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Filed Pursuant to Rule 424(b)(4)
Registration Nos. 333-196090 and 333-196890

PROSPECTUS

4,286,000 Shares

Common Stock

This is the initial public offering of shares of common stock of Ardelyx, Inc.

We are offering 4,286,000 shares of our common stock. Prior to this offering, there has been no public market for our common stock. Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "ARDX."

We are an emerging growth company under the federal securities laws and will be subject to reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 10.

	Per Share	Total
Initial public offering price	$14.00	$60,004,000
Underwriting discounts and commissions(1)	$ 0.98	$ 4,200,280
Proceeds, before expenses, to us	$13.02	$55,803,720

(1) See "Underwriting" for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

We have granted the underwriters the right to purchase up to 642,900 additional shares of common stock to cover over-allotments, if any. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

Certain of our existing investors have agreed to purchase an aggregate of 888,054 shares of our common stock (or approximately $12.4 million) in this offering at the initial public offering price.

The underwriters expect to deliver the shares against payment in New York, New York on or about June 24, 2014.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

Citigroup **Leerink Partners**

JMP Securities **Wedbush PacGrow Life Sciences**

June 18, 2014

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Neither we nor the underwriters have authorized anyone to provide you with information that is different from that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are offering to sell shares of common stock and seeking offers to buy shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock.

Until July 13, 2014 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Ardelyx® and our logo are some of our trademarks used in this prospectus. This prospectus also includes trademarks, tradenames, and service marks that are the property of other organizations. Solely for convenience, these trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbol, but, in the case of our trademarks and tradenames, those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights, or the right of the applicable licensor to these trademarks and tradenames.

Prospectus Summary

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before deciding to invest in our common stock, you should read this entire prospectus carefully, including the sections entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and related notes contained elsewhere in this prospectus. Unless the context otherwise requires, references in this prospectus to the "company," "Ardelyx," "we," "us" and "our" refer to Ardelyx, Inc.

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the gastrointestinal, or GI, tract to treat cardio-renal, GI and metabolic diseases. We have developed a proprietary drug discovery and design platform enabling us, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing our platform, we discovered and designed our lead product candidate, tenapanor, which in preclinical and clinical studies has consistently demonstrated the ability to reduce the absorption of dietary sodium and phosphorus, both of which are key factors in the progression of kidney disease. In 2012, we entered into a collaboration partnership with AstraZeneca AB, or AstraZeneca, for the worldwide development and commercialization of tenapanor. AstraZeneca is responsible for all of the development and commercialization costs for tenapanor, and we have retained an option to co-promote in the United States. Together with AstraZeneca, we are evaluating tenapanor in three Phase 2 clinical trials in patients with end stage renal disease, or ESRD, late-stage chronic kidney disease, or CKD, and constipation-predominant irritable bowel syndrome, or IBS-C. To enhance our proprietary drug discovery and design platform, we have developed a cell-culture system to simulate gut tissues called Ardelyx Primary Enterocyte and Colonocyte Culture System, or APECCS. We have also identified over 3,800 proteins on the inner surface of the gut, many of which we believe may be drug targets. In addition to tenapanor, we are evaluating small molecule NaP2b inhibitors for the treatment of elevated phosphorus, or hyperphosphatemia, in ESRD, a program we have licensed to Sanofi S.A., or Sanofi. We are also independently advancing three other discovery and lead development programs focused in cardio-renal, GI and metabolic diseases.

Our Product Pipeline

The following table summarizes key information about our product candidates:

Program	Indication	Research	Phase 1	Phase 2		Status	Development and Commercial Rights
				2a	2b		
Tenapanor *(NHE3 inhibitor)*	ESRD-PI					Results expected in 1H:2015	AstraZeneca • $870mm total potential deal size including $35mm up front and $237.5mm development milestones; tiered royalties • AZ funds and is responsible for all R&D • Ardelyx has right to co-promote in the United States
	IBS-C					Results expected in 4Q:2014	
	CKD					Results expected in 2H:2015	
RDX002 *(NaP2b inhibitor)*	ESRD-PI					Research	SANOFI • $198mm total potential deal size; tiered royalties • Sanofi funds and is responsible for all R&D • Ardelyx has right to co-promote in the United States
RDX009 *(TGR5 agonist)*	IBD					Research	ARDELYX
RDX013 *(K^+ channel modulator)*	Hyper-kalemia					Research	ARDELYX
RDX020 *(Cl^- channel modulator)*	Fluid Overload					Research	ARDELYX

Our lead product candidate, tenapanor, is a small molecule, orally administered inhibitor of NHE3, a transporter of sodium in the GI tract. We and AstraZeneca have evaluated tenapanor in eight human clinical trials in over 765 individuals. In Phase 1 and Phase 2 clinical trials, tenapanor has generally been well-tolerated and has shown the ability to divert dietary sodium into the stool in both healthy adult subjects and patients with ESRD. In Phase 1 clinical trials in healthy adults, we observed that tenapanor has a significant effect on the diversion of dietary phosphorus into the stool. Additionally, tenapanor has demonstrated activity consistent with an IBS-C drug by increasing the frequency of bowel movements in IBS-C patients in a Phase 2a clinical trial. We and AstraZeneca are continuing development in ongoing Phase 2a and Phase 2b clinical trials in three different indications:

- ESRD patients on hemodialysis to treat hyperphosphatemia: Phase 2b randomized, double-blind, placebo-controlled clinical trial in 150 patients to evaluate the effects of tenapanor on serum phosphorus. Enrollment is ongoing and the results of this clinical trial are expected in the first half of 2015.
- Stage 3 CKD patients with type 2 diabetes mellitus, the presence of the protein albumin in the urine, or albuminuria, and high blood pressure: Phase 2a randomized, double-blind, placebo-controlled clinical trial in 140 patients to evaluate the effects of tenapanor on kidney function and fluid overload. Enrollment is ongoing and the results of this clinical trial are expected in the second half of 2015.
- IBS-C patients: Phase 2b randomized, double-blind, placebo-controlled clinical trial in 371 patients to evaluate the effect of tenapanor on the frequency of bowel movements versus placebo. Enrollment is completed and the results of this clinical trial are expected in the fourth quarter of 2014.

We believe the market opportunity for tenapanor for these three potential patient populations is significant. We estimate, based on phosphate binder utilization, the only approved therapies for hyperphosphatemia, that there are about 270,000 ESRD patients with hyperphosphatemia in the United States. The worldwide market for phosphate binders in 2011 was reported to be approximately $1.5 billion and is projected to reach $2.3 billion by 2015. We believe there are approximately 1.8 million patients in the United States that have late-stage, or stage 3b or stage 4, CKD with type 2 diabetes, and approximately 4.4 million individuals in the United States with IBS-C.

In addition to tenapanor, we have discovered novel NaP2b inhibitors for the treatment of hyperphosphatemia in ESRD patients by inhibiting the active absorption of phosphorus. In February 2014, we entered into an option and license agreement with Sanofi under which we granted Sanofi an exclusive worldwide license to conduct research utilizing our small molecule NaP2b inhibitors. In addition, Sanofi has the option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors. Sanofi is advancing this program towards first-in-human clinical trials. Under our arrangement, Sanofi is responsible for all of the costs and expenses for research and preclinical activities and, should it exercise its option, for the development and commercialization efforts under the NaP2b program, while we retain an option to co-promote licensed products in the United States.

Utilizing our proprietary drug discovery and design platform, we are pursuing other internal discovery and lead-development programs that are currently in the research phase. While we have identified molecules that exhibit certain of the activity we are seeking in each of the following programs, we have not yet selected a lead molecule in these programs.

