Act, a healthcare reform measure, often called, the Affordable Care Act. The Affordable Care Act substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry.

The Affordable Care Act contains 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 Affordable Care Act:

- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- expands 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;

· expands access to commercial health insurance coverage through new state-based health insurance marketplaces, or exchanges;

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- requires manufacturers to participate in a coverage gap discount program, under which they must agree to offer 50 percent 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, beginning January 2011; and
- imposes 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 and Congressional challenges to certain aspects of the Affordable Care Act. We expect that the new presidential administration and U.S. Congress will likely continue to seek to modify, repeal, or otherwise invalidate all or certain provisions of, the Affordable Care Act. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the Affordable Care Act.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2 percent per fiscal year, which went into effect on April 1, 2013, and, due to subsequent legislative amendments, will remain in effect through 2025 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. 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. 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. 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.

Other regulations

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

EMPLOYEES

As of December 31, 2018, we had a total of 86 employees, all of which were full-time employees, including a total of 16 employees with Ph.D. degrees. Within our workforce, 61 employees are engaged in research and development and the remaining 25 in general management and administration, including finance, legal, and business development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We believe that we maintain good relations with our employees.

CORPORATE INFORMATION

We were incorporated in Delaware on October 17, 2007, under the name Nteryx and changed our name to Ardelyx, Inc. in June 2008. We operate in only one business segment, which is the research, development and commercialization of biopharmaceutical products. See Note 1 to our financial statements included in this Annual Report

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on Form 10 K. Our principal offices are located at 34175 Ardenwood Blvd., Suite 200, Fremont, CA 94555, and our telephone number is (510) 745 1700. Our website address is www.ardelyx.com.

We file electronically with the Securities and Exchange Commission, or 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 public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1 800 SEC 0330. 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.

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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 related notes 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 Limited Operating History, Financial Condition and Capital Requirements

We have a limited operating history, have incurred significant losses since our inception and we will incur losses in the future, which makes it difficult to assess our future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused substantially all of our efforts on our research and development activities, including developing tenapanor and developing our proprietary drug discovery and design platform. To date, we have not commercialized any products or generated any revenue from the sale of products.

We are not profitable and have incurred losses in each year since our inception in October 2007, and we do not know whether or when we will become profitable. We have only a limited operating history upon which to evaluate our business and prospects. We continue to incur significant research, development and other expenses related to our ongoing operations. As of December 31, 2018, we had an accumulated deficit of $365.5 million.

We expect that our operating losses will substantially increase for the foreseeable future as we prepare for the potential commercialization of, and incur manufacturing and development costs for, tenapanor, including costs associated with completing the ongoing Phase 3 development of tenapanor for the treatment of hyperphosphatemia in end stage renal disease, or ESRD, patients on dialysis, and if such Phase 3 development is successful, preparing the new drug application, or NDA, for submission to the U.S. Food and Drug Administration, or FDA, to request marketing authorization for tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, and continuing our discovery and research activities.

Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Further, the net losses we incur may fluctuate significantly from quarter-to-quarter and year-to-year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance.

We have substantial net operating loss and tax credit carryforwards for Federal and California income tax purposes. Such net operating losses and tax credits carryforwards may be reduced as a result of certain intercompany restructuring transactions. In addition, the future utilization of such net operating loss and tax credit carryforwards and credits will be subject to limitations, pursuant to Internal Revenue Code Sections 382 and 383, as a result of ownership changes that have occurred previously and additional limitations may be applicable as a result of ownership changes that could occur in the future.

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

We have no products approved for sale and have never generated any revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully complete the

development of, and obtain the regulatory and marketing approvals necessary to commercialize tenapanor for one or more indications, either on our own, or with one or more collaboration partners. We do not anticipate generating revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales or pursuant to milestone payments depends heavily on many factors, including but not limited to:

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- the successful completion of nonclinical and clinical development of tenapanor;
- obtaining regulatory approvals for tenapanor, either on our own, or with one or more collaboration partners;
- our ability to identify a collaboration partnership and negotiate acceptable terms for a collaboration partnership for the commercialization of tenapanor for IBS-C in the United States;
- our ability to successfully commercialize tenapanor, if approved, either on our own, or with one or more collaboration partners;
- developing a sustainable and scalable manufacturing process for tenapanor and 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 tenapanor, if approved;
- obtaining market acceptance of tenapanor, if approved, as a viable treatment option for the indications for which it is approved;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring, in-licensing and/or developing new product candidates;
- negotiating favorable terms in any collaboration partnership, licensing or other arrangements into which we may enter;
- 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.

In cases where we are successful in obtaining regulatory approvals to market tenapanor for one or more indications, our revenue will be dependent, in part, upon the size of the markets in the territories for which regulatory approval is granted, the accepted price for the product, the ability to get reimbursement at any price and whether we are commercializing the product or the product is being commercialized by a collaboration partner, and in such case, whether we have royalty and/or co-promotion rights for that territory, and whether any royalty we have a right to receive from a collaboration partner is in excess of the royalty we owe AstraZeneca as a result of the termination of our License Agreement with AstraZeneca in 2015. See NOTE 10. COLLABORATION AND LICENSING AGREEMENTS for details on our obligations to AstraZeneca. If the number of patients suitable for tenapanor is not as significant as we estimate, the indications approved by regulatory authorities are narrower than we expect, coverage and reimbursement for tenapanor are not available in the manner and to the extent which we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from the sale of tenapanor, even if approved. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to generate 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.

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

On May 16, 2018, we entered into a loan and security agreement with Solar Capital, Ltd. and Western Alliance Bank, or collectively the Lenders, pursuant to which the Lenders agreed to provide us a $50.0 million term loan facility with a maturity date of November 1, 2022. The full amount of the loan was funded on May 16, 2018. Until we have repaid such indebtedness, the loan and security agreement subjects us to various customary covenants, including requirements as to financial reporting and insurance and restrictions on our ability to dispose of our business or property, to change our line of business, to liquidate or dissolve, to enter into any change in control transaction, to merge or consolidate with any other entity or to acquire all or substantially all the capital stock or property of another entity, to incur additional indebtedness, to incur liens on our property, to pay any dividends or other distributions on capital stock other than dividends payable solely in capital stock, to redeem capital stock, to enter into licensing agreements, to engage in transactions with affiliates, and to encumber our intellectual property. Our business may be adversely affected by these restrictions on our ability to operate our business.

Additionally, we may be required to repay the outstanding indebtedness under the loan facility if an event of default occurs under the loan and security agreement. An event of default will occur if, among other things, we fail to make payments under the loan and security agreement; we breach any of our covenants under the loan and security agreement, subject to specified cure periods with respect to certain breaches; the Lenders determine that a material adverse change has occurred; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit the Lenders 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 delay, limit, reduce or terminate our product development or commercialization efforts or grant to others' rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. The Lenders could also exercise their 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.

We will require substantial additional financing to achieve our goals, and the inability to access this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our pre-commercialization efforts for tenapanor and our other product development and platform development activities.

Since our inception, most of our resources have been dedicated to our research and development activities, including developing our clinical product candidate tenapanor and developing our proprietary drug discovery and design platform. We believe that we will continue to expend substantial resources for the foreseeable future, including costs associated with completing the clinical program for tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, research and development, conducting preclinical studies and clinical trials for our other programs, obtaining regulatory approvals, developing and maintaining scalable manufacturing processes for our product candidates and sales and marketing. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization or co-promotion of any of our product candidates. Our future funding requirements will depend on many factors, including, but not limited to:

- the progress, timing, scope, results and costs of our clinical trial program evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, and if our clinical program is successful, the submission of an

NDA with the FDA to request marketing authorization for tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, as well as our decision whether or not to pursue other indications for tenapanor;

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- whether or not we receive approval from the FDA to market tenapanor for the treatment of patients with IBS-C;
- our ability to identify a collaboration partner and negotiate acceptable terms for a collaboration partnership for the commercialization of tenapanor in IBS-C in the United States;
- our ability to successfully commercialize tenapanor, if approved, either alone or with one or more collaboration partners;
- the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;
- the selling and marketing costs associated with tenapanor, including the cost and timing of building our sales and marketing capabilities, should we elect to do so;
- 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 sales of, or royalties on, tenapanor, if any;
- the sales price and the availability of adequate third-party reimbursement for tenapanor, if approved;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate, and any clinical trials we decide to pursue for other 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, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into with Solar Capital Ltd. and Western Alliance Bank during May 2018.

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 delay, limit, reduce or terminate our research activities, preclinical and clinical trials for our product candidates and our establishment and maintenance of sales and marketing capabilities or other activities that may be necessary to commercialize tenapanor, either alone or with collaboration partners. Additionally, our inability to access capital on a timely basis and on terms that are acceptable to us may force us to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor or certain of our product candidates through the use of alternative structures.

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Risks Related to Our Business

We are substantially dependent on the success of our lead product candidate, tenapanor, which may not be successful in further clinical trials, receive regulatory approval or be successfully commercialized.

To date, we have invested a significant amount of our efforts and financial resources in the research and development of tenapanor, which is currently our lead product candidate. The clinical and commercial success of tenapanor will depend on a number of factors, including the following:

- our ability to, in a timely manner and under terms that are acceptable to us, establish a collaboration partnership for the commercialization of tenapanor for the treatment of IBS-C in the United States;
- the ability of the third-party manufacturers we contract with to successfully execute and scale up the manufacturing processes for tenapanor, which has not yet been demonstrated, and to manufacture supplies of tenapanor and to develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMP, requirements;
- whether the FDA or foreign regulatory authorities require us or our collaboration partners to conduct clinical trials in addition to those anticipated prior to approval to market tenapanor, which could delay the commercialization of tenapanor;
- whether we will be required to conduct clinical trials in addition to those anticipated to obtain adequate commercial pricing;
- the prevalence and severity of adverse side effects of tenapanor;
- whether tenapanor's safety and efficacy profile is satisfactory to the FDA and foreign regulatory authorities to gain marketing approval;
- the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;
- our ability, either alone, or with a collaboration partner, to successfully commercialize tenapanor, if approved for marketing and sale by the FDA or foreign regulatory authorities, including educating physicians and patients about the benefits, administration and use of tenapanor;
- achieving and maintaining compliance with all regulatory requirements applicable to tenapanor;
- acceptance of tenapanor as safe, effective and well-tolerated by patients and the medical community;
- our ability, alone or with collaboration partners, to manage the complex pricing and reimbursement negotiations associated with marketing the same product at different doses for separate indications, if tenapanor is approved for marketing and sale by the FDA or foreign regulatory authorities for both IBS-C and hyperphosphatemia in dialysis patients;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of tenapanor compared to alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for tenapanor by third-party payors;
- enforcing intellectual property rights in and to tenapanor;

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- avoiding 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 tenapanor following approval.

As tenapanor is a first-in-class drug, there is a higher likelihood that approval may not be attained as compared to a class of drugs with approved products. While tenapanor met the primary endpoint in two Phase 3 clinical studies evaluating tenapanor for the treatment of patients with IBS-C, there can be no assurance that we will receive marketing authorization from FDA. In addition, a prolonged government shutdown may cause significant regulatory delays, and therefore, delay our efforts to seek and obtain approvals from the FDA, including approval of our NDA for tenapanor for the treatment of IBS-C. Although tenapanor met the primary endpoint in the first Phase 3 clinical trial for the treatment of hyperphosphatemia in ESRD patients on dialysis, there can be no assurances that the second Phase 3 trial of tenapanor in this indication will achieve the primary endpoint, or that our ongoing clinical trial evaluating tenapanor as adjuvant therapy to phosphate binders will achieve the primary endpoint. There can be no assurances that we will receive regulatory approval to market tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, either as monotherapy or as adjuvant therapy to phosphate binders. Further, it may not be possible or practicable to demonstrate, or if approved, to market tenapanor on the basis of certain of the benefits we believe tenapanor possesses. If the number of patients in the market for tenapanor or the price that the market can bear is not as significant as we estimate, or if we are not able to secure adequate coverage and reimbursement for tenapanor, we may not generate sufficient revenue from sales of tenapanor, if approved. Accordingly, there can be no assurance that tenapanor will ever be successfully commercialized or that we will ever generate income from sales of tenapanor. If we are not successful in completing the development of, obtaining approval for, and commercializing tenapanor, or are significantly delayed in doing so, our business will be materially harmed.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we may encounter substantial delays in completing our clinical development of tenapanor for the treatment of hyperphosphatemia. Furthermore, results of earlier studies and trials may not be predictive of future trial results.

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. Failure can occur at any time during the clinical trial process. The results of preclinical and clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. An unexpected adverse event profile, or the results of drug-drug interaction studies, may present challenges for the future development and commercialization of a product candidate for a particular condition despite receipt of positive efficacy data in a clinical study. We are currently conducting our second Phase 3 clinical trial for tenapanor as monotherapy for the treatment of hyperphosphatemia in ESRD patients on dialysis, as well as a Phase 3 clinical trial evaluating tenapanor as adjuvant therapy to phosphate binders for the treatment of hyperphosphatemia in this patient population. Although tenapanor met the primary endpoint in the first Phase 3 clinical trial for the treatment of hyperphosphatemia in ESRD patients on dialysis, there can be no assurances that the second Phase 3 trial results of tenapanor in that indication will show the desired safety and efficacy. There can also be no assurances that the ongoing clinical trial evaluating tenapanor as adjuvant therapy to phosphate binders will show the desired safety and efficacy for this indication. A number of companies in the pharmaceutical, biopharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials for similar indications that we are pursuing due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if our clinical development program for tenapanor for the treatment of hyperphosphatemia is completed, and despite the completion of our Phase 3 program for tenapanor for IBS-C, the results for indications sought may not be sufficient to obtain the desired regulatory approval for tenapanor, or if such regulatory approval is obtained, the content of the label approved by regulatory authorities may materially and adversely impact our ability to commercialize the product for the approved indication.

We do not know whether our clinical trial evaluating tenapanor as adjuvant therapy to phosphate binders for the treatment of hyperphosphatemia will enroll an adequate number of patients on time or whether that trial and our Phase 3 clinical trial for tenapanor monotherapy for the treatment of hyperphosphatemia will be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

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- reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtain institutional review board, or IRB, approval at each site;
- recruit suitable patients in a timely manner to participate in our trials;
- have patients complete a trial or return for post-treatment follow-up;
- ensure that clinical sites observe trial protocol, comply with good clinical practices, or GCPs, or continue to participate in a trial;
- address any patient safety concerns that arise during the course of a trial;
- address any conflicts with new or existing laws or regulations; or
- initiate or add a sufficient number of clinical trial sites.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating.

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

Further, if there are delays in the completion of, or termination of, either the Phase 3 clinical trial or the adjuvant therapy clinical trial for tenapanor for the treatment of hyperphosphatemia, the commercial prospects of tenapanor for such indication may be harmed, and our ability to generate revenue from product sales of tenapanor for such indication will be delayed. In addition, any delays in completing the clinical trial will increase costs, slow down our regulatory approval process for tenapanor for hyperphosphatemia and jeopardize the ability to commence product sales and generate revenue from product sales for this indication. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that may cause, or lead to, a delay in the completion of either or both of our ongoing hyperphosphatemia clinical trials may also ultimately lead to the denial of regulatory approval.

Even if we successfully obtain regulatory approval for tenapanor for one or more indications, it may never achieve market acceptance, sufficient third-party coverage or reimbursement, or commercial success, which will depend, in part, upon the degree of acceptance among physicians, patients, patient advocacy groups, health care payors and the medical community.

Even if we obtain FDA or other regulatory approvals required to market tenapanor, and it is ultimately commercialized for one or more indications, it may not achieve market acceptance among physicians, patients, third-party payors, patient advocacy groups, and the medical community. Market acceptance of tenapanor, in the event that marketing approval is obtained, depends on a number of factors, including:

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- with respect to tenapanor for IBS-C in the United States, our ability to obtain a collaboration partner for commercialization and the strength of such collaboration partner's financial resources and marketing and distribution organizations, as well as the commitment of such collaboration partner's sales organization to tenapanor;
- the efficacy demonstrated in clinical trials;
- the prevalence and severity of any side effects and overall safety and tolerability profile of the product;
- the clinical indications for which it is approved;
- advantages over new or traditional or existing therapies, including recently approved therapies or therapies that the physician community anticipate will be approved;
- acceptance by physicians, major operators of clinics and patients of tenapanor as a safe, effective and well-tolerated treatment;
- relative convenience and ease of administration of tenapanor;
- the potential and perceived advantages of tenapanor over current treatment options or alternative treatments, including future alternative treatments;
- the cost of treatment in relation to alternative treatments and willingness to pay for tenapanor, if approved, on the part of physicians and patients;
- the availability of alternative products and their ability to meet market demand; and
- the quality of our relationships with patient advocacy groups.

Any failure by us to obtain a collaboration partner for the commercialization of tenapanor in the United States for IBS-C and any failure of tenapanor to achieve market acceptance, sufficient third-party coverage or reimbursement, or commercial success, should it receive regulatory approval, would adversely affect our results of operations.

We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to commercialize tenapanor or any of our other product candidates.

We currently do not have a sales organization. In order to commercialize or co-promote tenapanor or any of our other product candidates, we must enter collaborative relationships with one or more third parties, or build internal marketing, sales, distribution, managerial and other non-technical capabilities. There can be no assurances that we will be successful in establishing collaborative relationships in a timely manner or on terms that are acceptable to us. If tenapanor receives regulatory approval and we have not entered collaborative relationships for the commercialization of tenapanor in the United States, we would have to establish appropriate sales organizations with technical expertise supporting distribution capabilities to commercialize the product candidate, which will be expensive and time consuming, or delay the commercial launch of tenapanor for such indication. As a company, we have no prior experience in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to secure the capital necessary to fund such efforts on acceptable terms, hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, comply with regulatory requirements applicable to the marketing and sale of drug products and effectively manage a geographically dispersed sales and marketing team.

If we are unable to enter collaborative relationships a timely manner, or on acceptable terms, and/or we fail or are delayed in the development of our internal sales, marketing and distribution capabilities, we may choose to delay the commercialization of our products and/or the commercialization of our products could be adversely impacted.