- RDX009 Program: Our focus is the discovery and development of non-systemic TGR5 agonists that stimulate GLP-2 and GLP-1 and have the potential when used in combination with a DPP4 inhibitor to heal the intestines and reduce inflammation in inflammatory bowel disease;
- RDX013 Program: Our focus is the discovery and development of drug candidates to treat hyperkalemia, or elevated serum potassium, also commonly seen in CKD and ESRD patients; and
- RDX020 Program: Our focus is the discovery and development of drug candidates that provide alternate ways to manage fluid overload and kidney function by inhibiting chloride transport in CKD patients, particularly those who also experience acid-base disorders due to their disease.

Our Proprietary Drug Discovery and Design Platform

Our platform, comprised of proprietary know-how and drug discovery and design tools such as APECCS, provides us with a competitive advantage in drug development. This platform enables us, in a rapid and cost-efficient manner, to discover and design novel drug candidates that work exclusively in the GI tract to treat cardio-renal, GI and metabolic diseases. By targeting receptors and transporters localized in the GI tract, we can modulate important functions of the gut, such as absorption of specific nutrients and minerals, or the gut's various hormonal functions, to treat and prevent diseases while avoiding systemic toxicities.

Traditional small molecule drug discovery and design focuses on drugs that are rapidly absorbed in the GI tract. Once absorbed, those molecules typically need to survive the first-pass metabolism that occurs in the liver in order to arrive at the targeted cells or tissues and provide the desired benefit or effect. Compared to the traditional approach employed by the pharmaceutical industry to develop systemic drugs, we believe our proprietary drug discovery and design platform has several key benefits:

- exploits the natural functions of the gut to affect disease;
- results in drug candidates with a superior safety profile that remain non-systemic;
- reduces discovery time; and
- promotes efficient phenotypic screens.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the GI tract to treat cardio-renal, GI and metabolic diseases. Our strategy involves the following:

- to advance tenapanor into late-stage and pivotal clinical trials in collaboration with AstraZeneca;
- to use non-dilutive financing from our existing collaboration partnerships and the proceeds of this offering to expand our product pipeline and advance our earlier-stage product candidates into clinical trials;
- to leverage our technological capabilities and drug discovery and design platform to expand our product pipeline;
- to develop commercial capabilities; and
- to leverage our management team's drug development and commercialization expertise to identify and secure complementary in-licensing opportunities.

Our Management Team

Our executive management team has extensive experience in the discovery, development and commercialization of products in the renal field. As the Senior Vice President and General Manager of Renagel at Genzyme Corporation, or Genzyme, a Sanofi company, our President and Chief Executive Officer, Michael Raab, launched and oversaw the sales growth of sevelamer, the leading phosphate binder for the treatment of hyperphosphatemia with over $1.0 billion in worldwide sales in 2013. Mr. Raab was also instrumental in the worldwide launch of both Ceredase and Cerezyme, Genzyme's $1.0 billion therapies for Gaucher disease. Other members of our executive team have discovered or developed important products and product candidates in the cardio-renal, GI and metabolic fields, including Renagel, patiromer and Welchol, in key roles in leading biopharmaceutical companies such as Ilypsa, Inc., MedImmune, LLC, a subsidiary of AstraZeneca Plc, GelTex Pharmaceuticals, Inc., Genzyme and PDL BioPharma, Inc.

Risk Associated With Our Business

Our business is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this prospectus summary. These risks include, among others:

- we have a limited operating history, have incurred significant losses and we will incur losses in the future;
- we have never generated any revenue from product sales and may never be profitable;
- we may require substantial additional financing;
- we are substantially dependent on the success of our lead product candidate, tenapanor, which is a first-in-class drug that has not been extensively studied in humans and, as 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;
- we are dependent on AstraZeneca for the development, regulatory approval, manufacture and commercialization of tenapanor;
- clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we may encounter substantial delays in our clinical studies;
- our product candidates may never achieve market acceptance or commercial success;
- the regulatory approval processes is lengthy, time consuming and inherently unpredictable; and
- our intellectual property may not be adequate to enable us to compete effectively in our market, and we may become subject to claims alleging infringement of third parties' intellectual property rights.

Corporate Information

We were founded in October 2007 as a Delaware corporation under the name Nteryx, Inc. Our principal executive offices are located at 34175 Ardenwood Blvd., Fremont, CA 94555, and our telephone number is (510) 745-1700. Our website address is www.ardelyx.com. The information on, or that can be accessed through, our website is not part of this prospectus. We have included our website address as an inactive textual reference only.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of this offering (December 31, 2019), (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startup Act of 2012 herein as the "JOBS Act," and references herein to "emerging growth company" shall have the meaning associated with it in the JOBS Act.

Certain of our existing investors have agreed to purchase an aggregate of 888,054 shares of our common stock (or approximately $12.4 million) in this offering at the initial public offering price.

The Offering

Issuer	Ardelyx, Inc.
Common stock we are offering	4,286,000 shares
Common stock to be outstanding after the offering	17,886,167 shares
Option to purchase additional shares to cover over-allotments, if any	642,900 shares
Use of proceeds	The net proceeds from this offering will be approximately $52.4 million, or approximately $60.8 million if the underwriters exercise their option to purchase additional shares in full, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We currently expect to use the net proceeds from this offering to fund continued discovery and development efforts for our preclinical product candidates, the exercise of our right to co-fund the first Phase 3 clinical development program for tenapanor, if we decide to exercise such right, expenses related to the development of APECCS, and the remainder for working capital and other corporate purposes, which will include facilities expansion and the pursuit of other research and discovery efforts and could also include the acquisition or in-license of other products, product candidates or technologies. See "Use of Proceeds" on page 53 for a more complete description of the intended use of proceeds from this offering.
Risk factors	See "Risk Factors" beginning on page 10 and other information included in this prospectus for a discussion of factors that you should consider carefully before deciding to invest in our common stock.
Symbol on The NASDAQ Global Market	"ARDX"

The number of shares of common stock to be outstanding after this offering is based on 13,600,167 shares of common stock outstanding as of March 31, 2014, and excludes the following:

- 880,497 shares of common stock issuable upon the exercise of outstanding stock options under our 2008 Stock Incentive Plan, as amended, as of March 31, 2014 having a weighted-average exercise price of $1.23 per share (which excludes 239,423 shares of early exercised stock options subject to a repurchase right);
- 26 shares of common stock reserved for issuance pursuant to future awards under our 2008 Stock Incentive Plan, as amended, as of March 31, 2014, which will become available for issuance under our 2014 Equity Incentive Award Plan after consummation of this offering;
- 1,419,328 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the consummation of this offering; and

- 202,762 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan.

Unless otherwise indicated, the number of shares of our common stock described above gives effect to:

- a 1-for-9 reverse stock split of our capital stock we have effected;
- the conversion of all outstanding shares of our convertible preferred stock pursuant to a stockholder vote under our amended and restated certificate of incorporation into an aggregate of 11,517,222 shares of common stock immediately prior to the consummation of this offering;
- the net exercise, based on the initial public offering price, of all of our Series B warrants into 571,244 shares of our common stock at an exercise price of $0.09 per share;
- the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering; and
- assumes no exercise of the underwriters' option to purchase additional shares to cover over-allotments.

We refer to our Series A and Series B convertible preferred stock collectively as "convertible preferred stock" in this prospectus, as well as for financial reporting purposes and in the financial tables included in this prospectus, as more fully explained in Note 7 to our audited financial statements. In this prospectus (other than for financial reporting purposes and in the financial tables included in this prospectus), we refer to our outstanding warrants to purchase shares of our Series B convertible preferred stock as our Series B warrants.

Summary Financial Data

The following tables present summary financial data for our business. We have derived the following statements of operations data for the years ended December 31, 2012 and 2013 from our audited financial statements included elsewhere in this prospectus. We have derived the statements of operations data for the three months ended March 31, 2013 and 2014 and the balance sheet data as of March 31, 2014 from our unaudited financial statements included elsewhere in this prospectus. We have prepared the unaudited financial statements on the same basis as the audited financial statements and have included, in our opinion, all adjustments, consisting only of normal recurring adjustments, that we consider necessary for a fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results that should be expected in the future, and our interim results are not necessarily indicative of the results that should be expected for the full year or any other period. You should read this data together with our financial statements and related notes appearing elsewhere in this prospectus and the information under the captions "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
	(in thousands, except per share data)			
			(unaudited)	
Statements of Operations Data:				
Revenue:				
Licensing revenue	$ 3,182	$ 8,063	$ 1,989	$ 3,236
Collaborative development revenue	2,228	20,865	4,567	5,314
Total revenue	5,410	28,928	6,556	8,550
Operating expenses:				
Research and development[1]	10,184	28,093	5,939	7,637
General and administrative[1]	4,031	3,700	1,027	1,377
Total operating expenses	14,215	31,793	6,966	9,014
Loss from operations	(8,805)	(2,865)	(410)	(464)
Other expense, net	(30)	(52)	(25)	(4)
Change in fair value of preferred stock warrant liability	(950)	(3,506)	—	(2,603)
Loss before provision for income taxes	(9,785)	(6,423)	(435)	(3,071)
Provision for income taxes	—	(141)	(35)	—
Net loss	$ (9,785)	$ (6,564)	$ (470)	$ (3,071)
Net loss per common share, basic and diluted[2]	$ (11.32)	$ (5.82)	$ (0.45)	$ (2.44)
Shares used to compute net loss per common share, basic and diluted[2]	864,020	1,127,948	1,042,675	1,256,245
Pro forma net loss per common share, basic and diluted (unaudited)[2]		$ (0.23)		$ (0.04)
Shares used to compute pro forma net loss per common share, basic and diluted (unaudited)[2]		13,216,414		13,344,711

(1) Included in the statement of operations data above are the following stock-based compensation expenses (in thousands):

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
			(unaudited)	
Research and development	$ 221	$ 200	$48	$ 37
General and administrative	252	152	59	27
Total stock-based compensation	$ 473	$ 352	$107	$ 64

(2) See Notes 2 and 12 to our audited financial statements and Note 5 to our unaudited financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per common share, pro forma net loss per common share, and the weighted-average number of shares used in the computation of the per share amounts.

The table below presents our balance sheet data as of March 31, 2014:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the conversion of all outstanding shares of our convertible preferred stock pursuant to a stockholder vote under our amended and restated certificate of incorporation into an aggregate of 11,517,222 shares of common stock immediately prior to the consummation of this offering;
  - the net exercise, based on the initial public offering price, of all of our Series B warrants into 571,244 shares of our common stock at an exercise price of $0.09 per share, and the related reclassification of our convertible preferred stock warrant liability to additional paid-in capital; and
  - the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale of 4,286,000 shares of common stock in this offering at the initial public offering price, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	As of March 31, 2014		
	Actual	Pro Forma	Pro Forma As Adjusted
		(unaudited) (in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 33,221	$ 33,221	$ 85,625
Working capital	20,347	20,347	72,751
Total assets	40,548	40,548	92,952
Preferred stock warrant liability	9,059	—	—
Convertible preferred stock	56,155	—	—
Accumulated deficit	(71,724)	(71,724)	(71,724)
Total stockholders' (deficit) equity	(66,458)	(1,244)	51,160

Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. 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. We have only one product candidate in clinical trials and no product sales, which, together with our limited operating history, 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 our lead product candidate, 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 you can evaluate our business and prospects. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the years ended December 31, 2012 and 2013 was $9.8 million and $6.6 million, respectively, and $3.1 million for the three months ended March 31, 2014. As of March 31, 2014, we had an accumulated deficit of $71.7 million.

If we do not receive anticipated milestone payments from our collaboration partners, AstraZeneca AB, or AstraZeneca and Sanofi S.A., or Sanofi, our operating losses will substantially increase for the foreseeable future as we continue our discovery, research, development, manufacturing and commercialization activities. We cannot assure you that we will receive any potential milestones under our agreements with AstraZeneca and/or Sanofi. For a discussion of the risks associated with our preclinical and clinical development programs with, and potential for milestone payments from, AstraZeneca and Sanofi, see below under "—Risks Related to Our Business."

Even if we receive the anticipated milestone payments or receive royalty payments from our collaboration partners, we may not be able to achieve or sustain profitability. For example, we may choose to exercise our right to co-fund a portion of the first Phase 3 clinical development program for tenapanor, incurring expenses of up to $40.0 million, and we would likely incur continued operating losses during the period we are co-funding the program. In addition, our receipt of milestone payments from our collaboration partners may not result in the recognition of revenue in the period received, as we may be required to amortize the milestone payment over a period of time. Depending upon such requirement and the period of amortization, we may continue to incur losses even after the receipt of such milestone payments. Therefore, there can be no assurance that our losses will not increase into the future. Our prior losses, combined with possible 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 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, and the ability of

our collaboration partners, to successfully complete the development of and obtain the regulatory and marketing approvals necessary to commercialize one or more of our product candidates. 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:

- the completion of research and preclinical and clinical development of our product candidates;
- together with our collaboration partners, obtaining regulatory approvals for our product candidates;
- the ability of our collaboration partners to successfully commercialize and/or our ability to commercialize or co-promote, if we so choose, our product candidates;
- developing a sustainable and scalable manufacturing process for any approved product candidates and establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products to support clinical development and the market demand for our product candidates, if approved;
- obtaining market acceptance of our product candidates, if approved, as viable treatment options;
- 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, or our collaboration partners, are successful in obtaining regulatory approvals to market one or more of our product candidates, 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 have royalty and/or co-promotion rights for that territory. If the number of patients suitable for our product candidates is not as significant as we estimate, the indication approved by regulatory authorities is narrower than 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 such products, 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 you to lose all or part of your investment.

We may require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development or other operations.

Since our inception, most of our resources have been dedicated to our research and development activities, including developing our lead product candidate, tenapanor, and developing our proprietary drug discovery and design platform. As of March 31, 2014, we had working capital of $20.3 million, including capital resources consisting of cash and cash equivalents of $33.2 million. We believe that we will continue to expend substantial resources for the foreseeable future, including costs associated with research and development, conducting preclinical studies and clinical trials, obtaining regulatory approvals 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.

Based on our current operating plan, we believe that our existing capital resources will allow us to fund our operating plan through at least the next 12 months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. Our future funding requirements will depend on many factors, including, but not limited to:

- our decision whether or not to exercise our right to co-fund the first Phase 3 clinical development program for tenapanor, in which case we may invest $20.0 million, $30.0 million or $40.0 million to acquire an increase of 1%, 2% or 3%, respectively, in the royalties payable to us by AstraZeneca on net sales of tenapanor;
- the achievement of development and regulatory milestones resulting in the payment to us from our collaboration partners of contractual milestone payments and the timing of receipt of such payments, if any;
- the progress, timing, scope, results and costs of our preclinical studies and clinical trials for our product candidates that have not been licensed, including the ability to enroll patients in a timely manner for clinical trials;
- the time and cost necessary to obtain regulatory approvals for our product candidates that have not been licensed and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability and the ability of our collaboration partners to successfully commercialize and/or co-promote our product candidates;
- the manufacturing, selling and marketing costs associated with product candidates, including the cost and timing of building our sales and marketing capabilities;
- our ability to establish and maintain collaboration partnerships, in-license/out-license or other similar arrangements and the financial terms of such agreements;
- the timing, receipt, and amount of sales of, or royalties on, our future products, if any;
- the sales price and the availability of adequate third-party reimbursement for our product candidates;
- 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;
- the time and cost necessary to respond to technological and market developments; and
- 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 our product candidates.