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

The pricing, coverage and reimbursement of our product candidates, if approved, must be adequate to support a commercial infrastructure. The availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates 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 our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

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

There is increased uncertainty related to insurance coverage and reimbursement for drugs, like tenapanor, which, if approved, will be marketed for the treatment of hyperphosphatemia in ESRD patients. In July 2010, CMS released its final rule to implement a bundled prospective payment system for the treatment of ESRD patients as required by the Medicare Improvements for Patients and Providers Act, or MIPPA. The bundled payment covers a bundle of items and services routinely required for dialysis treatments furnished to Medicare beneficiaries in Medicare-certified ESRD facilities or at their home, including the cost of certain routine drugs. The final rule delayed the inclusion of oral medications without intravenous equivalents in the bundled payment until January 1, 2014 and in April 2014, President Obama signed the Protecting Access to Medicare Act of 2014, which further extended this implementation date to January 1, 2024. Additionally, section 204 of the Stephen Beck, Jr., Achieving a Better Life Experience Act of 2014, or ABLE, provides that payment for oral-only ESRD drugs cannot be made under the ESRD Prospective Payment System prior to January 1, 2025. As a result, absent further legislation on this matter, beginning in 2025, oral-only ESRD-related drugs may be included in the bundle and separate Medicare reimbursement will no longer be available for such drugs, as it is today under Medicare Part D. While it is too early to project the full impact that bundling may have on the industry, the impact could potentially cause dramatic price reductions for tenapanor, if approved. We may be unable to sell tenapanor, if approved, to dialysis providers on a profitable basis if third-party payors reduce their current levels of payment, or if our costs of production increase faster than increases in reimbursement levels.

Outside the United States, 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 our product candidates. 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 United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient

to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States 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 any of our product candidates due to the trend

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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 may not be successful in our efforts to develop our product candidates that are at an early stage of development, or expand our pipeline of product candidates, as a result of numerous factors, which may include the inability to access capital necessary to fund such efforts on acceptable terms.

A key element of our strategy has been focused on the expansion of our pipeline of product candidates utilizing our proprietary drug discovery and design platform and to advance such product candidates through clinical development. Our inability to access capital in a timely manner or on acceptable terms to fund our early stage product candidates may force us to consider certain restructuring activities to enable the funding of those early assets through the use of alternative structures. In addition, of the large number of drugs in development, only a small percentage of such drugs successfully complete the FDA regulatory approval process and are commercialized. Accordingly, even if we are able to continue to fund our research and early stage development programs, there can be no assurance that any product candidates will reach the clinic or be successfully developed or commercialized.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Although our research and development efforts to date have resulted in several development programs, we may not be able to develop product candidates that are safe, effective and well-tolerated. Our research programs may initially show promise in identifying potential product candidates, and we may select candidates for development, yet we may fail to advance product candidates to clinical development for many reasons, including the following:

- we may be unable to access sufficient capital on acceptable terms to fund the development of all of our assets and as a result we may be forced to delay or terminate the development of certain product candidates, or to consider restructuring efforts to secure alternate funding for those assets;
- the research methodology used and our drug discovery and design platform may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- the market for a product candidate may change during our program so that the continued development of that product candidate is no longer reasonable;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective, well-tolerated or otherwise does not meet applicable regulatory or commercial criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe, effective and well-tolerated by patients, the medical community or third-party payors, if applicable.

Even if we are successful in continuing to expand our pipeline, through our own research and development efforts, the potential product candidates that we identify or for which we acquire rights may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that

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they are unlikely to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize a product pipeline, we may not be able to generate revenue from product sales in future periods or ever achieve profitability.

We rely on third parties to conduct some of our nonclinical studies and all of our 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 or commercialize our product candidates.

We do not have the ability to independently conduct clinical trials and, in some cases, nonclinical studies. 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 some of our nonclinical studies and all of our clinical trials, we remain responsible for ensuring that each of our studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third parties does not relieve us of our regulatory responsibilities. We, and these third parties are required to comply with current GLPs for nonclinical studies, and good clinical practices, or GCPs, for clinical studies. GLPs and GCPs are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our products in nonclinical and clinical development, respectively. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the European Medicines Agency, or EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Our product candidates may cause undesirable side effects or have other properties that could delay our clinical trials, or delay or prevent regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any regulatory approval that is achieved. If tenapanor or any of our other product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product candidate, the ability to market the product candidates could be compromised.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials, result in the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities or limit the commercial profile of an approved label. To date, patients treated with tenapanor have experienced drug-related side effects including diarrhea, nausea, vomiting, flatulence, abdominal discomfort, abdominal pain, abdominal distention and changes in electrolytes. In the event that trials conducted by us with tenapanor or trials we conduct with our other product candidates, reveal an unacceptable severity and prevalence of these or other side effects, such trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of tenapanor, or any such other product candidate, for any or all targeted indications. Additionally, despite a positive efficacy profile, the prevalence and/or severity of these or other side effects could cause us to cease further development of a product candidate for a particular indication, or entirely. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our

business, financial condition and prospects significantly.

In addition, in the event that any of our product candidates receives regulatory approval and we or others later identify undesirable side effects caused by one of our products, a number of potentially significant negative consequences could occur, including:

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- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or a collaboration partner, may be required to recall the product;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a Risk Evaluation and Mitigation Strategies, or REMS, plan that may require creation of a Medication Guide outlining the risks of such side effects for distribution to patients, as well as 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 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 a particular product candidate, if approved, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

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. If approved for marketing by the FDA or other regulatory agencies, tenapanor, as well as our other product candidates, would compete against existing treatments.

For example, tenapanor will, if approved for the treatment of hyperphosphatemia in ESRD patients on dialysis, compete directly with phosphate binders for the treatment of hyperphosphatemia in ESRD patients on dialysis. The various types of phosphate binders commercialized in the United States include the following:

- Calcium carbonate (many over-the-counter brands including Tums and Caltrate)
- Calcium acetate (several prescription brands including PhosLo and Phoslyra)
- Lanthanum carbonate (Fosrenol)
- Sevelamer hydrochloride (Renagel)
- Sevelamer carbonate (Renvela)
- Sucroferric oxyhydroxide (Velphoro)
- Ferric citrate (Auryxia)

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The hydrochloride form of sevelamer, Renagel, was launched in the United States by Genzyme Corporation in 1998 prior to its acquisition by Sanofi, and the carbonate form, Renvela, was launched in 2008. Sanofi booked €411 million ($470 million) in worldwide sales of sevelamer during 2018. Generic sevelamer carbonate has been approved in certain jurisdictions in Europe since 2015 and in the U.S. market since June 2017. In addition to the currently marketed phosphate binders, we are aware of at least two other binders in development, including fermagate (Alpharen), an iron-based binder in Phase 3 being developed by Opko Health, Inc., and PT20, an iron-based binder in Phase 3 being developed by Shield Therapeutics.

In respect of tenapanor for the treatment of IBS-C, numerous treatments exist for constipation and the constipation component of IBS-C, many of which are over-the-counter. These include psyllium husk (such as Metamucil), methylcellulose (such as Citrucel), calcium polycarbophil (such as FiberCon), lactulose (such as Cephulac), polyethylene glycol (such as MiraLax), sennosides (such as Exlax), bisacodyl (such as Ducolax), docusate sodium (such as Colace), magnesium hydroxide (such as Milk of Magnesia), saline enemas (such as Fleet) and sorbitol. These agents are generally inexpensive and work well to temporarily relieve constipation.

We are aware of three prescription products marketed for IBS-C, including Linzess (linaclotide), Amitiza (lubiprostone), and Trulance (plecanatide). Finally, we are also aware of two products that have recently received US FDA marketing authorization or are currently in review for marketing authorization by the US FDA: Motegrity (prucalopride) which was approved by FDA in December 2018 for the treatment of chronic idiopathic constipation in adults and tegaserod maleate, for which a supplemental new drug application was submitted for the treatment of women with IBS-C who are at low risk for cardiovascular disease.

It is possible that our competitors will develop and market drugs or other treatments that are less expensive and more effective than our product candidates, or that will 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 anticipate that we will 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.

Our proprietary drug discovery and design platform, and, in particular, APECCS, is a new approach to the discovery, design and development of new product candidates and may not result in any products of commercial value. Furthermore, the APECCS aspects of our drug discovery and design platform may have diminished relevance to our efforts focused on the discovery of targets and therapies for the treatment of renal diseases.

We have developed a proprietary drug discovery and design platform to enable the identification, screening, testing, design and development of new product candidates, and have developed APECCS as a component of this of this platform. We have utilized APECCS in the design of our small molecules and to identify new and potentially novel targets in the GI tract. However, there can be no assurance that APECCS will be able to identify new targets in the GI tract or that any of these potential targets or other aspects of our proprietary drug discovery and design platform will

yield product candidates that could enter clinical development and, ultimately, be commercially valuable. In addition, as we focus our efforts on the discovery and design of therapies for the treatment of cardiorenal diseases, we may need to further develop our proprietary drug discovery and design platform to enhance its usefulness in the identification, screening, testing, design and development of new product candidates for the treatment of cardiorenal diseases. There can be no assurances that we will be successful in such additional development of our platform or that our platform will yield product candidates for the treatment of renal diseases.

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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 clinical trials effectively, including the Phase 3 trial of tenapanor and the clinical trial evaluating tenapanor as adjuvant therapy to phosphate binders, both of which are being conducted at multiple trial sites;
- manage our internal research and 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 pre-commercialization activities, our business will be materially adversely affected.

We rely completely on third parties to manufacture our nonclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of tenapanor, if approved. Our business would be harmed if those third parties fail to obtain approval of the FDA or comparable regulatory authorities, fail to provide us with sufficient quantities of drug, or fail to do so at acceptable quality levels or prices.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture tenapanor or any of other our product candidates on a commercial scale, or to manufacture our drug supplies for use in the conduct of our nonclinical and clinical studies. The facilities used by our contract manufacturers to manufacture our drug supply must be approved by the FDA pursuant to inspections that will be conducted after an NDA is submitted to the FDA including the NDA we submitted in September 2018. Our ability to control the manufacturing process of our product candidates is limited to the contractual requirements and obligations we impose on our contract manufacturer. Although they are contractually required to so do, we are completely dependent on our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products.

If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would require a transfer of technology to such alternative facilities and potentially additional capital investment. In addition, the use of alternative manufacturing facilities would require qualification with the FDA or comparable foreign regulatory authorities, all of which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical studies. There are a limited number of suppliers for raw materials and certain processes, such as spray drying, that we use to manufacture our drugs, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product

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candidates for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials or processes by our manufacturers. Although we generally do not begin a clinical study unless we believe we have on hand, or will be able to manufacture, a sufficient supply of a product candidate to complete such study, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing, and potential regulatory approval of our product candidates, which could harm our business and results of operations.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

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

- decreased demand for our product candidates;
- 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 our product candidates.

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. We currently carry product liability insurance covering use in our clinical trials in the amount of $10.0 million in the aggregate. Although we maintain such 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.

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We are highly dependent on the services of our President and Chief Executive Officer, Michael Raab and our Chief Development Officer, David Rosenbaum, Ph.D. If we are not able to retain these members of our management team, or recruit additional management and clinical personnel, our business will suffer.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified personnel. In particular, we are highly dependent upon Michael Raab, our President and Chief Executive Officer and David Rosenbaum, Ph.D., our Chief Development Officer. The loss of services of any of these individuals could delay or impair the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates. Although we have entered into employment agreements with our senior management team, including Mr. Raab and Dr. Rosenbaum, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected. Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. In addition to the competition for personnel, the San Francisco Bay area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

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

We and our collaborators, CROs, and other contractors and consultants collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we and our collaborators, CROs and other contractors and consultants collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we and our collaborators, CROs and other contractors and consultants do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent a data compromise, and rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result a number of third-party vendors may or could have access to our confidential information. Our internal 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 damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, 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 cyber-attacks 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. 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. If such an event were to

occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. 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. In addition,

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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, including the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Clinical Health Act of 2009, or HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition.

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, or the 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, or Section 404, and the related rules of the Securities and Exchange Commission, or SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. We will remain an emerging growth company until December 31, 2019.

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 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 currently expect to form additional collaboration partnerships, create joint ventures or enter into additional

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licensing arrangements with third parties in the United States and abroad that we believe will complement or augment our existing business. In particular, we have formed collaboration partnerships with Kyowa Hakko Kirin Co., Ltd. for commercialization of tenapanor for hyperphosphatemia in Japan, with Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd. for commercialization of tenapanor for hyperphosphatemia and IBS-C in China and related territories, and in Canada with Knight Therapeutics Inc. for commercialization of tenapanor for IBS-C and hyperphosphatemia. We face significant competition in seeking appropriate collaboration partners, and the process to identify an appropriate partner and negotiate appropriate terms is time-consuming and complex. Any delays in identifying suitable additional collaboration partners and entering into agreements to develop our product candidates could also delay the commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. Moreover, we may not be successful in our efforts to establish such additional collaboration partnerships for tenapanor for IBS-C commercialization in the United States or for any future product candidates and programs on terms that are acceptable to us, or at all. With respect to tenapanor, this may be because third parties may not view tenapanor for the treatment of IBS-C as having sufficient potential to be successfully commercialized. If we are unable to establish a collaboration partnership for the commercialization of IBS-C in the United States, the commercialization of tenapanor for IBS-C, if approved, could be materially and adversely impacted, which could have a material adverse effect on our business, results of operations, financial condition and prospects. Additionally, we may not be successful in our efforts to establish collaboration partnerships for our other product candidates because our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, and/or third parties may not view such other product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile. There is no guarantee that our current collaboration partnerships or any such arrangements we enter into in the future will be successful, or that any collaboration partner will commit sufficient resources to the development, regulatory approval, and commercialization effort for such products, or that such alliances will result in us achieving revenues that justify such transactions.

We 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 restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor or certain of our product candidates 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 to pay for acquisitions;
- higher-than-expected acquisition and integration costs;
- write-downs of assets or goodwill or impairment charges;

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- 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 we seek and obtain approval to commercialize our product candidates outside of the United States, manufacture our product candidates outside of the United States, or otherwise engage in business outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

In addition to Japan, China and Canada, we or our collaboration partners may decide to seek marketing approval for certain of our product candidates outside the United States or otherwise engage in business outside the United States, including entering into contractual agreements with third-parties. We currently utilize contract manufacturing organizations located outside of the United States to manufacture our active drug substance for tenapanor. We expect that 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 United States and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- 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

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· 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.

Our research and development activities involve the controlled storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. 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 these hazardous materials. 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, research and development efforts and business operations, environmental damage resulting in costly clean-up and 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 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 United States, 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. The 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. We cannot anticipate all the ways in which the global economic climate and global financial market conditions could adversely impact our business in the future.

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

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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.

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

Risks Related to Government Regulation

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. Neither we nor any of our collaboration partners is permitted to market any drug product in the United States until we receive marketing approval from the FDA. In September 2018, we submitted our first NDA to the FDA seeking marketing approval for tenapanor for IBS-C. Neither we, nor our collaboration partners have submitted additional applications or obtained marketing approval for any of our product candidates anywhere in the world. Obtaining regulatory approval of a NDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaboration partners must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such drug candidates are safe and effective for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA approval varies

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depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all targeted indications.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical studies, and depends upon numerous factors. The FDA and comparable foreign authorities have substantial discretion in the approval process and we may encounter matters with the FDA or such comparable authorities that requires us to expend additional time and resources and delay or prevent the approval of our product candidates. For example, the FDA may require us to conduct additional studies or trials for drug product either prior to or post-approval, such as additional drug-drug interaction studies or safety or efficacy studies or trials, or it may object to elements of our clinical development program such as the number of subjects in our current clinical trials from the United States. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or result in a decision not to approve an application for regulatory approval. Despite the time and expense exerted, failure can occur at any stage.

Applications for our product candidates could fail to receive regulatory approval for many reasons, including but not limited to the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our, or our collaboration partners', clinical studies;
- the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which approval is sought;
- the FDA or comparable foreign regulatory authorities may disagree with the interpretation of data from preclinical studies or clinical studies;
- the data collected from clinical studies of our product candidates may not be sufficient to support the submission of a NDA or other submission or to obtain regulatory approval in the United States or elsewhere;
- we or our collaboration partners may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's risk-benefit ratio for its proposed indication is acceptable;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers responsible for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process, as well as the unpredictability of the results of clinical studies, may result in our failure and/or that of our collaboration partners to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. Additionally, if the FDA requires that we conduct additional clinical studies, places limitations in our label, delays approval to market our product candidates or limits the use of our products, our business and results of operations may be harmed.

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In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, any product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Even if a drug is approved by the FDA or foreign regulatory authorities, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, 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 contract manufacturers will be subject to continual review and periodic inspections to assess compliance with regulatory requirements. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Regulatory authorities may also impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance.

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

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

- warning letters, fines or holds on clinical trials;
- 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 contract manufacturers' operations; or
- product seizure or detention, or refusal to permit the import or export of products.

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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 our product candidates. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

In addition, the FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. 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 United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these Executive Orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

The regulatory authorities also may, at any time following approval of a product for sale, audit the manufacturing facilities of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable

regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent suspension of production or closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

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

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

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

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

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If tenapanor or our other product candidates receive marketing approval, we and our collaboration partners, if any, 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 intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations regarding off-label promotion. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our product candidates for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Over the past several years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission 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 Food, Drug and Cosmetic Act, the False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "qui tam" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim, or caused a false claim to be submitted, to the government for payment. The person bringing a qui tam suit is entitled to a share of any recovery or settlement. Qui tam suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a qui tam suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved

uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

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If approved, tenapanor and our other product candidates 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.

Some participants in clinical studies of tenapanor have reported adverse effects after being treated with tenapanor, including diarrhea, nausea, flatulence, abdominal discomfort, abdominal pain, abdominal distention and changes in electrolytes. If we are successful in commercializing any products, FDA and foreign regulatory agency regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory agency could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

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

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

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

In order to market any product in the EEA (which is composed of the 28 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, or MA. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment

of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by

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regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for regulatory approvals or to do so on a timely basis, and even if we do file we may not receive necessary approvals to commercialize our products in any market.

We and our collaboration partners may be 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.

Although we do not currently have any products on the market, once we begin commercializing our products, we and our collaboration partners may be 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;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;
- the federal physician sunshine requirements under the Affordable Care Act, 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, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers 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 state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and

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- 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. Further, the Affordable Care Act, among other things, amends the intent requirement of the federal anti-kickback and criminal health care fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the false claims statutes. 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 United States may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates and to produce, market and distribute our products after clearance or approval is obtained.

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

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

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

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the United States, the Affordable Care Act 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. The Affordable Care Act, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% 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

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outpatient drugs to be covered under Medicare Part D. The Bipartisan Budget Act of 2018 increases this discount to 70% beginning in 2019.

We currently expect that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation, and we currently expect that the current Presidential Administration will continue to seek to modify, or repeal all, or certain provisions of, the Affordable Care Act. There is still uncertainty with respect to any regulatory changes, and such regulatory changes could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were otherwise authorized by the Affordable Care Act. However, 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.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. These new laws, among other things, included aggregate reductions of Medicare payments of 2% per fiscal year to providers that will remain in effect through 2027 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. 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. 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.

Risks Related to Intellectual Property

We may become subject to claims alleging infringement of third parties' patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of tenapanor or our other product candidates, or prevent or delay the continued use of our drug discovery and development platform, including APECCS.

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. There can be no assurances that we will not be subject to claims alleging that the manufacture, use or sale of tenapanor or any other product candidates, or that the use of our drug discovery and development platform, including APECCS, 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 tenapanor or other product candidates or by the use of APECCS. 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 tenapanor or our other product candidates, or by the use of APECCS.

We may be subject to third-party patent infringement claims in the future against us or our that would cause us to incur substantial expenses and, if successful against us, 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 research, development, manufacturing or

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sales of the product or product candidate that is the subject of the suit. In addition, if a patent infringement suit were brought against us regarding the use of aspects of our drug discovery and development platform, we could be forced to stop our use of APECCS or of other aspects of our platform, or we could be forced to modify our processes to avoid infringement, which may not be possible at a reasonable cost, if at all, and which could result in substantial delay in our use of our platform for the discovery of new product candidates or potential targets. 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, or to cease our use of APECCS or some other aspect of our drug discovery and development platform or our business operations 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.

In addition to infringement claims against us, if third parties prepare and file patent applications in the United States that also claim technology similar or identical to ours, we may have to participate in interference or derivation proceedings in the United States Patent and Trademark Office, or 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.

If our intellectual property related to our product candidates is not adequate or if we are not able to protect our trade secrets or our confidential information, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates, our drug discovery and development platform and our development programs. Any disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in foreign countries. Additionally, our research and development efforts may result in product candidates for which patent protection is limited or not available. Even if patents do successfully issue, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. For example, U.S. patents can be challenged by any person before the new USPTO Patent Trial and Appeals Board at any time before one year after that person is served an infringement complaint based on the patents. Patents granted by the European Patent Office may be similarly opposed by any person within nine months from the publication of the grant. Similar proceedings are available in other jurisdictions, and in the United States, Europe and other jurisdictions third parties can raise questions of validity with a patent office even before a patent has granted. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. For example, a third party may develop a competitive product that provides therapeutic benefits similar to one or more of our product candidates but has a sufficiently different composition to fall outside the scope of our patent protection. If the breadth or strength of protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is successfully challenged, then our ability to commercialize such product candidates could be negatively affected, and

we may face unexpected competition that could have a material adverse impact on our business. Further, if we encounter delays in our clinical trials, the period of time during which we or our collaboration partners could market tenapanor or other product candidates under patent protection would be reduced.

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

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

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States 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.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, if any, one of the U.S. patents covering each of such approved product(s) or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon

regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

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

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

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

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

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. 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.

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 United States and foreign countries may affect our ability to obtain and enforce adequate intellectual property protection for our technology.

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

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

or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Risks Related to Our Common Stock

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

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

- results from, or any delays in, clinical trial programs relating to our product candidates, including the ongoing clinical trials for tenapanor for hyperphosphatemia;
- the success of our efforts to establish a collaboration partnership for the commercialization of tenapanor for IBS-C in the United States;
- our ability, alone or with collaboration partners, to commercialize or obtain regulatory approval for tenapanor, or delays in commercializing or obtaining regulatory approval;
- announcements of regulatory approval, a complete response letter with respect to our NDA filed with the FDA in September 2018 seeking marketing approval for tenapanor for IBS-C, results of regulatory inspections of our facilities or those of our contract manufacturing organizations, or specific label restrictions or patient populations for tenapanor’s use, or changes or delays in the regulatory review process;
- announcements relating to our current or future collaboration partnerships;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to 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 clinical development of any of our product candidates, including the ongoing Phase 3 and adjuvant therapy clinical trials for tenapanor for hyperphosphatemia;
- 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;

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- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacture, supply or distribution shortages;
- actual or anticipated fluctuations in our operating results;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry or other healthcare reform measures in the United States;
- 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 United States 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.

One of our stockholders owns a significant percentage of our stock and, together with our management, will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2018, entities affiliated with New Enterprise Associates, or NEA, a venture capital fund associated with one of our directors, collectively beneficially owned approximately 26.2% of our common stock, including shares that NEA has the right to acquire within 60 days of December 31, 2018. NEA together with our executive officers and directors beneficially owned approximately 29.3% of our capital stock, including outstanding restricted stock units that will vest within 60 days of December 31, 2018, and warrants and stock options exercisable for shares of our common stock within 60 days of December 31, 2018. Therefore, these stockholders may be able to determine all matters requiring stockholder approval, and the entities affiliated with NEA alone will have significant ability to influence decisions through their ownership position. For example, these stockholders may be able to influence or control elections of directors, amendments to our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that certain stockholders may feel are in their best interest as one of our stockholders.

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

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

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of December 31, 2018, we had 62,516,627 shares of common stock outstanding. Of those shares, approximately 15.8 million were held by current directors, executive officers and other affiliates, or may otherwise be subject to Rule 144 under the Securities Act of 1933, or the Securities Act.

As of December 31, 2018, approximately 1.0 million shares of common stock issuable upon vesting of outstanding restricted stock units and approximately 5.5 million shares of common stock issuable upon exercise of outstanding options were eligible for sale in the public market to the extent permitted by the provisions of the applicable vesting schedules, and Rule 144 and Rule 701 under the Securities Act. In addition, as of December 31, 2018, approximately 2.2 million shares of common stock issuable upon exercise of outstanding warrants were eligible for sale in the public market. If these additional shares of common stock are issued and sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

As of December 31, 2018, the holders of approximately 5.6 million shares of our outstanding common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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;

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- 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 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 indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

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- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
- We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

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

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

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our headquarters is currently located in Fremont, California, and consists of 61,784 square feet, plus a further 10,716 square feet beginning in September 2019, of leased office and laboratory space under a lease that currently expires in September 2021. In addition, we lease 3,520 square feet of office space in Boston, Massachusetts, under a lease that currently expires in October 2021. We believe that our existing facilities are adequate for our current needs. If we determine that additional or new facilities are needed in the future, we believe that sufficient options would be available to us on commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. We believe that as of December 31, 2018, 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 4. MINE SAFETY DISCLOSURES

Not applicable.

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PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Common Stock

Our common stock commenced trading on The Nasdaq Global Market under the symbol "ARDX" on June 19, 2014. Prior to that date, there was no public trading market for our common stock. As of December 31, 2018, there were 34 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.

Recent Sales of Unregistered Securities

None.

Use of Proceeds

Not applicable.

Issuer Purchases of Equity Securities

Not applicable.

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ITEM 6. SELECTED FINANCIAL DATA

The data set forth below is not necessarily indicative of the results of future operations and should be read in conjunction with the financial statements and the notes included elsewhere in this annual report on Form 10 K and also with "ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS" and our financial statements and the related notes included in this Annual Report on Form 10 K.

	Year Ended December 31,				
Statement of Operations Data:	2018	2017	2016	2015	2014
	(in thousands, except share and per share amounts)				
Revenue:					
Licensing revenue	$ 2,320	$ 42,000	$ —	$ 21,611	$ 18,394
Collaborative development revenue	—	—	—	2,415	13,229
Other revenue	287	—	—	—	—
Total revenue	2,607	42,000	—	24,026	31,623
Cost of revenue	466	8,400	—	—	—
Gross profit	2,141	33,600	—	24,026	31,623
Operating expenses:					
Research and development	69,373	75,484	94,161	39,885	25,900
General and administrative	23,715	23,231	18,734	13,530	7,287
Total operating expenses	93,088	98,715	112,895	53,415	33,187
Loss from operations	(90,947)	(65,115)	(112,895)	(29,389)	(1,564)
Interest expense	(3,534)	—	—	—	—
Other income (expense), net	3,187	1,955	508	(261)	10
Change in fair value of preferred stock warrant liability	—	—	—	—	(1,593)
Loss before provision for income taxes	(91,294)	(63,160)	(112,387)	(29,650)	(3,147)
Provision for (benefit from) income taxes	4	1,179	—	(29)	67
Net loss	$ (91,298)	$ (64,339)	$ (112,387)	$ (29,621)	$ (3,214)
Net loss per common share, basic and diluted	$ (1.62)	$ (1.36)	$ (2.80)	$ (1.29)	$ (0.31)
Shares used in computing net loss per share - basic and diluted	56,219,919	47,435,331	40,118,522	22,892,640	10,248,337

	As of December 31,				
Balance Sheet Data:	2018	2017	2016	2015	2014
	(in thousands)				
Cash, cash equivalents and short-term investments	$ 168,089	$ 133,976	$ 200,823	$ 107,004	$ 107,286
Total assets	183,332	157,903	213,131	116,946	113,414
Deferred revenue	—	—	—	—	47,053

Accumulated deficit	(365,512)	(278,214)	(213,875)	(101,488)	(71,867)
Total stockholders' equity	115,813	139,312	193,151	108,901	60,682

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

OVERVIEW

We are a biopharmaceutical company focused on developing first-in-class medicines to improve treatment choices for people with cardiorenal diseases. This includes patients with end-stage renal disease, or ESRD, suffering from elevated serum phosphorus, or hyperphosphatemia; and patients with chronic kidney disease, or CKD, and/or heart failure patients with elevated serum potassium, or hyperkalemia.

Our portfolio is led by the development of tenapanor, a first-in-class inhibitor of NHE3. In our cardiorenal pipeline, tenapanor is being evaluated in a second Phase 3 clinical trial, the PHREEDOM trial, for the treatment of hyperphosphatemia in patients with ESRD who are on dialysis, with topline results expected in the fourth quarter of 2019. This trial follows a successful first Phase 3 clinical trial completed in 2017, which achieved statistical significance for the primary endpoint. Tenapanor, if successfully developed and approved, would be the first therapy for phosphate management that is not a phosphate binder. We are also evaluating tenapanor in combination with phosphate binders in a Phase 3 clinical trial, the AMPLIFY trial, from which results are currently expected in the second half of 2019. If our AMPLIFY trial is successful, tenapanor would, if approved, be the first and only phosphate lowering therapy to be indicated as adjunctive therapy for use in combination with binders.

We are also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia. Hyperkalemia is a common problem in patients with heart and kidney disease, particularly in patients taking common blood pressure medications known as RAAS inhibitors, which inhibit of the renin-angiotensin-aldosterone system. We believe that RDX013 has the potential to lower elevated potassium with a much lower pill burden than potassium binders and may provide significant advantages as a stand-alone agent or also in combination with potassium binders.

In addition to the development of tenapanor for the treatment of hyperphosphatemia for ESRD patients on dialysis, we have developed tenapanor for the treatment of patients with IBS-C. On September 12, 2018, we submitted a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for the treatment of patients with irritable bowel syndrome with constipation, or IBS-C, and have been granted a target action date under the Prescription Drug User Fee Act, or PDUFA, of September 12, 2019. The NDA submission was supported by a clinical package encompassing more than 3,100 patients and healthy volunteers who have participated in Ardelyx clinical trials and extensive clinical and preclinical data supporting the safety profile. The data include results from the completed IBS-C registration T3MPO program, which consisted of two Phase 3 trials, T3MPO-1 and T3MPO-2, and a long-term safety extension trial, T3MPO-3. Both the T3MPO-1 and T3MPO-2 trials achieved statistical significance for their primary endpoint and demonstrated that tenapanor had a durable effect on reducing constipation and abdominal pain that patients with IBS-C experience. The favorable safety profile of tenapanor, which has been shown across all clinical trials, was further supported by the completed T3MPO-3 study.

We have developed a proprietary drug discovery and design platform to discover targets found in the GI tract that regulate processes in the body and design products candidates that act upon those targets to take advantage of the gut's ability to communicate with other organs.

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Since commencing operations in October 2007, substantially all our efforts have been dedicated to our research and development activities, including developing our clinical product candidate tenapanor and developing our proprietary drug discovery and design platform. We have not generated any revenues from product sales and have no products approved for commercialization. As of December 31, 2018, we had an accumulated deficit of $365.5 million.

On May 16, 2018, we entered into a loan and security agreement, or the Loan Agreement, with Solar Capital Ltd. and Western Alliance Bank. The Loan Agreement provides for a $50.0 million term loan facility with a maturity date of November 1, 2022. The full amount of the loan was funded on May 16, 2018. We received net proceeds from the loan of $49.3 million, after deducting the closing fee, legal expenses and issuance cost.

On May 25, 2018, we completed an underwritten public offering of 12,500,000 shares of our common stock at a price to the public of $4.00 per share, that were purchased by Jefferies LLC, or Jefferies, and Leerink Partners LLC, or Leerink, as representatives of several underwriters, or collectively the Underwriters, from the Company at a price of $3.76 per share, and on June 25, 2018, we sold an additional 1,875,000 shares of our common stock at a price to the public of $4.00 per share, that were purchased by the Underwriters from the Company at a price of $3.76 per share, following the full exercise of the underwriters' option to purchase additional shares of common stock. We received net proceeds from the offering of $53.8 million, after deducting the underwriting discounts, commissions and offering expenses.

We expect to incur operating losses for the foreseeable future as a result of our continued development of tenapanor and our preparations for the commercialization of tenapanor, including costs associated with completing the on-going Phase 3 development program for tenapanor for the treatment of hyperphosphatemia in patients with ESRD on dialysis, as well as the advancement of our research programs into the preclinical stage. To date, we have funded our operations from the sale and issuance of common stock, convertible preferred stock, funds from our former collaboration partnerships, funds from license agreements, and funds from our Loan Agreement with Solar Capital Ltd. and Western Alliance Bank.

FINANCIAL OPERATIONS OVERVIEW

Revenue

We have not generated any revenue from product sales. Prior to 2017, our revenue to date had been generated from non-refundable license payments and reimbursements for research and development expenses under license agreements with AstraZeneca AB, or AstraZeneca, and Sanofi, S.A., or Sanofi, both of which were terminated in 2015. We recognized revenue from upfront payments ratably over the term of our estimated period of performance under those agreements, which we recorded as licensing revenue. Reimbursements from AstraZeneca for development costs incurred under our license and collaboration agreement with them were classified as collaborative development revenue. There has been no recognition of collaborative development revenue since the termination of the AstraZeneca agreement in 2015.

In 2017, we executed license agreements with Kyowa Hakko Kirin Co., Ltd., or KHK, and Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd., or Fosun Pharma, for the development, commercialization and distribution of tenapanor for certain uses in Japan and China, respectively. Under the terms of the KHK and Fosun Pharma license agreements, the Company received an aggregate of $30.0 million and $12.0 million, respectively, in non-refundable up-front license fees. These amounts were recorded as revenue when the contracts were executed. These agreements also contain milestone payments, which will be recorded as revenue when we achieve the underlying milestone. See "ITEM 1. BUSINESS—OUR PRODUCT PIPELINE— Tenapanor: A New Approach for Treating Hyperphosphatemia in ESRD Patients on Dialysis" for additional detail regarding the KHK and Fosun Pharma license agreements

During the first quarter of 2018, we executed a license agreement with Knight Therapeutics, Inc., or Knight, for the development, commercialization and distribution of tenapanor for hyperphosphatemia and IBS-C in Canada. Under the terms of the Knight license agreement, the Company received a nonrefundable payment of CAD 3 million, or U.S. $2.3 million, in up-front license fees, which was recorded as revenue when the contract was executed. The agreement

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also provides for development and commercialization milestone payments, which will be recorded as revenue when we achieve the underlying milestone.

Our past revenue performance is not necessarily indicative of results to be expected for the future operating periods. Our non-product revenue cannot always be predicted since it is dependent upon achievement of certain milestones.

On January 1, 2018 we adopted the new standard for Revenue from Contracts with Customers, ASC 606, on a modified retrospective method as an adjustment to the opening balance of retained earnings of the annual reporting period. See “Note 2. Summary Of Significant Accounting Policies” under Revenue Recognition, for further detail.

Cost of Revenue

Cost of revenue represents payments due to AstraZeneca, who under the terms of a termination agreement entered into in 2015 are entitled to (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should we elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, up to a maximum of $75.0 million in aggregate for (i) and (ii). We recognize these expenses as cost of revenue when we recognize the revenue that generates our liability for these license payments. To date in aggregate, we have recognized $9.9 million of the $75.0 million, recorded as cost of revenue comprising (i) $6.0 million and $2.4 million related to the KHK license agreement and Fosun Pharma license agreement, respectively, recorded in 2017 (ii) $0.5 million related to the Knight license agreement recorded in the year ended December 31, 2018 and (iii) $1.0 million related to the KHK license agreement associated with a milestone that KHK achieved in February 2019.

Research and Development Expenses

We recognize all research and development expenses as they are incurred to support the discovery, development and manufacturing of our product candidates. Research and development expenses consist of the following:

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

We expect to continue to make substantial investments in research and development activities as we progress the development of tenapanor, as well as our other product candidates, advance our research programs into the preclinical stage and continue our early stage research. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for any of our product candidates, including tenapanor. Additionally, if marketing approval is received for tenapanor for the treatment of IBS-C, we may not be successful in securing one or more collaboration partners to commercialize tenapanor in the United States and other territories. The probability of success of each of the product candidates may be affected by numerous factors, including preclinical data, clinical data, market acceptance, sufficient third-party coverage or reimbursement, our ability to access capital on acceptable terms, competition, manufacturing capability and commercial viability.

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We anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to the scientific and clinical success of each product candidate, ongoing assessment as to each product candidate's commercial potential, and our ability to access capital on acceptable terms. We will need to raise additional capital and will seek additional collaboration partnerships in order to complete the development and commercialization of tenapanor. If we are unable to access capital on a timely basis and on terms that are acceptable to us, we may be forced to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor or certain of our product candidates through the use of alternative structures.

General and Administrative

General and administrative expenses consist primarily of salaries and related costs, including stock-based compensation. Other general and administrative expenses include facility related costs and professional fees for legal, accounting, investor relations and other consulting services.

We anticipate that our general and administrative expenses will increase in the future primarily because of (i) increased pre-commercial activities, personnel costs and professional fees for services to support the potential launch and commercialization of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis and (ii) expenses related to costs of operating as a public company primarily preparing for future integrated audits.

Provision for Income Taxes

The provision for income taxes was not material for year ending December 31, 2018, $1.2 million for year ending December 31, 2017 and zero for year ending December 31, 2016. We have a net loss for all three years ending December 31, 2018. Our deferred tax assets continue to be fully offset by a valuation allowance.

The Tax Cuts and Jobs Act of 2017, or TCJA, makes broad and complex changes to the U.S. tax code, including, but not limited to, reducing the U.S. federal corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, effective January 1, 2018. The Company is able to determine a reasonable estimate of certain effects of the TCJA and has therefore recognized the provisional tax impacts related to the revaluation of deferred tax assets and liabilities. As a result, the Company has recorded a decrease related to net deferred tax assets of $35.6 million, with an offsetting change in valuation allowance of $35.6 million for the year ended December 31, 2017. The SEC has provided accounting and reporting guidance that allows the Company to report provisional amounts within a measurement period of up to one year from the date of enactment due to the complexities inherent in adopting the TCJA. The Company completed its analysis during the measurement period and there were no measurement period adjustments recognized during the reporting period.