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 and development activities, preclinical and clinical trials for our product candidates for which we retain such responsibility and our establishment and maintenance of sales and marketing capabilities or other activities that may be necessary to commercialize or co-promote our product candidates.

Risks Related to Our Business

We are substantially dependent on the success of our lead product candidate, tenapanor, which may not be successful in nonclinical studies or 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 and only product candidate in clinical

trials. In particular, together with AstraZeneca, our collaboration partner for tenapanor, we have completed six Phase 1 and two Phase 2 trials and are currently conducting three Phase 2 trials and one Phase 1 study. Our near-term prospects, including our ability to finance our operations through the receipt of milestone payments and generate revenue from product sales, will depend heavily on the successful development and AstraZeneca's commercialization of tenapanor, if approved. The clinical and commercial success of tenapanor will depend on a number of factors, including the following:

- the timely completion of the ongoing clinical trials of tenapanor, which will depend substantially upon the satisfactory performance of third-party contractors;
- whether tenapanor's safety and efficacy profile is satisfactory to the U.S. Food and Drug Administration, or FDA, and foreign regulatory authorities to warrant marketing approval;
- the timely completion of the ongoing chronic kidney disease, or CKD, Phase 2a clinical trial, which will depend substantially upon our ability to identify principal investigators with patient populations suitable for study, and the ability of those principal investigators to successfully enroll those patients into the trial;
- the results of a long-term rat carcinogenicity study required for approval of tenapanor, which will not be known for at least two and half years, and which may be delayed for a significant period of time for reasons outside of the control of AstraZeneca, particularly if AstraZeneca is required to restart or modify the study for any reason;
- whether FDA or foreign regulatory authorities require additional clinical trials prior to approval to market tenapanor;
- the prevalence and severity of adverse side effects of tenapanor;
- the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;
- the ability of AstraZeneca and us through our co-promotion rights, if we choose to exercise such rights and are not precluded from doing so under the terms of our agreement with AstraZeneca or any subsequent co-promotion agreements, 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 and effective by patients and the medical community;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for tenapanor by third-party payors;
- the effectiveness of AstraZeneca's marketing, sales and distribution strategy and operations;
- the ability of AstraZeneca, or any third-party manufacturer it contracts with, to successfully scale up the manufacturing process for tenapanor, which has not yet been demonstrated, and to manufacture supplies of tenapanor and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practice, or cGMP, requirements;
- enforcing intellectual property rights in and to tenapanor;
- 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 profile of tenapanor following approval.

Most of these factors are beyond our control, including clinical development, the regulatory submission process, manufacturing, marketing and sales efforts of AstraZeneca.

As a first-in-class drug, tenapanor, has not been extensively studied in humans and the nonclinical and clinical data on its effect in the human body is limited to the trials and studies that we and AstraZeneca have completed. As 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. We cannot be certain that tenapanor will be successful in preclinical studies, clinical trials or receive regulatory approval. For example, like phosphate binders, treatment with tenapanor in patients with end stage renal disease, or ESRD, may be significantly impacted by such patient's adherence to a restrictive low phosphorus diet, and as such, adherence may be a factor in demonstrating the efficacy of tenapanor in clinical trials for this patient population. Further, it may not be possible or practicable to demonstrate, or if approved, to market on the basis of, certain of the benefits we believe tenapanor possesses, including the reduction of sodium absorption in patients with CKD, which is unlikely to be an endpoint to be considered for approval in CKD patients. Additionally, the reduction of serum phosphorus is currently an approvable endpoint in ESRD, but not in the broader CKD patient population in the United States. 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, we may not generate significant revenue from sales of tenapanor, if approved. Accordingly, we cannot assure you that tenapanor will ever be successfully commercialized or that we will ever generate revenue from sales of tenapanor. If we and AstraZeneca 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.

We are dependent on AstraZeneca for the development, regulatory approval, manufacture and commercialization of our small molecule NHE3 inhibitor program, which includes tenapanor, and if AstraZeneca fails to perform as expected, or is unable to obtain the required regulatory approvals for tenapanor, the potential for us to generate future revenue from milestone and royalty payments from tenapanor would be significantly reduced and our business would be materially and adversely harmed.

In October 2012, we entered into a license agreement with AstraZeneca granting it an exclusive worldwide license to our small molecule NHE3 inhibitor program, which includes our lead product candidate tenapanor, for all indications. Under this agreement, AstraZeneca has responsibility for completing all nonclinical and clinical development and obtaining and maintaining regulatory approval for tenapanor from the FDA and regulatory agencies outside of the United States. Ultimately, if tenapanor is advanced through clinical trials and receives marketing approval from the FDA or comparable foreign regulatory agencies, AstraZeneca will be responsible for the commercialization of tenapanor, subject to our right to elect to participate in certain co-promotion activities in the United States. The potential for us to obtain future development milestone payments and, ultimately, generate revenue from royalties from tenapanor depends entirely on the successful development, regulatory approval, marketing and commercialization of tenapanor by AstraZeneca. In addition to the risks inherent in the development of a drug product candidate, our collaboration partnership with AstraZeneca may not be successful due to a number of important factors, including the following:

- prior to the 175th day after the database lock for the ongoing Phase 2b clinical trial in hyperphosphatemic ESRD patients, AstraZeneca may terminate the license for any reason with 30 -days' prior written notice and thereafter AstraZeneca may terminate the license with 120- days' prior written notice;
- AstraZeneca has the unilateral ability to choose not to develop tenapanor for one or more indications for which it has been or is currently being evaluated, provided it pursues at least one indication, and AstraZeneca may choose to pursue an indication that is not in our strategic best interest or forego an indication, even if clinical data is supportive of further development for such indication;
- AstraZeneca may choose not to develop and commercialize tenapanor in all relevant markets;
- AstraZeneca may take considerably more time advancing tenapanor through the clinical and regulatory process than we currently anticipate, which could materially delay the achievement of milestones and, consequently the receipt of milestone payments from AstraZeneca;

- AstraZeneca's obligation to use "commercially reasonable efforts" with regard to the development, regulatory approval, manufacture and commercialization of tenapanor under our agreement leaves AstraZeneca with discretion in determining the efforts and resources that it will apply to the development, regulatory approval, manufacture and commercialization of tenapanor;
- subject to our right to elect to participate in co-promotion activities in the United States, AstraZeneca controls all aspects of the commercialization of tenapanor;
- AstraZeneca is obligated to reimburse a specified amount for the current constipation-predominant irritable bowel syndrome, or IBS-C, Phase 2b clinical trial, and despite our efforts to keep costs below that amount, we may be required to spend more than that to complete the trial, and if we do so, we will not be reimbursed for those excess amounts by AstraZeneca;
- AstraZeneca's recent strategic withdrawal from selling gastrointestinal, or GI, products and the differing treatment of the IBS-C indication in our agreement implies that AstraZeneca may choose not to develop the IBS-C indication, even if our current Phase 2b clinical trial were successful;
- AstraZeneca may change the focus of its development and commercialization efforts or pursue higher-priority programs and, accordingly, reduce the efforts and resources allocated to tenapanor, which will have the direct effect of reducing our co-promotion activities as our level of co-promotion is limited to a percentage of the overall commercialization activities;
- AstraZeneca may fail to develop a commercially viable formulation or manufacturing process for tenapanor, and may fail to manufacture or supply sufficient drug substance of tenapanor for commercial use, if approved, which could result in lost revenue;
- AstraZeneca may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- AstraZeneca may sublicense its rights with respect to tenapanor to one or more third parties without our consent;
- AstraZeneca may not dedicate the resources that would be necessary to carry tenapanor through clinical development or may not obtain the necessary regulatory approvals;
- if AstraZeneca is acquired during the term of our collaboration partnership, the acquiror may have different strategic priorities that could cause it to terminate our agreement or reduce its commitment to our collaboration partnership; and
- if our agreement with AstraZeneca terminates, we will no longer have rights to receive potential revenue under the agreement with AstraZeneca for future milestones or royalties, in which case we would need to identify alternative means to continue the development, manufacture and commercialization of tenapanor, alone or with others.