CRITICAL ACCOUNTING POLICES AND ESTIMATES

A detailed discussion of our significant accounting policies can be found in Note 1 of the Notes to Consolidated Financial Statements in Part II, Item 8, and the impact and risks associated with our accounting policies are discussed throughout this Annual Report on Form 10 K and in the footnotes to the financial statements. Critical accounting policies are those that require significant judgment and/or estimates by management at the time that financial statements are prepared such that materially different results might have been reported if other assumptions had been made. We consider certain accounting policies related to revenue recognition, accrued liabilities, and use of estimates to be critical policies. These estimates form the basis for making judgments about the carrying values of assets and liabilities. We base our estimates and judgments on historical experience and on various other assumptions that we

believe to be reasonable under the circumstances. Actual results could differ materially from these estimates.

We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain.

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Revenue Recognition

On January 1, 2018 we adopted the new standard for Revenue from Contracts with Customers, ASC 606, on a modified retrospective method as an adjustment to the opening balance of retained earnings of the annual reporting period. As a result of the adoption of the new standard, on January 1, 2018, we recorded the following: (i) an increase in current assets of $5.0 million representing a receivable related to the first milestone under our KHK license agreement, which was achieved by KHK in February 2019, (ii) an increase in current liabilities of $1.0 million representing a payable related to the corresponding payment to AstraZeneca in accordance with our termination agreement with AstraZeneca and (iii) a related decrease in its accumulated deficit of approximately $4.0 million as the new standard permits revenue from milestones that possess certain criteria to be recognized earlier as the new standard contains different recognition criteria related to milestones than under the previous standard, Revenue Recognition, Multiple-Element Arrangements - Licensing revenues, ASC 605.

We enter into licensing agreements which are within the scope of ASC 606, under which we license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us of one or more of the following: non-refundable, up-front license fees; development, regulatory and commercial milestone payments; and future royalties on net sales of licensed products. Each of these payments results in license, collaboration and other revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under each of our agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

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

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer’s discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If we are entitled to additional payments when the customer exercises these options, any payments are recorded in other revenues when the customer obtains control of the goods, which is upon delivery.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty

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has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our licensing arrangements.

Accrued Research and Development Expenses

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

· CROs in connection with clinical studies;
· investigative sites in connection with clinical studies;
· vendors related to product manufacturing, development and distribution of clinical supplies;
· collaborator entities in connection with our collaboration agreements; and
· vendors in connection with preclinical development activities.

We record expenses related to clinical studies and manufacturing development activities based on our estimates of the services received and efforts expended pursuant to contracts with our CROs and manufacturing vendors that conduct and manage these activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which each component of a service will be performed, and estimate, with vendor input if appropriate, the resulting level of completion of each component of the service, with such estimates often involving drivers that provide a surrogate measurement of completion such as number of enrolled subjects and/or number of sites activated in the calculation of clinical trial fee accruals. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrued or prepaid expense balance accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amounts actually incurred.

Stock-Based Compensation

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

Expected Term—We have limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock-option grants. As such, the expected term is estimated using the simplified method whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option.

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Expected Volatility— Since January 1, 2017, we have used 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. Prior to December 31, 2016, our stock had not been publicly traded for a sufficient period to enable us to use our own historic volatility, so the expected volatility was calculated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle, and financial leverage of the Company.

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.

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

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

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

RESULTS OF OPERATIONS

Comparison of the Years Ended December 31, 2018 and 2017

Revenue

	Year Ended December 31,	
	2018	2017
Licensing revenue	$ 2,320	$ 42,000
Other revenue	287	—
Total revenues	2,607	42,000
Dollar change from prior year	(39,393)	
Percent change from prior year	(94) %	

Total revenue was $2.6 million for the year ended December 31, 2018, a decrease of $39.4 million, or 94%, compared to $42.0 million for the year ended December 31, 2017. Total revenue of $2.6 million in the year ended December 31, 2018 included $2.3 million of licensing revenue related to the upfront payment from Knight and $0.3 million of other revenue related to the manufacturing supply of tenapanor and other materials to KHK, for KHK's product development and clinical trials in Japan, in accordance with our license agreement with KHK. Total revenue of $42.0 million in the year ended December 31, 2017 was comprised of licensing revenue related to upfront payments in accordance with our KHK and Fosun Pharma license agreements.

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Cost of revenue

	Year Ended December 31,	
	2018	2017
Cost of revenue	$ 466	$ 8,400
Dollar change from prior year	(7,934)	
Percent change from prior year	(94) %	

Cost of revenue was $0.5 million for the year ended December 31, 2018, a decrease of $7.9 million, or 94%, compared to $8.4 million for the year ended December 31, 2017. The cost of revenue in both periods represented license payments due to AstraZeneca. AstraZeneca, under the terms of a termination agreement entered into in 2015, is entitled to (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should we elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, with the maximum amount due to AstraZeneca for royalties and non-royalty revenue not to exceed $75.0 million in aggregate for (i) and (ii).

Research and Development

	Year Ended December 31,	
	2018	2017
Research and development	$ 69,373	$ 75,484
Dollar change from prior year	(6,111)	
Percent change from prior year	(8) %	

Research and development expenses were $69.4 million for the year ended December 31, 2018, a decrease of $6.1 million, or 8%, compared to $75.5 million for the year ended December 31, 2017. The decrease consisted of a $1.1 million decrease in our external program costs and a $5.0 million decrease in our internal program costs.

The decrease in our external program costs of $1.1 million included a $11.7 million decrease due to discontinuation of the RDX7675 program and a $1.7 million reduction of activities associated with the RDX8940 program that was partially offset by a $12.3 million increase in expense primarily related to our tenapanor programs. The $12.3 million increase included an increase in expense related to the start of our second tenapanor hyperphosphatemia Phase 3 study that was partially offset by a decrease in expenses for clinical development activities related to the completion of our tenapanor IBS-C Phase 3 clinical program as well as our first tenapanor hyperphosphatemia Phase 3 clinical trial.

The decrease in our internal costs of $5.0 million was primarily due to a decrease in personnel costs, including stock-based compensation costs as a result of a reduction in force during the third quarter of 2017, and a related decrease in research and development activities.

General and Administrative

	Year Ended December 31,	
	2018	2017
General and administrative	$ 23,715	$ 23,231
Dollar change from prior year	484	
Percent change from prior year	2 %	

General and administrative expenses were $23.7 million for the year ended December 31, 2018, an increase of $0.5 million, or 2%, compared to $23.2 million for the year ended December 31, 2017. The increase was primarily due to an increase in professional services and stock-based compensation expense, partially offset by a reduction in personnel costs due to reduction in force during the third quarter of 2017.

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Comparison of the Years Ended December 31, 2017 and 2016

Revenue

	Year Ended December 31,	
	2017	2016
	(in thousands)	
Licensing revenue	$ 42,000	$ —
Dollar change from prior year	42,000	
Percent change from prior year	*	%

* not meaningful

Licensing revenue for the year ended December 31, 2017, was $42.0 million, an increase of $42.0 million compared to the year ended December 31, 2016, when we generated no licensing revenue. Licensing revenue for 2017 was related to the recognition of revenue from upfront payments under our KHK and Fosun Pharma license agreements.

Cost of revenue

	Year Ended December 31,	
	2017	2016
	(in thousands)	
Cost of revenue	$ 8,400	$ —
Dollar change from prior year	8,400	
Percent change from prior year	*	%

* not meaningful

Cost of revenue for the year ended December 31, 2017, was $8.4 million, an increase of $8.4 million compared to the year ended December 31, 2016, when we generated no revenue and therefore incurred no related costs. Cost of revenue represents license payments due to AstraZeneca, which under the terms of a termination agreement entered into in 2015 is entitled to (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should we elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, with the maximum amount due AstraZeneca for royalties and non-royalty revenue not to exceed $75.0 million in aggregate for (i) and (ii).

Research and Development

	Year Ended December 31,	
	2017	2016
	(in thousands)	
Research and development	$ 75,484	$ 94,161
Dollar change from prior year	(18,677)	
Percent change from prior year	(20) %	

Research and development expenses were $75.5 million for the year ended December 31, 2017, a decrease of $18.7 million, or 20%, compared to $94.2 million for the year ended December 31, 2016. The decrease consisted of a $23.8 million decrease in our external program costs, partially offset by a $5.1 million increase in our internal program costs.

The decrease in our external program costs of $23.8 million was primarily due to a decrease of $22.3 million in expenses incurred for clinical development activities related to the completion of our T3MPO Phase 3 clinical program for tenapanor, our first Phase 3 clinical trial evaluating tenapanor for the treatment of hyperphosphatemia patients with

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ESRD on dialysis and a decrease in manufacturing development activities related to tenapanor. In addition, expenses incurred for clinical development activities, clinical manufacturing and process development activities associated with RDX8940 decreased by $3.2 million. These decreases were offset by an increase of $1.7 million in expenses incurred primarily for clinical development activities associated with RDX7675, including costs associated with the termination of that program.

The increase in our internal costs of $5.1 million was primarily due to an increase in salaries and related costs, including stock-based compensation, facilities-related costs, principally related to supporting the growth of our development team and severance costs relating to our reduction in workforce in the third quarter 2017.

General and Administrative

	Year Ended December 31,	
	2017	2016
	(in thousands)	
General and administrative	$ 23,231	$ 18,734
Dollar change from prior year	4,497	
Percent change from prior year	24 %	

General and administrative expenses were $23.2 million for the year ended December 31, 2017, an increase of $4.5 million, or 24%, compared to $18.7 million for the year ended December 31, 2016. The increase was primarily due to increases in salaries and related costs, including stock-based compensation and facilities costs including depreciation expense, due to an increase in headcount and an expansion of facilities late in 2016, increased legal fees, and severance costs due to the refocusing of resources towards late-stage programs and subsequent reduction in the workforce in the third quarter of 2017, offset by reductions in certain professional services.

LIQUIDITY AND CAPITAL RESOURCES

	December 31,	
	2018	2017
Cash and cash equivalents	78,768	75,383
Short-term investments	89,321	58,593
Total liquid funds	$ 168,089	$ 133,976

As of December 31, 2018, we had cash, cash equivalents and short-term investments totaling $168.1 million compared to $134.0 million as of December 31, 2017.

In January 2016, we completed an underwritten public offering of 8,625,000 shares of common stock at an offering price of $10.00 per share for gross proceeds of $86.3 million. This offering was completed under our shelf registration statement filed on July 13, 2015, and we received net proceeds from the offering of approximately $80.8 million, after deducting the underwriters' discounts and commissions and offering expenses.

In July 2016, we sold and issued an aggregate of 12,600,230 shares of common stock in a private placement transaction at an offering price of $8.73 per share for gross proceeds of $110.0 million. We received net proceeds from

the offering of approximately $109.8 million, after deducting offering expenses.

In November and December 2017, we executed license agreements with KHK and Fosun Pharma for the development, commercialization and distribution of tenapanor for certain indications in Japan and China, respectively, under which we were entitled to an aggregate of $30.0 million and $12.0 million, respectively, in up-front license fees. The $30.0 million was collected by December 31, 2017 and the remaining $12.0 million, less $1.2 million of withholding taxes, was collected in January 2018. We accrued a liability of $8.4 million to AstraZeneca in accordance with the terms of our termination agreement with AstraZeneca entered into in 2015, of which $6.0 million was paid by December 31, 2017 and the remainder of which was paid in February 2018.

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In March 2018, we entered into an exclusive license agreement with Knight for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. In March and April 2018, we collected $2.3 million related to the Knight license agreement, and $0.5 million of cost of revenue was paid pursuant to the AstraZeneca Termination Agreement.

On May 16, 2018, we entered into a loan and security agreement, or the Loan Agreement, with Solar Capital Ltd. and Western Alliance Bank. The Loan Agreement provides for a $50.0 million term loan facility with a maturity date of November 1, 2022. The full amount of the loan was funded on May 16, 2018. We received net proceeds from the loan of $49.3 million, after deducting the closing fee, legal expenses and issuance cost.

On May 25, 2018, we completed an underwritten public offering of 12,500,000 shares of our common stock at a price to the public of $4.00 per share, that were purchased by the Underwriters from the Company at a price of $3.76 per share, and on June 25, 2018, we sold an additional 1,875,000 shares of our common stock at a price to the public of $4.00 per share, that were purchased by the Underwriters from the Company at a price of $3.76 per share, following the full exercise of the underwriters' option to purchase an additional shares of common stock. We received net proceeds from the offering of $53.8 million, after deducting the underwriting discounts, commissions and offering expenses.

On August 9, 2018, we filed a prospectus supplement with the SEC pursuant to our previously filed shelf registration statement on Form S-3 (File No. 333-217441). The prospectus covers the offering, issuance and sale of up to $50.0 million of shares of common stock from time to time in "at the market" offerings pursuant to a Sales Agreement entered into with Leerink on August 9, 2018. As of December 31, 2018, no shares have been offered or issued or sold against the Sales Agreement with Leerink.

Our primary sources of cash have been from the sale and issuance of common stock, convertible preferred stock, funds from our former collaboration partnerships, funds from license agreements, and funds from our Loan Agreement with Solar Capital Ltd. and Western Alliance Bank. Our primary uses of cash are to fund operating expenses, primarily research and development expenditures, as well as general administrative expenditures and our obligations related to our license termination agreement with AstraZeneca. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe that our existing capital resources as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements for at least the next 12 months following our financial statement issuance date. 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 can change, and we may require significant additional capital to fund our operations, including to support the development, commercialization and manufacturing efforts for tenapanor. We may seek to obtain such additional capital through debt financings, credit facilities, additional equity offerings and/or strategic collaborations. We currently have no unutilized credit facility or committed sources of capital, and there can be no assurances that such sources of capital will be available to us when needed or on acceptable terms. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we may be able to secure additional collaboration partnerships with third-parties to participate in the development and commercialization of our potential products, our future funding requirements will depend on many factors, including the following:

- the progress, timing, scope, results and costs of our clinical trial program evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis alone and in combination with phosphate binders, and if our clinical programs are successful, the submission of an NDA with the FDA to request marketing authorization for tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis and as an adjunctive therapy with

phosphate binders, as well as our decision whether or not to pursue other indications for tenapanor;

- whether or not we receive approval from the FDA to market tenapanor for the treatment of patients with IBS-C;
- our ability to identify a collaboration partner and negotiate acceptable terms for a collaboration partnership for the commercialization of tenapanor in IBS-C in the United States;

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- our ability to successfully commercialize tenapanor, if approved, either alone or with one or more collaboration partners;
- the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;
- the selling and marketing costs associated with tenapanor, including the cost and timing of building our sales and marketing capabilities, should we elect to do so;
- 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 sales of, or royalties on, tenapanor, if any;
- the sales price and the availability of adequate third-party reimbursement for tenapanor, if approved;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate, and any clinical trials we decide to pursue for other 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, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into with Solar Capital and Western Alliance Bank during May 2018.

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		
	2018	2017	2016
Cash used in operating activities	$ (70,274)	$ (65,190)	$ (92,534)
Cash (used in) provided by investing activities	(29,894)	65,290	(131,076)
Cash provided by financing activities	103,553	685	191,204
Net increase (decrease) in cash and cash equivalents	$ 3,385	$ 785	$ (32,406)

Cash Flows from Operating Activities

Net cash used in operating activities during the year ended December 31, 2018, was approximately $70.3 million. The net loss of $91.3 million was adjusted for (i) non-cash charges of $2.4 million related to depreciation, amortization, non-cash interest expense and change in derivative liabilities and $9.2 million for stock-based compensation, (ii) a decrease of $10.7 million in accounts receivable related to the Fosun Pharma license upfront fee received, (iii) a $0.5 million decrease in prepaid expenses primarily advances to vendors for clinical development and manufacturing, and (iv) a decrease in accounts payable and accrued liabilities of $1.8 million primarily due to expenses incurred for the clinical manufacturing, process development, and clinical development activities for tenapanor.

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Net cash used in operating activities during the year ended December 31, 2017, was approximately $65.2 million. The net loss of $64.3 million was adjusted for (i) non-cash charges of $3.2 million for depreciation and amortization and $9.6 million for stock-based compensation, (ii) an increase of $10.8 million in accounts receivable, solely related to the Fosun Pharma license upfront fee after withholding taxes, (iii) an increase of $2.1 million in prepaid expenses and (iv) a decrease in accounts payable and accrued liabilities of $0.7 million primarily due to expenses incurred for the clinical manufacturing, process development, and clinical development activities for tenapanor and RDX7675.

Net cash used in operating activities during the year ended December 31, 2016, was approximately $92.5 million. The net loss of $112.4 million was adjusted for (i) an increase of accounts payable and accrued liabilities of $11.2 million primarily due to expenses incurred for the clinical manufacturing, process development, and clinical development activities for tenapanor, RDX7675 and RDX8940, (ii) non-cash charges of $1.8 million for depreciation and amortization and $5.3 million for stock-based compensation and (iii) pre-payments of $1.6 million to vendors for clinical development and manufacturing activities.

Cash Flows from Investing Activities

Net cash used in investing activities was $29.9 million for the year ended December 31, 2018, primarily due to purchases of short-term investments of $169.0 million and purchase of property and equipment of $0.3 million offset by maturities of short-term investments and redemptions of $139.4 million.

Net cash provided by investing activities was $65.3 million for the year ended December 31, 2017, primarily due to maturities and sales, less purchases, of short-term investments of $67.7 million. This was offset by the acquisition of property and equipment of $2.4 million related to the purchase of laboratory equipment and leasehold improvements.

Net cash used by investing activities was $131.1 million for the year ended December 31, 2016, primarily due to purchases of marketable securities of $133.8 million and acquisition of property and equipment of $4.9 million related to the expansion of our laboratory and related equipment. These uses of cash were partially offset by maturities of short-term investments of $7.6 million.

Cash Flows from Financing Activities

Net cash provided by financing activities for the year ended December 31, 2018, was $103.6 million, primarily due to (i) net proceeds of $53.8 million from an underwritten public offering of our common stock in 2018 after deducting the underwriting discounts and commissions and offering expenses, (ii) net proceeds of $49.3 million from the term loan provided by Solar Capital Ltd. and Western Alliance Bank after deducting the closing fee, legal expenses and issuance costs, and (iii) net proceeds of $0.5 million from issuance of common stock under the employee stock purchase plan, or ESPP.

Net cash provided by financing activities for the year ended December 31, 2017, was $0.7 million, due to proceeds from issuance of common stock under ESPP.

Net cash provided by financing activities for the year ended December 31, 2016, was $191.2 million and was primarily due to net proceeds of $190.6 million from public and private offerings of our common stock.

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CONTRACTUAL OBLIGATIONS AND OTHER COMMITMENTS

	Payments Due by Period (in thousands)				
Contractual Obligation:	Less than 1 year	1 to 3 Years	3 to 5 Years	More Than 5 Years	Total
Lease obligations (1)	$ 2,697	$ 5,329	$ —	$ —	$ 8,026
Contract manufacturing obligations (2)	—	682	1,364	1,365	3,411
Long-term debt obligations (3)	5,193	37,050	26,081	—	68,324
Total contractual obligations	$ 7,890	$ 43,061	$ 27,445	$ 1,365	$ 79,761

(1) These amounts are comprised of total future estimated remaining payments under our non-cancelable existing operating lease agreements.
(2) These amounts are comprised of contractual obligations related to minimum purchase commitment of drug supply for our proposed commercial supply of our product candidates.
(3) The long-term debt obligation is comprised of a Loan and Security Agreement that was executed in May 2018 and includes estimated principle and interest payments thereupon.

OFF-BALANCE SHEET ARRANGEMENTS

As of December 31, 2018, we did not have any off-balance sheet arrangements as defined in Item 303(a)(4) of Regulation S-K as promulgated by the SEC.

RECENT ACCOUNTING PRONOUNCEMENTS

Refer to Note 2 in the notes to our consolidated financial statements in Part I, Item 8 of this Annual Report on Form 10 K, for a discussion of new accounting pronouncements.

JOBS ACT ACCOUNTING ELECTION

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. In addition, as an emerging growth company, we have reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will remain an emerging growth company until December 31, 2019.

SMALLER REPORTING COMPANY

On June 28, 2018, the SEC adopted amendments that raise the thresholds in the smaller reporting company, or SRC, definition, whereby we were determined to qualify as an SRC. We elected to reflect that determination and avail ourselves with most of the SRC scaled disclosure accommodations in our subsequent filings.

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ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include risk related to interest rate sensitivities. We had cash, cash equivalents and short-term investments of $168.1 million as of December 31, 2018, which consist of bank deposits and money market funds, as well as high quality fixed income instruments including corporate bonds, commercial paper, and asset-backed securities collateralized by non-mortgage consumer receivables. 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 AAAm/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 a 10% movement in market interest rates would not have a significant impact on the total value of our portfolio, as specified below. We do not enter into investments for trading or speculative purposes.

We are subject to interest rate fluctuation exposure both through our borrowings under the Loan Agreement and our investment in money market accounts each of which bears a variable interest rate. Borrowings under the Loan Agreement bear interest at a rate equal to one-month LIBOR plus 7.45% per annum. A hypothetical increase in one-month LIBOR of 100 basis points above the current one-month LIBOR rates would have increased our interest expense by approximately $0.4 million as of December 31, 2018. We had $49.2 million aggregate principal amount of loan outstanding as of December 31, 2018.

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

Foreign Currency Exchange Risk

The majority of our transactions occur in U.S. dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. dollar, primarily, Swiss francs and the euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. dollar against other currencies affects the reported amounts of expenses, assets and liabilities. During the year ended December 31, 2018, we entered into forward currency exchange contracts denominated in Swiss francs, that are not designated as cash flow hedges, to secure a foreign currency exchange rate to minimize cash flow exposure to fluctuating exchange rates.

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 counterparty to these forward foreign currency exchange contracts is a creditworthy commercial bank, which minimizes the risk of counterparty nonperformance.

As of December 31, 2018, we had open forward foreign currency exchange contracts with notional amounts of $3.4 million. A hypothetical 10% strengthening in foreign currency exchange rates compared with the U.S. dollar relative to exchange rates at December 31, 2018 would have resulted in a reduction in the value of the Swiss francs, expressed in U.S. Dollars, of approximately $0.4 million which would negatively affect earnings during the remaining life of the contracts.

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ITEM 8. CONSOLIDATED FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

ARDELYX, INC.
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Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ardelyx, Inc. (the Company) as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

Adoption of ASU No. 2014-09

As discussed in Note 2 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), and the related amendments effective January 1, 2018.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

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

Redwood City, California

March 6, 2019

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ARDELYX, INC.

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share amounts)

	December 31, 2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 78,768	$ 75,383
Short-term investments	89,321	58,593
Accounts receivable	85	10,796
Unbilled license revenue	5,000	—
Prepaid expenses and other current assets	3,197	4,940
Total current assets	176,371	149,712
Property and equipment, net	5,611	8,032
Other assets	1,350	159
Total assets	$ 183,332	$ 157,903
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,148	$ 3,933
Accrued compensation and benefits	2,723	3,229
Uncharged license fees	1,000	—
Accrued and other liabilities	12,857	10,709
Total current liabilities	17,728	17,871
Loan payable, long term	49,209	—
Other long-term liabilities	582	720
Total liabilities	67,519	18,591
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized; no shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively.	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized; 62,516,627 and 47,534,979 shares issued and outstanding as of December 31, 2018 and December 31, 2017, respectively.	6	5
Additional paid-in capital	481,357	417,568
Accumulated deficit	(365,512)	(278,214)
Accumulated other comprehensive loss	(38)	(47)
Total stockholders' equity	115,813	139,312
Total liabilities and stockholders' equity	$ 183,332	$ 157,903

See accompanying notes.

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ARDELYX, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share amounts)

	Year Ended December 31,		
	2018	2017	2016
Revenues:			
Licensing revenue	$ 2,320	$ 42,000	$ —
Other revenue	287	—	—
Total revenues	2,607	42,000	—
Cost of revenue	466	8,400	—
Gross profit	2,141	33,600	—
Operating expenses:			
Research and development	69,373	75,484	94,161
General and administrative	23,715	23,231	18,734
Total operating expenses	93,088	98,715	112,895
Loss from operations	(90,947)	(65,115)	(112,895)
Interest expense	(3,534)	—	—
Other income (expense), net	3,187	1,955	508
Loss before provision for income taxes	(91,294)	(63,160)	(112,387)
Provision for income taxes	4	1,179	—
Net loss	$ (91,298)	$ (64,339)	$ (112,387)
Net loss per common share, basic and diluted	$ (1.62)	$ (1.36)	$ (2.80)
Shares used in computing net loss per share - basic and diluted	56,219,919	47,435,331	40,118,522
Comprehensive loss:			
Net loss	$ (91,298)	$ (64,339)	$ (112,387)
Unrealized gain (loss) on available-for-sale securities, net of tax	9	24	(71)
Comprehensive loss	$ (91,289)	$ (64,315)	$ (112,458)

See accompanying notes.

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ARDELYX, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands, except share amounts)

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive Income	Total Stockholders'
	Shares	Amount	Capital	Deficit	(Loss)	Equity
Balance as of December 31, 2015	25,964,886	$ 3	$ 210,386	$ (101,488)	$ —	$ 108,901
Issuance of common stock in connection with PIPE, net of expenses of $263	12,600,230	1	109,735	—	—	109,736
Issuance of common stock in connection with public offering, net of expenses of $5,413	8,625,000	1	80,836	—	—	80,837
Issuance of common stock under employee stock purchase plan	69,054	—	576	—	—	576
Issuance of common stock for services	20,118	—	187	—	—	187
Issuance of common stock upon exercise of options	25,134	—	55	—	—	55
Issuance of common stock upon vesting of restricted stock units	5,000	—	—	—	—	—
Stock-based compensation	—	—	5,317	—	—	5,317
Other comprehensive loss	—	—	—	—	(71)	(71)
Net loss	—	—	—	(112,387)	—	(112,387)
Balance as of December 31, 2016	47,309,422	$ 5	$ 407,092	$ (213,875)	$ (71)	$ 193,151
Issuance of common stock under employee stock purchase plan	99,343	—	623	—	—	623
Issuance of common stock for services	46,858	—	201	—	—	201
Issuance of common stock upon exercise of options	35,759	—	62	—	—	62
Issuance of common stock upon vesting of restricted stock units	43,597	—	—	—	—	—
Stock-based compensation	—	—	9,590	—	—	9,590
Other comprehensive income	—	—	—	—	24	24

Net loss	—	—	—	(64,339)	—	(64,339)
Balance as of December 31, 2017	47,534,979	$ 5	$ 417,568	$ (278,214)	$ (47)	$ 139,312
Issuance of common stock under employee stock purchase plan	120,959	—	491	—	—	491
Issuance of common stock for services	75,183	—	303	—	—	303
Issuance of common stock upon exercise of options	—	—	—	—	—	—
Issuance of common stock upon vesting of restricted stock units	410,506	—	—	—	—	—
Stock-based compensation	—	—	9,226	—	—	9,226
Other comprehensive income	—	—	—	—	9	9
Issuance of common stock upon underwritten public offering	14,375,000	1	53,769	—	—	53,770
Adoption of ASU No. 2014-09 on January 1, 2018	—	—	—	4,000	—	4,000
Net loss	—	—	—	(91,298)	—	(91,298)
Balance as of December 31, 2018	62,516,627	$ 6	$ 481,357	$ (365,512)	$ (38)	$ 115,813

See accompanying notes.

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ARDELYX, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Operating activities			
Net loss	$ (91,298)	$ (64,339)	$ (112,387)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation expense	2,678	2,639	1,295
Amortization of deferred financing costs	236	375	346
Amortization of deferred compensation for services	253	192	194
Amortization of premium on investment securities	(1,136)	11	(86)
Stock-based compensation	9,226	9,590	5,317
Change in derivative liabilities	111	—	—
Non-cash interest associated with debt discount accretion	303	—	—
Changes in operating assets and liabilities:			
Accounts receivable	10,711	(10,796)	—
Prepaid expenses and other assets	525	(2,148)	1,562
Accounts payable	(2,730)	(1,027)	2,148
Accrued compensation and benefits	(506)	68	795
Accrued and other liabilities	1,353	245	8,282
Net cash used in operating activities	(70,274)	(65,190)	(92,534)
Investing activities			
Proceeds from maturities of investments	138,600	133,701	7,600
Sales and redemptions of investments	850	17,957	—
Purchases of investments	(169,033)	(84,013)	(133,810)
Purchases of property and equipment	(311)	(2,355)	(4,866)
Net cash (used in) provided by investing activities	(29,894)	65,290	(131,076)
Financing activities			
Proceeds from loan payable, net of issuance costs	49,292	—	—
Proceeds from issuance of common stock, net of issuance costs	53,770	—	190,573
Proceeds from issuance of common stock under stock plans	491	685	631
Net cash provided by financing activities	103,553	685	191,204
Net decrease in cash and cash equivalents	3,385	785	(32,406)
Cash and cash equivalents at beginning of period	75,383	74,598	107,004
Cash and cash equivalents at end of period	$ 78,768	$ 75,383	$ 74,598
Supplementary disclosure of cash flow information:			
Income taxes paid	$ 4	$ 3	$ —
Supplementary disclosure of non-cash financing information:			
Issuance of derivative in connection with issuance of loan payable	546	—	—
Acquisition of property and equipment included in accounts payable and accrued liabilities	$ —	$ 55	$ 730
Services settled through the issuance of common stock	$ 303	$ 201	$ 187

See accompanying notes.

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ARDELYX, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. ORGANIZATION AND BASIS OF PRESENTATION

Ardelyx, Inc., or "the Company," is a specialized biopharmaceutical company focused on developing first-in-class medicines to improve treatment choices for people with cardiorenal disease. Tenapanor, a first-in-class inhibitor of NHE3, is being evaluated in a second Phase 3 clinical trial for the treatment of hyperphosphatemia in patients with end-stage renal disease, or ESRD, who are on dialysis and in an additional Phase 3 clinical trial as an adjunctive therapy with phosphate binders in the same patient population. The Company is also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia. In November 2018, the Company obtained acceptance of its New Drug Application, or NDA, from the United States Food and Drug Administration, or FDA, for tenapanor for the treatment of people with irritable bowel syndrome with constipation, or IBS-C.

The Company operates in only one business segment, which is the development of biopharmaceutical products.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation

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

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Ardelyx and its wholly-owned subsidiary, Ardelyx Cayman Islands, which was placed into voluntary liquidation in December 2017. Intercompany transactions and balances have been eliminated upon consolidation.

Use of Estimates

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

Liquidity

The Company has never been profitable on an annual basis and, as of December 31, 2018, the Company has an accumulated deficit of $365.5 million. The Company has incurred net losses of approximately $91.3 million, $64.3 million and $112.4 million in the years ended December 31, 2018, 2017 and 2016, respectively. The Company expects to continue to incur net operating losses for the foreseeable future, as the Company continues the development of, seeks regulatory approval for, and if approved, begins to commercialize and manufacture tenapanor, either directly by the Company or through one or more of its collaboration partners. The Company will need additional funding to support its future operating activities and adequate funding may not be available to the Company on acceptable terms,

or at all. The Company's failure to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the business, results of operations, and financial condition. The Company will need to generate significant revenues to achieve profitability and may never do so. The Company believes that its current available cash, cash equivalents and short-term investments will be sufficient to fund its planned expenditures and meet the Company's obligations for at least 12 months following its financial statement issuance date.

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Cash and Cash Equivalents

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

Short-Term Investments

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

Concentration of Credit Risk

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

Accounts Receivable

An allowance for doubtful accounts will be recorded based on a combination of historical experience, aging analysis, and information on specific accounts. Account balances will be written off against the allowance after all means of collection have been exhausted and the potential for recovery is considered remote. No provision was made for doubtful accounts as of December 31, 2018 or 2017.

Property and Equipment

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

Impairment of Long-Lived Assets

The carrying value of long-lived assets, including property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the asset may not be recoverable. An impairment loss is recognized when the total of estimated future undiscounted cash flows, expected to result from the use of the asset and its eventual disposition, are less than its carrying amount. Impairment, if any, would be assessed using discounted cash flows or other appropriate measures of fair value. Through December 31, 2018, there have been no such impairment losses.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences

are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

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Revenue Recognition

On January 1, 2018 the Company adopted the new standard for Revenue from Contracts with Customers, ASC 606, on a modified retrospective method as an adjustment to the opening balance of retained earnings of the annual reporting period. As a result of the adoption of the new standard, on January 1, 2018, the Company recorded the following: (i) an increase in current assets of $5.0 million representing a future receivable related to the first milestone under the Company's license agreement with Kyowa Hakko Kirin Co., Ltd., or KHK, that KHK achieved in February 2019, (ii) an increase in current liabilities of $1.0 million representing a future payable related to the corresponding payment to AstraZeneca AB, or AstraZeneca, in accordance with the Company's termination agreement with AstraZeneca and (iii) a related decrease in its accumulated deficit of approximately $4.0 million as the new standard permits revenue from milestones that possess certain criteria to be recognized earlier as the new standard contains different recognition criteria related to milestones than under the previous standard, Revenue Recognition, Multiple-Element Arrangements - Licensing revenues, ASC 605.

The Company enters into licensing agreements which are within the scope of ASC 606, under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; development, regulatory and commercial milestone payments; and future royalties on net sales of licensed products. Each of these payments results in license, collaboration and other revenues, except for revenues from royalties on net sales of licensed products, which are classified as royalty revenues.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Milestone Payments: At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration and other revenues and earnings in the period of adjustment.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the customer's discretion are generally considered as options. The Company assess if these options provide a material right to the licensee and if so, they are accounted for

as separate performance obligations. If the Company is entitled to additional payments when the customer exercises these options, any payments are recorded in other revenues when the customer obtains control of the goods, which is upon delivery.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company

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recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Research and Development Costs

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

Accrued Research and Development Expenses

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

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

The Company records expenses related to clinical studies and manufacturing development activities based on its estimates of the services received and efforts expended pursuant to contracts with multiple CROs and manufacturing vendors that conduct and manage these activities on its behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, the Company estimates the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the Company will adjust the accrued or prepaid expense balance accordingly. To date, there have been no material differences from the Company's estimates to the amounts actually incurred.

Stock-Based Compensation

The Company recognizes compensation expense for all stock-based payment awards made to employees and directors based on estimated fair values. For employee stock options, the Company determines the grant date fair value of the awards using the Black-Scholes option-pricing model and generally recognizes the fair value as stock-based compensation expense on a straight-line basis over the vesting period of the respective awards. For restricted stock and performance-based restricted stock, to the extent they are probable, the compensation cost for these awards is

based on the closing price of the Company's common stock on the date of grant and recognized as compensation expense on a straight-line basis over the requisite service period. Stock-based compensation expense is based on the value of the

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portion of stock-based payment awards that is ultimately expected to vest. As such, the Company's stock-based compensation is reduced for the estimated forfeitures at the date of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

The Company accounts for equity instruments issued to nonemployees based on their fair values on the measurement dates using the Black-Scholes option-pricing model. The estimated fair values of the options granted to nonemployees are remeasured as they vest. As a result, the noncash charge to operations for nonemployee options with vesting conditions is affected each reporting period by changes in the fair value of the Company's common stock.

Derivatives and Hedging Activities

The Company accounts for its derivative instruments as either assets or liabilities on the consolidated balance sheet and measures them at fair value. Derivatives are adjusted to fair value through other (expense) income, net in the consolidated statements of operations and comprehensive loss.

Comprehensive Loss

Comprehensive loss is composed of two components: net loss and other comprehensive income (loss). Other comprehensive income (loss) refers to gains and losses that under U.S. GAAP are recorded as an element of stockholders' equity, but are excluded from net loss.

Net Loss per Share

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

Recent Accounting Pronouncements

New Accounting Pronouncements - Recently Adopted

In August 2018, the SEC adopted amendments to certain disclosure requirements in Securities Act Release No. 33-10532, Disclosure Update and Simplification. These amendments eliminate, modify, or integrate into other SEC requirements certain disclosure rules. Among the amendments is the requirement to present an analysis of changes in stockholders' equity in the interim financial statements included in quarterly reports on Form 10-Q. The analysis, which can be presented as a footnote or separate statement, is required for the current and comparative quarter and year-to-date interim periods. The amendments are effective for all filings made on or after November 5, 2018. In light of the anticipated timing of effectiveness of the amendments and expected proximity of effectiveness to the filing date for most filers' quarterly reports, the SEC's Division of Corporate Finance issued a Compliance and Disclosure Interpretation related to Exchange Act Forms, or CDI – Question 105.09, that provides transition guidance related to this disclosure requirement. CDI – Question 105.09 states that the SEC would not object if the filer's first presentation of the changes in shareholders' equity is included in its Form 10-Q for the quarter that begins after the effective date of the amendments. As such, the Company adopted these SEC amendments on November 5, 2018 and will present the analysis of changes in stockholders' equity in its interim financial statements in its March 31, 2019 Form 10-Q. The Company does not anticipate that the adoption of these SEC amendments will have a material effect on the Company's financial position, results of operations, cash flows or shareholders' equity.

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, which amends the guidance for accounting for revenue from contracts with customers. This ASU supersedes the revenue recognition requirements in Topic 605, Revenue Recognition, and creates a new Topic 606, Revenue from Contracts with Customers. In 2015 and 2016, the FASB issued additional ASUs related to Topic 606 that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance, including principal versus agent considerations, identifying performance obligations, and licensing, and they include other improvements

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and practical expedients. The Company adopted this new standard on January 1, 2018 using the modified retrospective transition method.