The timing and amount of any milestone and royalty payments we may receive under our agreement will depend on, among other things, the efforts, allocation of resources, and successful development and commercialization of tenapanor by AstraZeneca under our agreement. There can be no assurance that any of the development and regulatory milestones will be achieved or that we will receive any future milestone payments under the agreement. In addition, in certain circumstances we may believe that we have achieved a particular milestone and AstraZeneca may disagree with our belief. In that case, receipt of that milestone payment may be delayed or may never be received, which may require us to adjust our operating plans.

If AstraZeneca does not perform in the manner we expect or fulfill its responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to tenapanor could be delayed or terminated and it could become necessary for us to assume the responsibility at our own expense for the clinical development of tenapanor. In that event, we would likely be required to substantially limit the size and scope of the development and commercialization of tenapanor or seek additional financing to fund further development, or to identify alternative collaboration partners for tenapanor, and our potential to generate future revenue from royalties and milestone payments from tenapanor would be significantly reduced or delayed and our business would be materially and adversely harmed.

Our election to co-fund the first Phase 3 clinical development program for tenapanor must be made in a limited time period prior to the initiation of the first pivotal clinical trial for tenapanor and, as a result, we may make a substantial capital investment for a product candidate based on limited clinical data.

Under our agreement with AstraZeneca, we may elect to participate in the funding of the first Phase 3 clinical development program for the first indication of tenapanor by investing a co-funding amount of $20.0 million, $30.0 million or $40.0 million to acquire an increase of 1%, 2% or 3%, respectively, in the royalties payable to us by AstraZeneca on net sales of tenapanor. We may exercise this right only for a limited period of 60 days following AstraZeneca's determination to proceed to the first Phase 3 clinical development program for tenapanor for a specific indication. An election to participate in the co-fund will be based, in part, on our analysis as to the likelihood of success of the Phase 3 clinical development program and the potential for regulatory approval to commercialize tenapanor. As a result, we will be required to make a substantial capital investment in tenapanor prior to the initiation of the first pivotal clinical trial and if tenapanor is unsuccessful in its pivotal trial or if it never receives regulatory approval, we will not receive any financial return on this capital investment.

We have not yet negotiated our agreement with AstraZeneca specifying all of the terms of our co-promotion right.

Pursuant to our license agreement with AstraZeneca, we have retained a co-promotion right with respect to tenapanor in the United States. While the license agreement includes the material terms of our co-promotion right, we and AstraZeneca mutually agreed to negotiate a separate agreement specifying the detailed activities and responsibilities in respect of the marketing and co-promotion of tenapanor following our election to exercise our co-promotion rights. If we elect to exercise our co-promotion rights, the separate agreement we negotiated with AstraZeneca may place restrictions or additional obligations on us, including financial obligations. Any restrictions or additional obligations may restrict our co-promotion activities or involve more significant financial obligations than we currently anticipate.

Exercising our co-promotion right under our license agreement with AstraZeneca may restrict our future commercialization and/or co-promotion activities.

Our agreement with AstraZeneca prohibits us from using the same sales force to co-promote tenapanor as we do to promote other products that compete with tenapanor or with any other products that are then being actively promoted by AstraZeneca or its affiliates. If we elect to co-promote tenapanor, we may therefore be required to have a separate sales forces to promote other products we may elect to co-promote under our agreement with Sanofi, or other products we develop and commercialize on our own, should any of such products be competitive with tenapanor or with any other products promoted by AstraZeneca or its affiliates. The exercise of the co-promotion right under our agreement with AstraZeneca, could adversely affect the efficiency and cost of our promotion efforts for our products and, effectively, may prohibit us from exercising our co-promotion rights under our agreement with Sanofi or with respect to other co-promotion rights with future collaboration partners.

If Sanofi does not exercise its option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors or if it exercises the option and subsequently terminates any development program under its collaboration partnership with us, any potential milestone payments or revenue from product sales under this collaboration partnership will be significantly reduced or non-existent, and our results of operations and financial condition will be materially and adversely affected.

In February 2014, we entered into a license option and license agreement with Sanofi under which we granted Sanofi an exclusive worldwide license to conduct research utilizing our small molecule NaP2b inhibitors, which we refer to as our RDX002 program, solely for the purpose of completing activities under a preclinical development plan. We believe the inhibition of NaP2b, an intestinal phosphate transporter, would provide utility for the treatment of hyperphosphatemia in ESRD patients, which is also the lead indication for which we and AstraZeneca are developing tenapanor.

Under the terms of this agreement, Sanofi has the option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors. Sanofi may exercise this option at any time following the effective date of the agreement and ending 45 days after the filing of an investigational new drug application, or IND, subject to certain exceptions, and if Sanofi does not file an IND on or before the 40th month anniversary of the completion of the technology transfer phase, the agreement will terminate.

If Sanofi does not exercise its option under its agreement with us, or terminates its rights and obligations with respect to the development program or the entire agreement, then depending on the timing of such event:

- the development of our NaP2b inhibitor program may be terminated or significantly delayed;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the agreement if we decided to continue work under the NaP2b inhibitor program independently;
- we would not be eligible to receive any of the remaining development or regulatory milestone payments or royalties on product sales;
- in order to fund further development and commercialization of the NaP2b program, we may need to raise additional capital if we choose to internally pursue the development of the program, or we may need to seek out and establish alternative collaboration partnerships with third-party collaboration partners for the program, which may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of the programs or increase our expenditures and seek additional funding by other means; and
- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of the NaP2b program.

Any of these events would have a material adverse effect on our results of operations and financial condition.

In addition, we may be effectively prohibited from co-promoting any product candidates arising from the NaP2b program if we have previously exercised our co-promotion right under our agreement with AstraZeneca. For additional information regarding the effect of exercising our co-promotion right with AstraZeneca, see the risk factor above titled “Exercising our co-promotion right under our license agreement with AstraZeneca may restrict our future commercialization and/or co-promotion activities.”

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we may encounter substantial delays in our clinical studies. 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, or our collaboration partners, 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. For example, in a Phase 2a study evaluating tenapanor in ESRD patients with fluid overload, while pharmacological activity of tenapanor was confirmed, the study failed to meet the primary endpoint of a statistically significant difference between tenapanor and placebo in change in interdialytic weight gain from baseline to week 4. The results of preclinical and clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. For example, the positive results generated to date in preclinical and clinical studies for tenapanor do not ensure that the ongoing Phase 2a and Phase 2b clinical trials, or future clinical trials, will demonstrate similar results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through preclinical studies and initial clinical trials. 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 trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates.

We may experience delays in our ongoing or future trials, and we do not know whether future clinical trials will begin on time, need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- obtain regulatory approval to commence a trial, if applicable;
- 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;
- initiate or add a sufficient number of clinical trial sites; or
- manufacture sufficient quantities of product candidate for use in clinical trials.

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 and AstraZeneca have experienced a delay in the enrollment of the ongoing Phase 2a clinical trial in CKD patients due to the restrictive eligibility criteria, and, although we have initiated efforts to increase enrollment by initiating new sites and amending the protocol, there can be no assurances that our efforts will be successful in increasing the rate of enrollment to complete this study on time, if at all.

We could also encounter delays if a clinical trial is suspended or terminated by us, our collaboration partner for the product candidate, by the IRBs of the institutions in which such trials are being conducted, by an independent data safety monitoring board, or DSMB, for such trial 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, conducting clinical trials in foreign countries presents additional risks that may delay completion of clinical trials. These risks include the failure of physicians or enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes and political and economic risks relevant to such foreign countries. In addition, the FDA may determine that the clinical trial results obtained in foreign subjects do not represent the safety and efficacy of a product candidate when administered in U.S. patients and

are thus not supportive of an NDA approval in the United States. As part of our effort to increase the rate of enrollment in the ongoing Phase 2a clinical trial in CKD patients, we and AstraZeneca have plans to initiate sites in Germany. For the reasons stated above, these efforts may not improve the rate of enrollment in this study, or generate results that can be used to support the development of tenapanor.

If there are delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate revenue from product sales from any of these product candidates will be delayed. In addition, any delays in completing the clinical trials will increase costs, slow down our product candidate development and approval process and jeopardize the ability to commence product sales and generate revenue from product sales. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Our unlicensed product candidates are at an early stage of development and we may not be successful in our efforts to develop these products or expand our pipeline of product candidates.

A key element of our strategy is to expand our pipeline of products candidates utilizing our proprietary drug discovery and design platform and to advance such product candidates through clinical development. Our current unlicensed product candidates, which include candidates in our RDX009, RDX013 and RDX020 programs, are in the discovery and lead identification stages of preclinical development and will require substantial preclinical and clinical development, testing and regulatory approval prior to commercialization. In particular, tenapanor is our only product candidate in clinical trials and our other product candidates are in the preclinical stage with significant research and development required before we could file an IND with regulatory authorities to begin clinical studies. 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 development programs, we cannot assure you 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 and effective. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development or commercialization for many reasons, including the following:

- 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 or otherwise does not meet applicable regulatory 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 and effective 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 or by pursuing in-licensing or acquisition of product candidates, the potential product candidates for which we identify or 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 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.

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.

We have developed a proprietary drug discovery and design platform to enable the identification, screening, testing, design and development of new product candidates, and we recently we enhanced this platform with the addition of APECCS. We plan to utilize APECCS to identify new and potentially novel targets in the GI tract. We have also identified over 3,800 proteins on the inner surface of the gut, many of which we believe may be drug targets. However, we cannot assure you APECCS will work nor 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.

Although we expect to continue to enhance the capabilities of our APECCS system by advancing the cell culture and screening process and/or acquiring new technologies to broaden the scope of APECCS, we may not be successful in any of our enhancement and development efforts. For example, we may not be able to enter into agreements on suitable terms to obtain technologies required to develop certain capabilities of APECCS. In addition, we may not be successful in developing the conditions necessary to grow multiple segments of intestine or from multiple species, or otherwise develop assays or cell cultures necessary to expand these capabilities. If our enhancement or development efforts are unsuccessful, we may not be able to advance our drug discovery capabilities as quickly as we expect or identify as many potential drugable targets as we desire.

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

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

We rely on third parties to conduct some of our preclinical and 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, preclinical or nonclinical studies. We rely on medical institutions, clinical investigators, contract laboratories, collaboration partners 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 we are conducting with AstraZeneca, as well as

those third parties with whom we will contract for execution of clinical trials for our internal programs, 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 preclinical and 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 good laboratory practices, or GLPs, for preclinical and 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 preclinical 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. We cannot assure you 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.

Even if our product candidates obtain regulatory approval, they may never achieve market acceptance 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 our product candidates obtain FDA or other regulatory approvals, and are ultimately commercialized, our product candidates may not achieve market acceptance among physicians, patients, third-party payors, patient advocacy groups, health care payors and the medical community. Market acceptance of our product candidates for which marketing approval is obtained depends on a number of factors, including:

- the efficacy of the products as demonstrated in clinical trials;
- the prevalence and severity of any side effects and overall safety profile of the product;
- the clinical indications for which the product is approved;
- advantages over existing therapies;
- acceptance by physicians, major operators of clinics and patients of the product as a safe and effective treatment;
- relative convenience and ease of administration of our products;
- the potential and perceived advantages of our product candidates 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 our products, if approved, on the part of physicians and patients;
- the availability of alternative products and their ability to meet market demand;
- the strength of our or our collaboration partners' marketing and distribution organizations;
- the quality of our relationships with patient advocacy groups; and
- sufficient third-party coverage or reimbursement.

Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our results of operations.

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 regulatory approval, if any. If any of our 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, our collaboration partners, 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, flatulence, abdominal discomfort, abdominal pain, and abdominal distention. In the event that trials conducted by us or AstraZeneca 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 AstraZeneca or us to cease further development of or deny approval of tenapanor, or any such other product candidate, for any or all targeted indications. 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:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or our collaboration partners, 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 our collaboration partners, 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 our collaboration partners, 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, or our other product candidates, would compete against existing treatments. For example, tenapanor will, if approved, compete directly with

phosphate binders for the treatment of hypophosphatemia in patients with ESRD, including sevelamer hydrochloride (Renagel) and sevelamer carbonate (Renvela), which were launched by Genzyme. Impax Laboratories, Inc. launched a generic version of sevelamer carbonate in April 2014 and is expected to launch a generic version of sevelamer hydrochloride in September 2014. In addition to the currently marketed phosphate binders, we are aware of several other binders in development such as ferric citrate (Zerenex), an iron-based binder in Phase 3 being developed in the United States by Keryx and approved in Japan, fermagate (Alpharen), an iron-based binder in Phase 2 being developed by Opko Health, and sucroferric oxyhydroxide (Velphoro), an iron-based binder.

While there are no treatments for CKD that have been proven to reverse the disease, we are aware of one agent, CLP-1001, being developed by Sorbent Therapeutics, which is an orally administered, non-systemic exchange resin that binds both sodium and potassium as well as protons that showed positive effects in CKD patients with heart failure in a Phase 2a clinical trial and which showed the ability to increase fecal sodium. We believe this agent, if approved, may be competitive with tenapanor to treat CKD and ESRD patients. We are aware of certain investigational drugs that were being developed for delaying kidney decline as measured by estimated glomerular filtration rate, or eGFR. Among other products, Concert Pharmaceuticals is developing CTP-499 which showed protective effects on kidney function at 48 weeks in a Phase 2 clinical trial in patients with CKD and type 2 diabetes.

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 relieve temporary constipation. We are also aware of two prescription drugs currently on the U.S. market that are approved to treat IBS-C, Linzess (linaclotide), which was developed by Ironwood Pharmaceuticals and was approved in 2012 and 2013 for IBS-C and chronic constipation in both the United States and in Europe, and Amitiza (lubiprostone), which was first approved in the United States in 2006 and is currently marketed by Sucampo and Takeda for treatment of chronic idiopathic constipation, or CIC, IBS-C and opioid induced constipation, or OIC.

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.

For additional information regarding the competitive landscape for our product candidates, see “Business—Competition.”

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 co-promote tenapanor, if approved, or commercialize or co-promote any of our other product candidates.

We currently do not have a sales organization. In order to co-promote tenapanor or commercialize or co-promote any of our other product candidates, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If one or more of our product candidates receives regulatory approval, we expect to establish a specialty sales organization with technical expertise and supporting distribution capabilities to co-promote and/or commercialize our product candidates, which will be expensive and time consuming. 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 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. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products.

We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates.