Impact of Adoption

The Company, on adopting Topic 606 on January 1, 2018, has used the modified retrospective transition method with the cumulative effect of initially applying the standard as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application. The following adjustments were recorded in the opening balance on January 1, 2018.

	December 31, 2017	Adjustments Due to Topic 606	January 1, 2018
Total current assets	$ —	5,000	$ 5,000
Total current liabilities	—	1,000	1,000
Accumulated deficit	$ —	4,000	$ 4,000

As a result of adopting Topic 606 on January 1, 2018, the following financial statement line items in the Company's Consolidated Balance Sheet at December 31, 2018 and the Consolidated Statement of Income for the year ended December 31, 2018 were affected.

	December 31, 2018		
	As Reported	Under Topic 605	Effect of Change
Total current assets	$ 176,371	171,371	$ 5,000
Total current liabilities	17,728	16,728	1,000
Accumulated deficit	(365,512)	(369,512)	4,000

	Year Ended December 31, 2018		
	As Reported	Under Topic 605	Effect of Change
Revenue:			
Licensing revenue	$ 2,320	2,320	$ —
Other revenue	287	287	—
Cost of revenue	466	466	—

In May 2017, FASB issued ASU No. 2017-09, Compensation-Stock Compensation (Topic 718) - Scope of Modification Accounting (ASU 2017-09). The amendments included in this update provide guidance about which

changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting. The amendments in this update will be applied prospectively to an award modified on or after the adoption date.

New Accounting Pronouncements – Adoption on January 1, 2019

In February 2016, the FASB issued ASU No. 2016-02—Leases, (Topic 842) (ASU 2016-02), as amended, which generally requires lessees to recognize operating and financing lease liabilities and corresponding right-of-use assets on the balance sheet and to provide enhanced disclosures surrounding the amount, timing and uncertainty of cash flows arising from leasing arrangements. In July 2018, the FASB issued ASU No. 2018-11, Leases (Topic 842): Targeted Improvements, or ASU No. 2018-11. In issuing ASU No. 2018-11, the FASB is permitting another transition method for ASU 2016-02, which allows the transition to the new lease standard by recognizing a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. We will elect this transition method and package of practical expedients permitted under the transition guidance, which allows us to carryforward our historical lease classification, our assessment on whether a contract is or contains a lease, and our initial direct costs for any leases that exist prior to adoption of the new standard. We will also elect to combine lease and non-lease components and to keep leases with an initial term of 12 months or less off the balance sheet and recognize the associated lease payments in the statements of operations on a straight-line basis over the lease term. We will adopt the ASU on January 1, 2019 using a modified retrospective approach and are finalizing our assessment of the impact of the adoption of the ASU and expect to record a right-of-use asset and a

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corresponding lease liability to account for our facility lease as a cumulative-effect adjustment to the opening balance of accumulated deficit in the period of adoption.

In June 2018, the FASB issued ASU No. 2018-07, Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. ASU 2018-07 is intended to reduce the cost and complexity and to improve financial reporting for nonemployee share-based payments. ASU 2018-07 expands the scope of Topic 718, Compensation-Stock Compensation (which currently only includes share-based payments to employees) to include share-based payments issued to nonemployees for goods or services. Consequently, the accounting for share-based payments to nonemployees and employees will be substantially aligned. ASU 2018-07 supersedes Subtopic 505-50, Equity-Based Payments to Non-Employees. ASU 2018-07 is effective for the Company for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year and early adoption is permitted. The Company assessed there will be no material impact of this standard on its consolidated financial statements.

New Accounting Pronouncements Not Yet Adopted

In August 2018, the FASB issued ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement. ASU 2018-13 considers cost and benefits, and removes, modifies and adds disclosure requirements in Topic 820. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty is to be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments are to be applied retrospectively to all periods presented. ASU 2018-13 is effective for the Company for fiscal years beginning after December 15, 2019, including interim periods within that fiscal year and early adoption is permitted. The Company is currently assessing the impact of this standard on its consolidated financial statements.

The Company has reviewed all other significant newly-issued accounting pronouncements and concluded that they either are not applicable to the Company’s operations or no material effect is expected on its consolidated financial statements as a result of future adoption.

3. CASH, CASH EQUIVALENTS AND INVESTMENTS

Securities classified as cash, cash equivalents and short-term investments as of December 31, 2018 and December 31, 2017 are summarized below (in thousands). Estimated fair value is based on quoted market prices for these investments.

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 3,733	—	—	$ 3,733
Money market funds	73,238	—	—	73,238
Commercial paper	1,797	—	—	1,797

Total cash and cash equivalents	$ 78,768	$ —	$ —	$ 78,768
Short-term investments				
U.S. treasury securities	3,996	—	—	3,996
Corporate bonds	34,611	—	(21)	34,590
Commercial paper	41,371	—	(14)	41,357
Asset-backed securities	9,381	—	(3)	9,378
Total short-term investments	$ 89,359	$ —	$ (38)	$ 89,321
Total cash equivalents and investments	$ 168,127	$ —	$ (38)	$ 168,089

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	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 5,882	$ —	$ —	$ 5,882
Money market funds	68,651	—	—	68,651
Commercial paper	850	—	—	850
Total cash equivalents and investments	$ 75,383	$ —	$ —	$ 75,383
Short-term investments				
U.S. treasury securities	$ 3,994	—	(1)	$ 3,993
Corporate bonds	26,853	—	(26)	26,827
Commercial paper	19,584	—	(14)	19,570
Asset-backed securities	8,209	—	(6)	8,203
Total short-term investments	$ 58,640	$ —	$ (47)	$ 58,593
Total cash equivalents and investments	$ 134,023	$ —	$ (47)	$ 133,976

Cash equivalents consist of money market funds and other debt securities with original maturities of three months or less at the time of purchase, and the carrying amount is a reasonable approximation of fair value. The Company invests its cash in high quality securities of financial and commercial institutions. These securities are carried at fair value, which is based on readily available market information, with unrealized gains and losses included in “accumulated other comprehensive loss” within stockholders’ equity on the Company’s consolidated balance sheets. The Company uses the specific identification method to determine the amount of realized gains or losses on sales of marketable securities. Realized gains or losses have been insignificant and are included in “other income (expense), net” in the consolidated statement of operations.

All available-for-sale securities held as of December 31, 2018 and 2017, had contractual maturities of less than one year. The Company’s available-for-sale securities are subject to a periodic impairment review. The Company considers a debt security to be impaired when its fair value is less than its carrying cost, in which case the Company would further review the investment to determine whether it is other-than-temporarily impaired. When the Company evaluates an investment for other-than-temporary impairment, the Company reviews factors such as the length of time and extent to which fair value has been below cost basis, the financial condition of the issuer and any changes thereto, intent to sell, and whether it is more likely than not the Company will be required to sell the investment before the recovery of its cost basis. If an investment is other-than-temporarily impaired, the Company writes it down through the statement of operations to its fair value and establishes that value as a new cost basis for the investment. The Company did not identify any of its available-for-sale securities as other-than-temporarily impaired in any of the periods presented. As of December 31, 2018 and 2017, no investment was in a continuous unrealized loss position for more than one year and the Company believes that it is more likely than not that the investments will be held until maturity or a forecasted recovery of fair value.

4. FAIR VALUE MEASUREMENTS

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

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

Level 1 – Valuations are based on quoted prices in active markets for identical assets or liabilities and readily accessible by the Company at the reporting date. Examples of assets and liabilities utilizing Level 1 inputs are certain money market funds, U.S. treasuries and trading securities with quoted prices on active markets.

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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. Examples of assets and liabilities utilizing Level 2 inputs are corporate bonds, commercial paper, certificates of deposit and over-the-counter derivatives.

Level 3 – Valuations based on unobservable inputs in which there is little or no market data, which require the Company to develop its own assumptions.

The following table sets forth the fair value of the Company's financial assets measured on a recurring basis by level within the fair value hierarchy:

	December 31, 2018			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 73,238	$ 73,238	$ —	$ —
U.S. treasury securities	3,996	3,996	—	—
Corporate bonds	34,590	—	34,590	—
Commercial paper	43,154	—	43,154	—
Asset-backed securities	9,378	—	9,378	—
Total	$ 164,356	$ 77,234	$ 87,122	$ —
Liabilities:				
Derivative liability for exit fee	$ 533	$ —	$ —	$ 533
Foreign currency derivative contracts	52	$ —	$ 52	$ —
Total	$ 585	$ —	$ 52	$ 533

	December 31, 2017			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 68,651	$ 68,651	$ —	$ —
U.S. treasury securities	3,993	3,993	—	—
Corporate bonds	26,827	—	26,827	—
Commercial paper	20,420	—	20,420	—
Asset-backed securities	8,203	—	8,203	—
Total	$ 128,094	$ 72,644	$ 55,450	$ —

Where quoted prices are available in an active market, securities are classified as Level 1. The Company classifies money market funds and U.S. treasury securities as Level 1. When quoted market prices are not available for the specific security, the Company estimates fair value by using benchmark yields, reported trades, broker/dealer quotes and issuer spreads. The Company classifies corporate bonds, commercial paper, asset-backed securities and foreign currency derivative contracts as Level 2. In certain cases, where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. There were no transfers between Level 1 and Level 2 during the periods presented.

In May 2018, pursuant to the loan and security agreement with Solar Capital Ltd. and Western Alliance Bank (see "Note 6. Borrowings"), the Company entered into an Exit Fee Agreement under which the Company agreed to pay $1.5 million in cash, or the Exit Fee, upon any change of control transaction in respect of the Company or if the Company obtains both (i) FDA approval of tenapanor in the treatment of hyperphosphatemia in ESRD patients on dialysis and (ii) FDA approval of tenapanor for the treatment of patients with IBS-C. Notwithstanding the prepayment or termination of the Term Loan, the Company's obligation to pay the Exit Fee will expire May 16, 2028. The Company evaluated that the Exit Fee is a freestanding derivative which should be accounted for at fair value on a recurring basis. The estimated fair value of the Exit Fee is recorded as a derivative liability and included in accrued and other liabilities on the accompanying

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consolidated balance sheet. As of December 31, 2018, the estimated fair value of the Exit Fee was determined to be $533,000, a decrease of $13,000 compared with $546,000, the initial estimated fair value in May 2018, primarily as a result of changes to the inputs in the calculation including the estimated timing of payment and the time value of money, which is presented as a component of change in derivative liabilities in the Company's consolidated statements of operations.

The fair value of the derivative liability was determined using a discounted cash flow analysis and is classified as a Level 3 measurement within the fair value hierarchy since the Company's valuation utilized significant unobservable inputs. Specifically, the key assumptions included in the calculation of the estimated fair value of the derivative instrument include: i) the Company's estimates of both the probability and timing of a potential $1.5 million payment to Solar Capital Ltd. and Western Alliance Bank as a result of the FDA approvals, and ii) a discount rate which was derived from the Company's estimated cost of debt. Generally, increases or decreases in the probability of occurrence would result in a directionally similar impact in the fair value measurement of the derivative instrument and it is estimated that a 10% increase (decrease) in the probability of occurrence would result in a fair value fluctuation of approximately $0.1 million.

Changes in the fair value of recurring measurements included in Level 3 of the fair value hierarchy are presented as changes in derivative liabilities for Exit Fee in the Company's consolidated statements of operations and were as follows for the year ended December 31, 2018 (in thousands):

	Estimated Fair Value of Derivative Liability
Balance of Level 3 Liabilities at December 31, 2017	$ —
Initial estimated fair value of derivative liability for exit fee	546
Change in estimated fair value of derivative liability for exit fee	(13)
Balance of Level 3 Liabilities at December 31, 2018	$ 533

The carrying amounts reflected in the balance sheets for cash equivalents, short-term investments, accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at both December 31, 2018 and December 31, 2017, due to their short-term nature.

5. DERIVATIVE FINANCIAL INSTRUMENTS

Foreign Currency Exchange Rate Exposure

The Company uses forward foreign currency exchange contracts to secure a foreign currency exchange rate when a contract is executed involving payment in a foreign currency in order to minimize cash flow exposure to fluctuating exchange rates. Such exposure results from portions of the Company's forecasted cash outflows being denominated in currencies other than the U.S. dollar, primarily the Swiss franc. The derivative instruments the Company uses to hedge this exposure are not designated as cash flow hedges, and as a result, changes in their fair value are recorded in other income (expense), net, on the Company's consolidated statements of operations and comprehensive loss.

The fair values of forward foreign currency exchange contracts are estimated using current exchange rates and interest rates and take into consideration the current creditworthiness of the counterparties. Information regarding the specific instruments used by the Company to hedge its exposure to foreign currency exchange rate fluctuations is provided below.

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The following table summarizes the Company's forward foreign currency exchange contracts outstanding as of December 31, 2018 (notional amounts in thousands):

Foreign Exchange Contracts	Number of Contracts	Aggregate Notional Amount in Foreign Currency	Maturity
Swiss francs	1	3,281	March 2019
Total	1		

The maximum length of time over which the Company is hedging its exposure to changes in exchange rates is March 2019.

The derivative liability balance of $51,756 is recorded in accrued and other liabilities on the consolidated balance sheet as of December 31, 2018, and the net loss associated with the Company's derivative instruments of $124,194 is recognized in other (expense) income, net on the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018. There were no expenses related to such derivative instruments during 2017 and 2016.

As of December 31, 2018, we had open forward foreign currency exchange contracts with notional amounts of $3.4 million.

6. BORROWINGS

Solar Capital and Western Alliance Bank Loan Agreement

On May 16, 2018, the Company entered into a loan and security agreement, or the Loan Agreement, with Solar Capital Ltd. and Western Alliance Bank, or collectively the Lenders. The Loan Agreement provides for a $50.0 million term loan facility with a maturity date of November 1, 2022, or the Term Loan. The full amount of the loan was funded on May 16, 2018. The Company received net proceeds from the loan of approximately $49.3 million, after deducting the closing fee, legal expenses and issuance cost.

Borrowings under the Term Loan bear interest at a floating per annum rate equal to 7.45% plus the one-month LIBOR. The Company is permitted to make interest-only payments on the Term Loan through June 1, 2020, unless the Company achieves its primary endpoint in the Phase 3 study of tenapanor for the treatment of hyperphosphatemia in end-stage renal disease patients on dialysis, prior to June 1, 2020, in which case the Company is permitted to make interest-only payments on the Term Loan through December 1, 2020. Accordingly, beginning on either June 1, 2020

or December 1, 2020, as applicable, through the maturity date, the Company will be required to make monthly payments of interest plus repayment of the Term Loan in consecutive equal monthly installments of principal. The Company paid a closing fee of 1% of the Term Loan, or $0.5 million, upon the closing of the Term Loan. The Company is obligated to pay a final fee equal to 3.95% of the Term Loan upon the earliest to occur of the maturity date, the acceleration of the Term Loan, the prepayment or repayment of the Term Loan or the termination of the Loan Agreement. The Company may voluntarily prepay the outstanding Term Loan, subject to a prepayment premium of (i) 3% of the principal amount of the Term Loan if prepaid prior to or on the first anniversary of the Closing Date, (ii) 2% of the principal amount of the Term Loan if prepaid after the first anniversary of the Closing Date through and including the second anniversary of the Closing Date, or (iii) 1% of the principal amount of the Term Loan if prepaid after the second anniversary of the Closing Date and prior to the maturity date. The Term Loan is secured by substantially all the Company's assets, except for our intellectual property and certain other customary exclusions. Additionally, in connection with the Term Loan, the Company entered into an Exit Fee Agreement, whereby the Company agreed to pay an exit fee in the amount of 3% of the Term Loan, or the Exit Fee, upon any change of control transaction in respect of the Company or if the Company obtains both (i) FDA approval of tenapanor in the treatment of hyperphosphatemia in ESRD patients on dialysis and (ii) FDA approval of tenapanor for the treatment of patients with IBS-C. Notwithstanding the prepayment or termination of the Term Loan, the obligation to pay the Exit Fee will expire 10 years from the Closing Date.

The Loan Agreement contains customary representations and warranties and customary affirmative and negative covenants. Additionally, if the Company elects to enter into an exclusive license agreement for the use of its intellectual

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property in the United States (other than for tenapanor for hyperphosphatemia or for our FXR and TGR5 agonist programs) and has not obtained the written consent of the Lenders to enter into such license agreement, the Company has agreed to maintain unrestricted cash and cash equivalents of at least $50.0 million, until the Company achieves its primary endpoint in the second Phase 3 study of tenapanor for the treatment of hyperphosphatemia in end-stage renal disease patients on dialysis. As of December 31, 2018, the Company was in compliance with all of the covenants set forth in the Loan Agreement.

In addition, the Loan Agreement contains customary events of default that entitle the Lender to cause the Company's indebtedness under the Loan Agreement to become immediately due and payable, and to exercise remedies against the Company and the collateral securing the Term Loan, including our cash. Upon the occurrence and for the duration of an event of default, an additional default interest rate equal to 4.0% per annum will apply to all obligations owed under the Loan Agreement. As of December 31, 2018, to the Company's knowledge, there were no facts or circumstances in existence giving rise to an event of default.

As of December 31, 2018, assuming the principal payments start on December 1, 2020, the Company's future debt payment obligations towards the principal and final fee, excluding interest payments and exit fee, for the respective fiscal years are as follows (in thousands):

2019	$ —
2020	2,083
2021	25,000
2022	24,892
Total principal and final fee payments	51,975
Less: Unamortized discount and debt issuance costs	(1,094)
Less: Unaccreted value of final fee	(1,672)
Loan payable, long term	$ 49,209

7. SHAREHOLDERS EQUITY

On May 22, 2018, the Company entered into an underwriting agreement with Jefferies LLC and Leerink Partners LLC, as representatives of several underwriters, or collectively the Underwriters, pursuant to which the Company agreed to issue and sell 12,500,000 shares of its common stock, par value $0.0001 per share, or Common Stock, to the Underwriters, or the Offering. The shares were sold at a public offering price of $4.00 per share and were purchased by the Underwriters from the Company at a price of $3.76 per Share. Under the terms of the underwriting agreement, the Company granted the Underwriters the option, for 30 days, to purchase up to 1,875,000 additional shares of

Common Stock at the public offering price.

On May 25, 2018, the Offering closed and the Company completed the sale and issuance of 12,500,000 shares of Common Stock. The Company received net proceeds from the Offering of approximately $46.7 million, after deducting the Underwriters' discounts and commissions and offering expenses payable by the Company. Subsequently, on June 25, 2018, the Underwriters exercised their option to purchase the full 1,875,000 shares of Common Stock at the public offering price of $4.00 per share that were purchased by the Underwriters from the Company at a price of $3.76 per Share and the Company received additional net proceeds of $7.1 million, after deducting the Underwriters' commissions. In aggregate, the Company completed the sale and issuance of 14,375,000 shares of Common Stock and received net proceeds from the Offering of approximately $53.8 million, after deducting the Underwriters' discounts, commissions and offering expenses.