We rely completely on third parties to manufacture our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidate. Our business would be harmed if those third parties fail to obtain approval of the FDA, Competent Authorities of the Member States of the EEA or comparable regulatory authorities, fail to provide us with sufficient quantities of drug product, 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 our preclinical and clinical drug supplies for use in the conduct of our preclinical and clinical studies, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. The facilities used by our contract manufacturers to manufacture any drug products must be approved by the FDA pursuant to inspections that will be conducted after an NDA is submitted to the FDA. We do not control the manufacturing process of our product candidates, and, other than with respect to tenapanor, 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. Under our agreement with AstraZeneca, the manufacturing of tenapanor is the responsibility of AstraZeneca. We are entirely dependent on AstraZeneca for all aspects of the manufacturing and validation process, as well as providing all commercial supply of tenapanor. For additional information regarding the risks of our dependence on AstraZeneca, see the risk factors above titled “We are substantially dependent on the success of our lead product candidate, tenapanor, which may not be successful in nonclinical studies or clinical trials, receive regulatory approval or be successfully commercialized” and “We are dependent on AstraZeneca for the development, regulatory approval, manufacture and commercialization of our small molecule NHE3 inhibitor program, which includes tenapanor, and if AstraZeneca fails to perform as expected, or is unable to obtain the required regulatory approvals for tenapanor, the potential for us to generate future revenue from milestone and royalty payments from tenapanor would be significantly reduced and our business would be materially and adversely harmed.”

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 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 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 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 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.

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 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.

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 extends this implementation date to January 1, 2024. As a result of the recent legislation, beginning in 2024, 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 bundling may have on the industry, the impact could potentially cause dramatic price reductions for tenapanor, if approved. We and AstraZeneca 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, 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 new products approved 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 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.

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.

We are highly dependent on the services of our President and Chief Executive Officer, Michael Raab, our Chief Scientific Officer, Dominique Charmot, Ph.D., and our Vice President of Drug Development, David Rosenbaum, Ph.D., and if we are not able to retain these members of our management or recruit additional management, clinical and scientific 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, Dominique Charmot, Ph.D., our Chief Scientific Officer, and David Rosenbaum, Ph.D., our Vice President of Drug Development. The loss of services of any of these individuals could delay or prevent 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 Drs. Charmot and 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 will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

As of March 31, 2014, we had 37 full-time employees. We will need to continue to expand our managerial, operational, finance and other resources in order to manage our operations, preclinical and clinical trials, research and development activities, regulatory filings, manufacturing and supply activities, and any marketing and commercialization activities, including co-promotion activities. Our management, personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- expand our general and administrative functions;
- establish and build a marketing and commercial organization;
- identify, recruit, retain, incentivize and integrate additional employees;
- manage our internal development efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, legal, financial and management controls, reporting systems and procedures.

If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We will 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 will 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, and we will likely need to hire additional accounting and financial staff with appropriate public company reporting experience and technical accounting knowledge. 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.

In addition, we expect that we will need to implement an enterprise resource planning, or ERP, system for our company. An ERP system is intended to combine and streamline the management of our financial, accounting, human resources, sales and marketing and other functions, enabling us to manage operations and track performance more effectively. However, an ERP system would likely require us to complete many processes and procedures for the effective use of the system or to run our business using the system, which may result in substantial costs. Additionally, during the conversion process, we may be limited in our ability to convert any business that we acquire to the ERP. Any disruptions or difficulties in implementing or using an ERP system could adversely affect our controls and harm our business, including our ability to forecast or make sales and collect our receivables. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention.

After this offering, we will be 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. Beginning with the second annual report that we will be required to file with the SEC, 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 not 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 the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of this offering (December 31, 2019), (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, or (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

To date, we have never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, 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 will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

We may form additional collaboration partnerships in the future with respect to our independent programs, and we may not realize the benefits of such collaborations.

We may form collaboration partnerships, create joint ventures or enter into licensing arrangements with third parties with respect to our independent programs that we believe will complement or augment our existing business. We have historically engaged, and intend to continue to engage, in partnering discussions with a range of pharmaceutical and biotechnology companies and could enter into new collaboration partnerships at any time. We face significant competition in seeking appropriate collaboration partners, and the negotiation process to secure appropriate terms is time-consuming and complex. Any delays in identifying suitable 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 a collaboration partnership for any future product candidates and programs on terms that are acceptable to us, or at all. This may be 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 our product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile. Even if we are successful in entering into a collaboration partnership or license arrangement, there is no guarantee that the collaboration partnership will be successful, or that any future 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 intend to consider strategic transactions, such as acquisitions of companies, asset purchases, and or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, 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;
- 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, or otherwise engage in business outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We 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 expect that we will be subject to additional risks related to entering into 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
- 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 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.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

We may be adversely affected by the current 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 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 recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. We cannot anticipate all the ways in which the current global economic climate and global financial market conditions could adversely impact our business.

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, the 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,

prior to the effectiveness of 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, 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.

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. We have not submitted an application or obtained marketing approval for any of our product candidates anywhere in the world. Obtaining regulatory approval of a new drug application, or 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 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.

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 GCPs 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.

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 and our collaboration partners and 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 and AstraZeneca, and those contract manufacturers it may rely upon with respect to the manufacture of tenapanor, 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. 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, our collaboration partners, 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. Some of our contract manufacturers have never produced a commercially approved pharmaceutical product and therefore have not obtained the requisite regulatory authority approvals to do so. The facilities and quality systems of some or all of our collaboration partners and 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, other than with respect to tenapanor, our contract manufacturing partners for compliance with the regulatory requirements. AstraZeneca is fully responsible for the manufacture of tenapanor, and we are entirely dependent upon AstraZeneca 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 collaboration partners and third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time consuming for us or a third party to implement, and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent suspension of production or closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we, our collaboration partners, 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, receives marketing approval, we and our collaborating partners 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.

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, and abdominal distention. 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: (1) FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA; (2) manufacturing standards; (3) federal and state healthcare fraud and abuse laws and regulations; or (4) laws that require the reporting of true and accurate financial information and data. 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 be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, 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 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 our 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 the 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 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
- 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 outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for

spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, the ATRA was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We 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.

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 any other product candidates.

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. We cannot assure you that we will not be subject to claims alleging that the manufacture, use or sale of tenapanor or any other product candidates nor that any activities conducted by us, 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 operation of our business. 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.

We may be subject to third-party patent infringement claims in the future against us or our collaboration partners 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 or our collaboration partners, we or they could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we or our collaboration partners 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 or our collaboration partners were able to obtain a license, 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 some aspect of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaboration partners are unable to enter into licenses on acceptable terms. 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. 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.

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 or our collaboration partners 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 or our collaboration partners 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.

If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we or our collaboration partners request, the period during which we or our collaboration partners 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.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both

technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation, including the Leahy-Smith America Invents Act signed into law on September 16, 2011. That Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and new venues and opportunities for competitors to challenge patent portfolios. Because of that Act, the U.S. patent system is now a "first to file" system, which may make it more difficult to obtain patent protection for inventions and increase the uncertainties and costs surrounding the prosecution of our or our collaboration partners' patent applications and the enforcement or defense of our or our collaboration partners' issued patents, all of which could materially adversely affect our business, results of operations and financial condition.

The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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.

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 and This Offering

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

The trading price of our common stock following this offering could be 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 of this prospectus and others such as:

- results from, or any delays in, clinical trial programs relating to our product candidates, including the ongoing and planned clinical trials for tenapanor;
- ability to commercialize or obtain regulatory approval for our product candidates, or delays in commercializing or obtaining regulatory approval;
- announcements of regulatory approval or a complete response letter to tenapanor, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements relating to future collaboration partnerships or our existing collaboration partnerships with AstraZeneca and/or Sanofi, including decisions regarding the exercise by AstraZeneca or Sanofi of their options or any termination by them of any development program under their collaboration partnerships with us;
- our election, and the related announcement, to exercise our co-fund right with respect to the first Phase 3 clinical development program for tenapanor;
- 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;
- any adverse changes to our relationship with any manufacturers or suppliers;

- the success of our testing and clinical trials;
- 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;
- 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;
- 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.