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8. PROPERTY AND EQUIPMENT

Property and equipment consist of the following:

	December 31, 2018	2017
	(in thousands)	
Laboratory equipment	$ 6,965	$ 6,857
Office equipment and furniture	889	815
Leasehold improvements	7,949	7,949
Property and equipment, gross	15,803	15,621
Less: accumulated depreciation	(10,192)	(7,589)
Total property and equipment, net	$ 5,611	$ 8,032

Depreciation expense totaled $2.7 million, $2.6 million and $1.3 million for the years ended December 31, 2018, 2017 and 2016, respectively.

9. ACCRUED AND OTHER LIABILITIES

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

	December 31, 2018	2017
Accrued clinical and non-clinical expenses	$ 9,790	$ 5,447
Accrued contract manufacturing expenses	1,971	3,980
Derivative liability for exit fee	533	—
Accrued professional and consulting services	112	530
Foreign currency derivative contract	52	—
Other	399	752
	$ 12,857	$ 10,709

10. COLLABORATION AND LICENSING AGREEMENTS

Kyowa Hakko Kirin Co., Ltd., or KHK

In November 2017, the Company entered into an exclusive license agreement with KHK, or the KHK Agreement, for the development, commercialization and distribution of tenapanor in Japan for cardiorenal indications. The Company assessed these arrangements in accordance with Topic 606 and concluded that the contract counterparty, KHK, is a customer. Under the terms of the KHK Agreement, the Company received $30.0 million in up-front license fees which was recognized as revenue when the agreement was executed. Based on the Company's assessment, it identified that the license and the manufacturing supply services were its material performance obligations at the inception of the agreement, and as such each of the performance obligations are distinct. Additionally, on January 1, 2018, the Company recorded an increase in current assets of $5.0 million and an increase in current liabilities of $1.0 million

related to the first milestone under the KHK Agreement that KHK achieved in February 2019, reflecting revenues and cost of revenue, respectively, that would have been recognized in the fourth quarter 2017 if the Company had adopted Topic 606 prior to January 1, 2018.

In addition to the up-front license fee of $30.0 million, the Company may be entitled to receive up to $55.0 million in total development milestones, of which $5.0 million has been recognized to date and 8.5 billion yen in commercialization milestones, worth up to $77.5 million at the currency exchange rate on December 31, 2018, as well as reimbursement of cost, plus a reasonable overhead for the supply of product and high-teen royalties on net sales throughout the term of the agreement.

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For the year ended December 31, 2018, $0.3 million of other revenue was recorded for manufacturing supply of tenapanor and other materials to KHK, for KHK's product development and clinical trials in Japan, in accordance with the Company's agreement with KHK, and a negligible cost of revenue was recorded pursuant to the AstraZeneca Termination Agreement.

Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd., or Fosun Pharma

In December 2017, the Company entered into an exclusive license agreement with Fosun Pharma, or the Fosun Agreement, for the development, commercialization and distribution of tenapanor in China for both hyperphosphatemia and irritable bowel syndrome with constipation, or IBS-C. The Company assessed these arrangements in accordance with Topic 606 and concluded that the contract counterparty, Fosun Pharma, is a customer. Under the terms of the Fosun Agreement, the Company received $12.0 million in up-front license fees which was recognized as revenue when the agreement was executed. Based on the Company's assessment, it identified that the license and the manufacturing supply services were its material performance obligations at the inception of the agreement, and as such each of the performance obligations are distinct.

In addition, the Company may be entitled to additional development and commercialization milestones of up to $113.0 million, as well as reimbursement of cost plus a reasonable overhead for the supply of product and tiered royalties on net sales ranging from the mid-teens to 20%.

For the year ended December 31, 2018, there was no revenue recorded related to the Fosun Agreement.

Knight Therapeutics, Inc., or Knight

In March 2018, the Company entered into an exclusive license agreement with Knight Therapeutics, Inc., or the Knight Agreement, for the development, commercialization and distribution of tenapanor in Canada for hyperphosphatemia and IBS-C. The Company assessed these arrangements in accordance with Topic 606 and concluded that the contract counterparty, Knight, is a customer. Based on the Company's assessment, it identified that the license and the manufacturing supply services were its material performance obligations at the inception of the agreement, and as such each of the performance obligations are distinct.

Under the terms of the agreement, the Company is eligible to receive up to CAD 25 million in total payments including an up-front payment and development and sales milestones, reimbursement of supply costs on a schedule specifying cost per tablet, with a reasonable mark up for overhead, as well as tiered royalty rates on net sales ranging from the mid-single digits to the low twenties.

For the year ended December 31, 2018, $2.3 million of revenue was recorded related to the Knight Agreement, and $0.5 million of cost of revenue was recorded pursuant to the AstraZeneca Termination Agreement.

AstraZeneca

In June 2015, the Company entered into a termination agreement with AstraZeneca, or the AstraZeneca Termination Agreement, pursuant to which the Company remains liable to pay AstraZeneca license fees for (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by the Company or its licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should the Company elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, up to a maximum of $75.0 million in aggregate for (i) and (ii). To date in aggregate, the Company has recognized $9.9 million of the $75.0 million, recorded as cost of revenue comprising (i) $6.0 million and $2.4 million related to the KHK Agreement and Fosun Agreement, respectively, recorded in 2017 (ii) $0.5 million related to the Knight Agreement recorded in the year

ended December 31, 2018 and (iii) $1.0 million related to the KHK Agreement associated with a future milestone that KHK achieved in February 2019 for which the Company recorded an increase in current liabilities in the year ended December 31, 2018 reflecting the amount that is owed to AstraZeneca upon achievement of the KHK milestone in February 2019.

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11. EQUITY INCENTIVE PLANS

2008 Plan

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

2014 Plan

The 2014 Equity Incentive Award Plan (the "2014 Plan") became effective on June 18, 2014. Under the 2014 Plan, 1,419,328 shares of common stock were initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, stock appreciation rights, or SARs, restricted stock awards, service-based restricted stock unit ("RSU") awards, performance-based restricted stock unit ("PRSU") awards, deferred stock awards, deferred stock unit awards, dividend equivalent awards, stock payment awards and performance awards. In addition, 35,221 shares that had been available for future awards under the 2008 Plan as of June 18, 2014, were added to the initial reserve available under the 2014 Plan, bringing the total reserve upon the effective date of the 2014 Plan to 1,454,549. The number of shares initially reserved for issuance or transfer pursuant to awards under the 2014 Plan will be increased by (i) the number of shares represented by awards outstanding under 2008 Plan on June 18, 2014, that are either forfeited or lapse unexercised or that are repurchased for the original purchase price thereof, up to a maximum of 1,153,279 shares, and (ii) if approved by the Administrator of the 2014 Plan, an annual increase on the first day of each fiscal year ending in 2024 equal to the lesser of (A) four percent (4.0%) of the shares of stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (B) such smaller number of shares of stock as determined by our board of directors; provided, however, that no more than 10,683,053 shares of stock may be issued upon the exercise of incentive stock options. Effective January 1, 2019, the 2014 Plan share reserve was increased by 2,490,417 shares.

2016 Plan

In November 2016, the Company's board of directors approved the 2016 Employment Commencement Incentive Plan (the "Inducement Plan") under which 1,000,000 shares were reserved. As of December 31, 2018, no shares of the Company's common stock were subject to inducement grants that were issued pursuant to the Inducement Plan.

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Stock Plan Activity

The following table summarizes activity under the 2008 Plan and the 2014 Plan, including grants issued to nonemployees, in the three years ended December 31, 2018:

		Options Issued and Outstanding			
	Shares Available for Grant	Number of Shares	Weighted-Average Exercise Price per Share	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2015	1,634,420	1,281,086	$ 9.78		
Options authorized	1,038,595	—	$ —		
Options granted	(1,524,014)	1,524,014	$ 11.42		
Options exercised	—	(25,134)	$ 2.19		
Options canceled	67,743	(67,743)	$ 16.67		
Issuance of common stock for services and restricted stock units, net of 5,000 forfeitures	(189,507)	—	—		
Balance at December 31, 2016	1,027,237	2,712,223	$ 10.60		
Options authorized	1,892,376	—	$ —		
Options granted	(1,723,906)	1,723,906	$ 11.73		
Options exercised	—	(35,759)	$ 1.70		
Options canceled	445,029	(445,029)	$ 14.15		
Issuance of common stock for services and restricted stock units, net of 79,850 forfeitures	(601,008)	—	—		
Balance at December 31, 2017	1,039,728	3,955,341	$ 10.78		
Options authorized	1,901,339	—	$ —		
Options granted	(2,566,339)	2,566,339	$ 6.01		
Options exercised	—	—	$ —		
Options canceled	1,014,920	(1,014,920)	$ 12.05		
Issuance of common stock for services and restricted stock units, net of 197,437 forfeitures	(781,120)	—	—		
Balance at December 31, 2018	608,528	5,506,760	$ 8.32	7.44	$ 648
Vested and expected to vest at December 31, 2018		5,015,765	$ 8.45	7.28	$ 648

Exercisable at December 31, 2018	2,916,825	$ 8.92	6.19	$ 648

The aggregate intrinsic value represents the difference between the total pre-tax value (i.e., the difference between the Company’s stock price and the exercise price) of stock options outstanding as of December 31, 2018, based on the Company’s common stock closing price of $1.79 per share, which would have been received by the option holders had all their in-the-money options been exercised as of that date.

For the year ended December 31, 2018, zero options were exercised to purchase shares of the Company's common stock. The intrinsic value of options exercised during the years ended December 31, 2018, 2017 and 2016, was zero, $0.3 million and $0.3 million, respectively.

The weighted-average grant-date estimated fair value of options granted during the years ended December 31, 2018, 2017 and 2016 was $4.29, $8.19 and $7.69 per share, respectively. The estimated grant date fair value of

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employee stock options was calculated using the Black-Scholes option-pricing model, based on the following weighted-average assumptions:

	Year Ended December 31,		
	2018	2017	2016
Expected term (years)	6.01	5.93	5.99
Expected volatility	83 %	82 %	77 %
Risk-free interest rate	2.60 %	2.08 %	1.62 %
Dividend yield	— %	— %	— %

Expected Term—The Company has limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock-option grants. As such, the expected term was estimated using the simplified method whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option.

Expected Volatility—Since January 1, 2017, the Company has used the historic volatility of its own stock over the retrospective period corresponding to the expected remaining term of the options, or the period since its shares were first quoted on The Nasdaq Global Market, if that is shorter, to compute its expected stock price volatility. Prior to December 31, 2016, the expected stock price volatility was calculated based on the average historical volatility for comparable publicly traded pharmaceutical companies, and the Company selected companies with comparable characteristics, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the Company's stock-based awards.

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 the Company's stock option grants.

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

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Restricted Stock Units

The following table summarizes restricted stock unit activity under the 2014 Plan in the three years ended December 31, 2018, and includes restricted stock units with time or service based vesting, or RSUs, and those restricted stock units with performance based vesting, or PRSUs:

	Number of Service-Based RSUs	Weighted-Average Grant Date Fair Value Per Share	Number of Performance-Based RSUs	Weighted-Average Grant Date Fair Value Per Share
Non-vested restricted stock units at December 31, 2015	10,000	$ 18.04	—	$ —
Granted	174,389	$ 14.34	—	$ —
Vested	(5,000)	$ 18.04	—	$ —
Forfeited	(5,000)	$ 18.04	—	$ —
Non-vested restricted stock units at December 31, 2016	174,389	$ 14.34	—	$ —
Granted	472,135	$ 4.70	161,865	$ 13.90
Vested	(43,597)	$ 14.34	—	$ —
Forfeited	(61,865)	$ 13.36	(17,985)	$ 13.90
Non-vested restricted stock units at December 31, 2017	541,062	$ 6.04	143,880	$ 13.90
Granted	—	$ —	903,374	$ 4.30
Vested	(284,611)	$ 5.55	(125,895)	$ 13.90
Forfeited	(170,842)	$ 7.53	(26,595)	$ 10.79
Non-vested restricted stock units at December 31, 2018	85,609	$ 4.70	894,764	$ 4.30

RSUs and PRSUs are generally subject to forfeiture if employment terminates prior to the release of vesting restrictions. The related compensation expense, which is based on the grant date fair value of the Company's common stock multiplied by the number of units granted, is recognized ratably over the period during which the vesting restrictions lapse.

In January 2017, the Company granted 161,865 PRSUs to certain employees that vest upon the achievement of specified performance conditions, subject to the employees' continued service relationship with the Company through the date of achievement, of which 125,895 PRSUs vested in November 2018. None of the PRSUs vested during the year ended December 31, 2017. The related compensation cost was recognized as an expense over the estimated vesting period ratably when achievement of the milestone was considered probable. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted. The Company recognized $0.6 million, $1.0 million and zero of related expense during the year ended December 31, 2018, 2017 and 2016, respectively.

In July 2018, the Company granted 903,374 PRSUs to its employees that vest upon the achievement of certain performance conditions, subject to the employees' continued service relationship with the Company through the achievement date. At December 31, 2018, 894,764 of these PRSUs were outstanding and none vested. Based on the evaluation of the performance conditions at December 31, 2018, the Company has not recorded stock-based

compensation expense for the year ended December 31, 2018 related to these PRSUs. The Company will continue to evaluate the performance conditions for these PRSUs at each reporting period and will record compensation expense related to the PRSUs accordingly.

With respect to RSUs, we recognize expense over the estimated vesting period ratably, contingent on continued service. The Company recognized $0.9 million, $0.9 million and $0.4 million of related expense during the year ended December 31, 2018, 2017 and 2016, respectively. The total estimated fair value of RSUs vested during the years ended December 31, 2018, 2017 and 2016 was $0.6 million, $0.4 million and $0.1 million, respectively.

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Issuance of Common Stock for Services

During the years ended December 31, 2018, 2017 and 2016, the Company issued 75,183, 46,858 and 20,118 shares, respectively, of its common stock to members of the board of directors who elected to receive stock in lieu of their cash fees under the Company's Non-Employee Director Compensation Program. The shares issued were valued at $0.3 million, $0.2 million and $0.2 million, respectively, based on the fair value of the common stock on the date of grant.

Employee Stock Purchase Plan

The Company adopted the 2014 Employee Stock Purchase Plan ("ESPP") and initially reserved 202,762 shares of common stock as of its effective date of June 18, 2014. If approved by the Administrator of the ESPP, on the first day of each calendar year, ending in 2024, the number of shares in the reserve will increase by an amount equal to the lesser of (i) one percent (1.0%) of the shares of common stock outstanding on the last day of the immediately preceding fiscal year and (ii) such number of shares of common stock as determined by the board of directors; provided, however, no more than 2,230,374 shares of our common stock may be issued under the ESPP. Effective January 1, 2019, the ESPP Plan share reserve was increased by 622,604 shares.

The following table summarizes ESPP activity in the three years ended December 31, 2018:

	Shares Available for Grant	Number of Shares Purchased	Purchase Price per Share	Gross Proceeds (in thousands)
Balance at December 31, 2015	347,074	41,580		
Shares purchased	(69,054)	69,054	$ 8.34	$ 576
Balance at December 31, 2016	278,020	110,634		
Shares purchased	(99,343)	99,343	$ 6.27	$ 623
Balance at December 31, 2017	178,677	209,977		
Shares authorized	622,604	—		
Shares purchased	(120,959)	120,959	$ 4.06	$ 492
Balance at December 31, 2018	680,322	330,936		

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 employees:

	Year Ended December 31,		
	2018	2017	2016
Expected term (years)	0.5	0.5	0.5
Expected volatility	76 %	80 %	76 %
Risk-free interest rate	2.08 %	0.97 %	0.48 %
Dividend yield	— %	— %	— %

Stock-based Compensation

Total stock-based compensation recognized was as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
	(in thousands)		
Research and development	$ 3,666	$ 4,585	$ 2,786
General and administrative	5,560	5,005	2,531
Total	$ 9,226	$ 9,590	$ 5,317

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As of December 31, 2018, the Company had $11.1 million, $0.3 million, zero and immaterial amount of total unrecognized compensation expense, net of estimated forfeitures, related to stock options, RSUs, PRSUs and ESPP, respectively, that will be recognized over an average vesting period of 3.0 years, 1.9 years, zero years and 0.2 years, respectively.

12. WARRANTS

Offering of Common Stock and Warrants

In June 2015, the Company sold and issued an aggregate of 7,242,992 shares of its common stock and warrants to purchase 2,172,899 shares of common stock for aggregate gross proceeds of approximately $77.8 million or net proceeds, after deducting issuance costs, of approximately $74.3 million. The purchase price for the common stock was $10.70 per share and the purchase price for the warrants was $0.125 per warrant. The warrants are exercisable for an exercise price of $13.91 per share at any time prior to the earlier of (i) 5 years from the date of issuance or (ii) certain changes in control of the Company. The Company has determined that the warrants should be classified as equity. In July 2015, the Company filed a registration statement with the SEC with respect to the common stock and warrants.

Other than with respect to warrants issued to holders affiliated with New Enterprise Associates, the warrants contain limitations that prevent each holder of warrants from acquiring shares upon exercise of the warrants that would cause the number of shares beneficially owned by it and its affiliates to exceed 9.99% of the total number of shares of the Company’s common stock then issued and outstanding. In addition, upon certain changes in control of the Company, each holder of a warrant can elect to receive, subject to certain limitations and assumptions, securities in a successor entity. None of the warrants issued in June 2015 have been exercised during each of the years ended December 31, 2016, 2017 and 2018.

13. INCOME TAXES

The components of the provision for income taxes for the year ended December 31, 2018, 2017 and 2016, are as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Current:			
Federal	$ —	$ —	$ —
State	4	5	—
Foreign	—	1,204	—
Total current	4	1,209	—
Deferred:			
Federal		(30)	—
State	—	—	—
Foreign	—	—	—
Total deferred	—	(30)	—
Provision for (benefit from) income taxes	$ 4	$ 1,179	$ —

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The following is a reconciliation of the statutory federal income tax rate to the Company's effective tax rate:

	December 31,					
	2018		2017		2016	
Income tax at the federal statutory rate	21.0	%	35.0	%	35.0	%
State taxes, net of federal benefit	0.6		0.5		0.3	
Net impact related to foreign subsidiary	—		(1.2)		—	
Change in valuation allowance	(22.5)		19.9		(36.2)	
Impact of tax reform rate change	—		(56.4)		—	
Tax credits	1.4		1.0		0.3	
Stock Based Compensation	(1.2)		(0.8)		0.1	
Other	0.7		0.1		0.5	
Income tax provision	—	%	(1.9)	%	—	%

Deferred income taxes reflect the tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows as of December 31, 2018 and 2017 (in thousands):

	December 31,	
	2018	2017
	(in thousands)	
Deferred tax assets:		
Fixed assets and intangibles	$ 38,376	$ 30,804
Net operating loss carryforwards	31,621	22,355
Tax credits	8,200	5,209
Stock-based compensation	3,763	3,159
Other	888	754
Gross deferred tax assets	82,848	62,281
Valuation allowance	(81,645)	(61,911)
Deferred tax assets net of valuation allowance	1,203	370
Deferred tax liabilities		
Adoption of New Accounting Standards	(1,054)	—
Other	(149)	(370)
Net deferred tax assets	$ —	$ —

The Company assesses 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 piece of objective negative evidence evaluated was the cumulative loss incurred over the three-year periods ended December 31, 2018, December 31, 2017 and December 31, 2016. Such objective evidence limits the ability to consider other subjective evidence, such as the Company's projections for future growth. On the basis of this evaluation, as of December 31, 2018, December 31, 2017 and December 31, 2016, full valuation allowance has been recorded against Company's net deferred tax asset. The amount of the deferred tax asset considered realizable, however, could be adjusted if estimates of future taxable income during the carryforward period are reduced or increased or if objective negative evidence in the form of cumulative losses is no longer present and additional weight is given to subjective evidence such as our projections for growth.

Realization of deferred tax assets is dependent on future taxable income, if any, the timing and the amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by approximately $19.7 million for the year ended December 31, 2018, decreased by approximately $12.6 million for the year ended December 31, 2017, and increased by approximately $40.7 million for the year ended December 31, 2016.

The increase in the valuation allowance in the year ended December 31, 2018 primarily relates to the Company's net operating loss and research and development tax credit generated in the current year.

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The TCJA makes broad and complex changes to the U.S. tax code, including, but not limited to, reducing the U.S. federal corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, effective January 1, 2018. The Company is able to determine a reasonable estimate of certain effects of the TCJA and has therefore recognized the provisional tax impacts related to the revaluation of deferred tax assets and liabilities. As a result, the Company has recorded a decrease related to net deferred tax assets of $35.6 million, with an offsetting change in valuation allowance of $35.6 million for the year ended December 31, 2017. The Securities and Exchange Commission has provided accounting and reporting guidance that allows the Company to report provisional amounts within a measurement period of up to one year from the date of enactment due to the complexities inherent in adopting the TCJA. The Company completed its analysis during the measurement period and there were no measurement period adjustments recognized during the reporting period.

As of December 31, 2018, the Company has net operating loss carryforwards for federal income tax purposes of approximately $193.3 million, of which approximately $47.0 million can be carried forward indefinitely and the remaining net operating losses expire beginning in 2030 if not utilized. Federal research and development tax credit carryforwards of approximately $8.7 million that expire beginning in 2027 if not utilized, and foreign tax credit carryforwards of approximately $1.2 million that expire in 2027 if not utilized.

In addition, the Company had net operating loss carryforwards for California income tax purposes of approximately $88.3 million that expire beginning of 2030 if not utilized, and state research and development tax credit carryforwards of approximately $6.9 million which can be carried forward indefinitely.

The Company had other state net operating losses of approximately $2.5 million that begin to expire in 2025. The Company had approximately $0.1 million of minimum tax credit carryovers for California income tax purposes. The minimum tax credits have no expiration date.

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

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows:

	December 31,		
	2018	2017	2016
	(in thousands)		
Balance at beginning of year	$ 20,734	$ 3,892	$ 3,298
Additions (subtractions) based on tax positions related to prior year	1,634	16,103	45
Additions based on tax positions related to current year	684	739	549
Balance at end of year	$ 23,052	$ 20,734	$ 3,892

The unrecognized tax benefits, if recognized and in absence of full valuation allowance, would impact the income tax provision by $9.8 million, $8.6 million and $3.5 million as of December 31, 2018, 2017 and 2016, respectively.

The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2018, 2017 and 2016, the Company 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, the Company does not anticipate that the amount of existing unrecognized tax benefits will change significantly during the next

12 months.

The Company files income tax returns in the U.S. federal, California, Maryland, Massachusetts, New Hampshire, New Jersey and Oregon tax jurisdictions. Due to the Company's net operating loss and tax credit

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carryforwards, the income tax returns remain open to U.S. federal and California state tax examinations. The Company is not currently under examination in any tax jurisdiction.

14. GEOGRAPHIC INFORMATION AND CONCENTRATIONS

Revenue by geographic areas for the years ended December 31, 2018, 2017 and 2016, are as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
United States	$ —	$ —	$ —
International:			
North America (1)	2,320	—	—
Asia Pacific (2, 3)	287	42,000	—
Total revenue	$ 2,607	$ 42,000	$ —

(1)Revenues from North America in 2018 comprised of $2.3 million from Canada in accordance with the Knight Agreement.

(2)Revenues from Asia Pacific in 2018 comprised $0.3 million from Japan in accordance with the KHK Agreement.

(3) Revenues from Asia Pacific in 2017 included $30.0 million from Japan in accordance with the KHK Agreement and $12.0 million from China in accordance with the Fosun Agreement.

Revenues are attributed to geographical areas based on the domicile of the Company’s collaboration partners.

Revenues recorded in the years ended December 31, 2018, 2017 and 2016, were wholly from collaboration partnerships. Collaboration partnerships accounting for more than 10% of total revenues during the years ended December 31, 2018, 2017 and 2016, are as follows:

	Year Ended December 31,		
	2018	2017	2016
Knight	89 %	—	—
KHK	11 %	71 %	—
Fosun Pharma	—	29 %	—

15. NET LOSS PER SHARE

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period, less shares subject to repurchase, and excludes any dilutive effects of stock-based awards and warrants. Diluted net loss per common share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, and unvested restricted common stock and stock units. As the Company had net losses for the years ended December 31, 2018, 2017 and 2016, all potential common shares

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were determined to be anti-dilutive. The following table sets forth the computation of net loss per common share (in thousands, except share and per share amounts):

	Year Ended December 31,		
	2018	2017	2016
Numerator:			
Net loss	$ (91,298)	$ (64,339)	$ (112,387)
Denominator:			
Weighted average common shares outstanding - basic and diluted	56,219,919	47,435,331	40,118,522
Net loss per share - basic and diluted	$ (1.62)	$ (1.36)	$ (2.80)

For the years ended December 31, 2018, 2017 and 2016, 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,		
	2018	2017	2016
Options to purchase common stock	5,378,008	3,977,160	2,464,089
Warrants to purchase common stock	2,172,899	2,172,899	2,172,899
Restricted stock units	199,135	323,819	87,079
Performance-based restricted stock units	395,791	148,216	—
ESPP shares issuable	63,413	60,524	37,227
Total	8,209,246	6,682,618	4,761,294

The number of potential common shares that would have been included in diluted income per share were it not 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, 2018, 2017 and 2016, was approximately 1.0 million, 1.0 million and 0.8 million, respectively.

16. COMMITMENTS AND CONTINGENCIES

Leases

The Company has a lease agreement for a facility in Fremont, California that was amended in December 2012 to extend the lease agreement to September 2016. In September 2014, the Company signed the second amendment to its facility lease agreement in Fremont, California to add space and to extend the lease term through September 2019. In addition, the amended lease agreement provides for a tenant improvement allowance of up to $0.6 million. In May 2016, the Company signed a third amendment to its facility lease agreement in Fremont, California to add space and to extend the lease term through September 2021 (the “Third Amendment”). The Third Amendment provides for a tenant improvement allowance of up to $0.4 million and the extended lease has rent escalation clauses throughout the

lease term. It also provides a lease extension option for five years on the entire premises at the higher of (i) a 3% annual escalation of the then-current base rent and (ii) the then-current fair market value for comparable premises.

Rent increases, including the impact of a rent holiday and leasehold improvement allowance from the landlord, will be recognized as deferred rent and amortized on a straight-line basis over the term of the lease. Under the terms of the lease agreement, the Company provided the lessor with a security deposit in the amount of $0.1 million. The lessor shall be entitled to draw on the security deposit in the event of any uncured default by the Company under the terms of the lease.

The Company had a lease agreement for a facility in Boston, Massachusetts for 16 months commencing March 1, 2017 and terminating June 30, 2018, with no extension option. On July 26, 2018 the Company entered into a new lease agreement for 36 months effective October 1, 2018 with an annual rent of $0.1 million as well as a separate agreement that extended the previous lease until the new lease was made available.

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The future minimum payments under noncancelable operating leases at December 31, 2018, are as follows (in thousands):

Year Ended December 31,	Amounts
2019	$ 2,697
2020	3,116
2021	2,213
2022	—
2023	—
Thereafter	—
Total	$ 8,026

Rent expense under operating leases was $1.8 million, $1.7 million and $1.3 million for the years ended December 31, 2018, 2017 and 2016, respectively.

Guarantees and Indemnifications

The Company indemnifies each of its 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, the Company currently holds director and officer liability insurance. This insurance allows the transfer of risk associated with our exposure and may enable the Company to recover a portion of any future amounts paid. The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, the Company has not recognized any liabilities relating to these obligations for any period presented.

Legal Proceedings and Claims

From time to time the Company may be involved in claims arising in connection with its business. Based on information currently available, the Company believes that the amount, or range, of reasonably possible losses in connection with any pending actions against it in excess of established reserves, in the aggregate, not to be material to its consolidated financial condition or cash flows. However, losses may be material to the Company’s operating results for any particular future period, depending on the level of income or loss for such period.

17. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

Selected quarterly financial results from operations for the years ended December 31, 2018 and 2017 are as follows (in thousands, except per share amounts):

	2018 Quarter End			
	March 31	June 30	September 30	December 31
Total revenue	$ 2,320	$ 30	$ 172	$ 85
Gross profit	1,856	30	170	85

Operating expenses	19,541	22,184	23,902	27,461
Net loss	(17,019)	(22,291)	(24,126)	(27,862)
Net loss per share - basic and diluted	$ (0.36)	$ (0.42)	$ (0.39)	$ (0.45)

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	2017 Quarter End			
	March 31	June 30	September 30	December 31
Total revenue	$ —	$ —	$ —	$ 42,000
Gross profit	—	—	—	33,600
Operating expenses	28,434	26,418	21,225	22,638
Net income (loss)	(28,008)	(25,721)	(20,724)	10,114
Net income (loss) per share - basic	$ (0.59)	$ (0.54)	$ (0.44)	$ 0.21
Net income (loss) per share - diluted	$ (0.59)	$ (0.54)	$ (0.44)	$ 0.21

18. SUBSEQUENT EVENTS

In February 2019, the company received a $5.0 million milestone payment from KHK in accordance with the terms of the license agreement with KHK, pursuant to KHK’s announcement in February 2019 of its initiation of a Phase 2 clinical study of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis.

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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, 2018, management, with the participation of our Chief Executive Officer and Chief Financial Officer, 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 Chief Executive Officer and the Chief Financial Officer, 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 Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2018, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed by, or under the supervision of, our CEO and CFO, and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

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

Our management assessed our internal control over financial reporting as of December 31, 2018, the end 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, 2018, our internal control over financial reporting was effective.

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or

detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known

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features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10 K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies.”

Changes in Internal Control over Financial Reporting

There were no changes in our internal controls over financial reporting during the quarter ended December 31, 2018, identified in connection with the evaluation required by Rule 13a 15(d) and 15d 15(d) of the Exchange Act that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

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PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2019 Annual Meeting of Stockholders (the "Proxy Statement"), which will be filed not later than 120 days after the end of our fiscal year ended December 31, 2018, under the headings "Executive Officers," "Election of Directors," "Corporate Governance," and " Section 16(a) Beneficial Ownership Reporting Compliance," and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our website at www.ardelyx.com. 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. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

ITEM 11. EXECUTIVE COMPENSATION

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

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

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

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

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

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

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

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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.

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Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation	8 K	6/24/2014	3.1	
3.2	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	Form of Warrant issued pursuant to the Securities Purchase Agreement by and among Ardelyx, Inc. and the purchasers signatory thereto, dated June 2, 2015	S 3	7/13/2015	4.3	
10.1	Termination Agreement, dated June 2, 2015, by and between AstraZeneca AB and Ardelyx, Inc.	10 Q	8/12/2015	10.1	
10.2	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)	
10.3	Amended and Restated Investor's Rights Agreement dated June 23, 2011, by and among Ardelyx, Inc. and the investors listed therein	S 1	5/19/2014	10.3	
10.4(a)	Lease, dated August 8, 2008, by and between 34175 Ardenwood Venture, LLC and Ardelyx, Inc.	S 1	5/19/2014	10.4(a)	
10.4(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)	
10.4(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	
10.4(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	
10.5(a)#	Ardelyx, Inc. 2008 Stock Incentive Plan, as amended	S 1	5/19/2014	10.5(a)	
10.5(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)	
10.5(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)	
10.6(a)#	Ardelyx, Inc. 2014 Equity Incentive Award Plan	S 8	7/14/2014	99.3	
10.6(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)	
10.6(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)	
10.7#		S 1/A	6/9/2014	10.7	

	Form of Indemnification Agreement for directors and officers				
10.8#	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
10.9#	Amended and Restated Change in Control Severance Agreement, dated June 6, 2014, by and between Ardelyx, Inc. and Mark Kaufmann	S	1/A	6/9/2014	10.15

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Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
	Amended and Restated Change in Control	S 1/A	6/9/2014	10.16	
10.10#	Severance Agreement, dated June 6, 2014, by and between Ardelyx, Inc. and Elizabeth Grammer, Esq.				
10.11#	Amended and Restated Change in Control Severance Agreement, dated June 6, 2014, by and between Ardelyx, Inc. and Jeffrey Jacobs, Ph.D.	S 1/A	6/9/2014	10.17	
10.12#	Amended and Restated Change in Control Severance Agreement, dated June 6, 2014, by and between Ardelyx, Inc. and David Rosenbaum, Ph.D.	S 1/A	6/9/2014	10.19	
10.13#	Offer Letter, dated August 11, 2011, by and between Ardelyx, Inc. and Mark Kaufmann	S 1/A	6/9/2014	10.10	
10.14#	Offer Letter, dated May 2, 2008, by and between Ardelyx, Inc. and Jeff Jacobs, Ph.D.	S 1/A	6/9/2014	10.12	
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#	Offer Letter, dated November 21, 2012, by and between Ardelyx, Inc. and Elizabeth Grammer, Esq.	S 1/A	6/9/2014	10.14	
10.19#	Offer Letter, dated November 21, 2014, by and between Ardelyx, Inc. and Jeremy S. Caldwell, Ph.D.	10 K	3/5/2015	10.22	
10.20#	Change in Control Severance Agreement, dated December 19, 2014, by and between Ardelyx, Inc. and Jeremy S. Caldwell, Ph.D.	10 K	3/4/2016	10.23	
10.21#	Offer Letter, dated December 12, 2015, by and between Ardelyx, Inc. and Paul Korner, MD, MBA	10 K	3/4/2016	10.21	
10.22#	Ardelyx, Inc. 2014 Employee Stock Purchase Plan	S 8	7/14/2014	99.6	
10.23(a)#	Non-Employee Director Compensation Program	S 1/A	6/9/2014	10.21	
10.23(b)#	Description of amendments to Non-Employee Director Compensation Program	8 K	3/9/2017	N/A	
10.24	Securities Purchase Agreement by and among Ardelyx, Inc. and the purchasers signatory thereto, dated June 2, 2015	10 Q	8/12/2015	10.2	
10.25	Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated June 2, 2015	S 3	7/13/2015	99.1	
10.26	Securities Purchase Agreement by and among Ardelyx, Inc. and the purchasers signatory thereto, dated July 14, 2016	10 Q	8/8/2016	10.1	
10.27	Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated July 14, 2016	10 Q	8/8/2016	10.2	
10.28(a)#		S 8	11/10/2016	99.1	

	Ardelyx, Inc. 2016 Employment Commencement Incentive Plan				
10.28(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
10.28(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
10.28(d)#	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2016 Employment Commencement Incentive Plan	S	8	11/10/16	99.4

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Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
10.29#	Change in Control Severance Agreement, dated January 4, 2016, by and between Ardelyx, Inc. and Paul Korner, MD, MBA	10 K	2/17/2017	10.29	
10.30#	Offer Letter, dated October 1, 2016, by and between Ardelyx, Inc. and Reginald Kim Seeto, MB.BS; B.Sc.	10 K	2/17/2017	10.30	
10.31#	Change in Control Severance Agreement, dated October 22, 2016, by and between Ardelyx, Inc. and Reginald Kim Seeto, MB.BS; B.Sc.	10 K	2/17/2017	10.31	
10.32#	Offer Letter, dated November 15, 2016, by and between Ardelyx, Inc. and Bryan Shaw	10 K	2/17/2017	10.32	
10.33#	Change in Control Severance Agreement, dated December 6, 2016, by and between Ardelyx, Inc. and Bryan Shaw	10 K	2/17/2017	10.33	
10.34#	Transition and Separation Agreement dated August 21, 2017, by and between the Company and Dr. Paul Korner	10 Q	11/7/2017	10.1	
10.35††	License Agreement, dated November 27, 2017, by and between Kyowa Hakko Kirin Co., Ltd. and Ardelyx, Inc.	10 K	3/14/2018	10.35	
10.36††	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	
10.37#	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	
10.38#	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	
10.39	Loan and Security Agreement, dated May 16, 2018, by and between the Company and Solar Capital Ltd. and Western Alliance Bank.	10-Q	8/7/2018	10.1	
10.40	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	
10.41#	Transition and Separation Agreement dated July 8, 2018, by and between the Company and Reginald Seeto, MBBS.	10-Q	8/7/2018	10.3	
21.1	Subsidiaries of the Registrant				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				X

	Exchange Act of 1934, as amended	
32.1	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a 14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C §1350	X
101.INS	XBRL Instance Document	X
101.SCH	XBRL Taxonomy Extension Schema Document	X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X

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Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document				X
101.PRE	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 have been omitted pursuant to a confidential treatment request. Omitted information has been filed separately with the Securities and Exchange Commission.

#Indicates management contract or compensatory plan.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Ardelyx, Inc.

Date: March 6, 2019 By: /s/ Michael Raab
Michael Raab
President Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Michael Raab and Mark Kaufmann, 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.

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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)	March 6, 2019
/s/ Mark Kaufmann Mark Kaufmann	Chief Financial Officer (Principal Financial and Accounting Officer)	March 6, 2019
/s/ David Mott David Mott	Chairman of the Board of Directors	March 6, 2019
/s/ Robert Bazemore Robert Bazemore	Director	March 6, 2019
/s/ William Bertrand, Jr. William Bertrand, Jr.	Director	March 6, 2019
/s/ Annalisa Jenkins Annalisa Jenkins, MBBS, FRCP	Director	March 6, 2019
/s/ Jan M. Lundberg Jan M. Lundberg, Ph.D.	Director	March 6, 2019
/s/ Gordon Ringold Gordon Ringold, Ph.D.	Director	March 6, 2019
/s/ Richard Rodgers Richard Rodgers	Director	March 6, 2019