We have broad discretion to determine how to use the funds raised in this offering, and may use them in ways that may not enhance our operating results or the price of our common stock.

Our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. We currently intend to use substantially all of the net proceeds of this offering to fund continued discovery and development efforts for our preclinical product candidates, the exercise of our right to co-fund the first Phase 3 clinical development program for tenapanor, if we decide to exercise such right, expenses related to the development of APECCS, and the balance for working capital and general corporate purposes, which will include facilities expansion and the pursuit of other research and discovery efforts and could also include the acquisition or in-license of other products, product candidates or technologies. However, our use of these proceeds may differ substantially from our current plans. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause our stock price to decline.

An active, liquid and orderly market for our common stock may not develop, and you may not be able to resell your common stock at or above the public offering price.

Prior to this offering, there has been no public market for shares of our common stock, and an active public market for our shares may not develop or be sustained after this offering. We and the representatives of the underwriters have determined the initial public offering price of our common stock through negotiation. This

price will not necessarily reflect the price at which investors in the market will be willing to buy and sell our shares following this offering. In addition, an active trading market may not develop following the consummation of this offering or, if it is developed, may not be sustained. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses or technologies or in-license new product candidates using our shares as consideration.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, 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 cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year following the fifth anniversary of the completion of this offering (December 31, 2019), (2) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, or (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

The initial public offering price of our common stock is substantially higher than the pro forma net tangible book value per share of our common stock before giving effect to this offering. Accordingly, if you purchase our common stock in this offering, you will incur immediate substantial dilution of approximately $11.13 per share, based on the initial public offering price, and our pro forma net tangible book value as of March 31, 2014. In addition, following this offering, purchasers in this offering will have contributed approximately 51% of the total gross consideration paid by stockholders to us to purchase shares of our common stock, but will own only approximately 24% of the shares of common stock outstanding immediately after this offering. Furthermore, if the underwriters exercise their option to purchase additional shares, or outstanding options or convertible

securities are exercised, you could experience further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section titled "Dilution."

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

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

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 after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the trading price of our common stock could decline. Based upon the number of shares outstanding as of March 31, 2014, upon the closing of this offering, we will have outstanding a total of 17,886,167 shares of common stock, assuming no exercise of the underwriters' option to purchase additional shares. Of these shares, approximately 4,286,000 shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering. Citigroup and Leerink, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, as of March 31, 2014, up to an additional 13,600,167 shares of common stock will be eligible for sale in the public market, 11,998,993 of which shares are held by current directors, executive officers and other affiliates and may be subject to Rule 144 under the Securities Act of 1933, or the Securities Act.

In addition, as of March 31, 2014, 1.1 million shares of common stock that are subject to outstanding options, will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

After this offering, the holders of approximately 12.4 million shares of our outstanding common stock as of March 31, 2014, will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting schedules and to the lock-up agreements described above. 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.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of March 31, 2014, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 97.7% of our outstanding voting stock and, upon the

closing of this offering, that same group will hold approximately 79.0% of our outstanding voting stock (assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options). Therefore, even after this offering these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of 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 you may feel are in your best interest as one of our stockholders.

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 that will be in effect immediately prior to the consummation of this offering will 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 will 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 66 2/3% 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 acquiror;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least 66 2/3% 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 acquiror from conducting a solicitation of proxies to elect the acquiror'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. For a description of our capital stock, see "Description of Capital Stock."

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

Our 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 to be effective immediately prior to the completion of this offering 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.
- 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, your ability to achieve a return on your 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 restrict our ability to pay dividends. Therefore, you are not likely to receive any dividends on your common stock for the foreseeable future. Since we do not intend to pay dividends, your ability to receive a return on your 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.

Special Note Regarding Forward-Looking Statements

This prospectus contains forward-looking statements concerning our business, operations and financial performance and condition, as well as our plans, objectives and expectations for our business operations and financial performance and condition. 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," "contemplate," "continue," "could," "due," "estimate," "expect," "goal," "intend," "may," "objective," "plan," "predict," "potential," "positioned," "seek," "should," "target," "will," "would," and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the timing of data from ongoing Phase 2a and 2b trials of tenapanor and the timing of commencement of the Phase 3 development program of tenapanor;
- our receipt of future milestone payments from our collaboration partners, and the expected timing of such payments;
- our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use;
- our development plans with respect to our NaP2b inhibitor program, as well as our RDX009, RDX013 and RDX020 programs;
- the likelihood and our expectations that we elect to exercise our co-promotion rights with respect to tenapanor or an NaP2b inhibitor product, or exercise our co-fund rights with respect to the first Phase 3 clinical development program for tenapanor;
- the likelihood and potential for Sanofi to exercise its option to exclusively license our NaP2b inhibitor program;
- our ability to maintain existing and our intention to establish new collaboration partnerships;
- our ability to develop, acquire and advance product candidates into, and successfully complete, clinical trials;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- the commercialization of our product candidates, including tenapanor and our NaP2b inhibitors;
- our commercialization, marketing and manufacturing capabilities;
- the implementation of our business model and strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering tenapanor and our NaP2b inhibitors;
- estimates of our expenses, future revenue, capital requirements, our needs for additional financing and our ability to obtain additional capital;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our use of proceeds from this offering;
- our financial performance; and
- developments and projections relating to our competitors and our industry.

These forward-looking statements are based on management's current expectations, estimates, forecasts, and projections about our business and the industry in which we operate and management's beliefs and assumptions and are not guarantees of future performance or development and involve known and unknown risks, uncertainties, and other factors that are in some cases beyond our control. As a result, any or all of our forward-looking statements in this prospectus may turn out to be inaccurate. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under "Risk Factors" and elsewhere in this prospectus. Potential investors are urged to consider these factors carefully in evaluating the forward-looking statements. These forward-looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future. You should, however, review the factors and risks we describe in the reports we will file from time to time with the SEC after the date of this prospectus. See "Where You Can Find More Information."

Market, Industry and Other Data

This prospectus contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates, including data regarding the estimated patient population in those markets, their projected growth rates, the perceptions and preferences of patients and physicians regarding certain therapies for the treatment of ESRD patients with hyperphosphatemia, patients with CKD and patients with IBS-C and other disease indications that we are pursuing or may pursue, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

Use of Proceeds

The net proceeds from the sale of 4,286,000 shares of common stock in this offering will be approximately $52.4 million at the initial public offering price, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that net proceeds will be approximately $60.8 million after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently expect to use our net proceeds from this offering as follows:

- approximately $15.0 million to $20.0 million to fund continued discovery and development efforts for our preclinical product candidates;
- if we exercise our right to co-fund the first Phase 3 clinical development program for tenapanor, we may invest a portion of the net proceeds of this offering, alone or together with cash on hand, in an amount of $20.0 million, $30.0 million or $40.0 million to acquire an increase of 1%, 2% or 3%, respectively, in the royalties payable to us by AstraZeneca on net sales of tenapanor;
- approximately $5.0 million to $10.0 million to advance and expand the development of APECCS, which amount is expected to fund our planned development activities for at least two years including acquiring equipment to monitor, miniaturize and automate the APECCS cell culture and screening processes, and enhancing the capabilities to develop intestinal cells in the APECCS format, APECCS cultures from intestinal tissues and assays with the APECCS system; and
- the remainder for working capital and other corporate purposes, which will include facilities expansion and the pursuit of other research and discovery efforts and could include the acquisition or in-license of other products, product candidates or technologies.

However, due to the uncertainties inherent in the clinical development and regulatory approval process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering that may be used for the above purposes. As such, our management will retain discretion over the use of the net proceeds from this offering. The amounts and timing of our expenditures will depend upon numerous factors, including, among others:

- the timing of the results of our ongoing Phase 2a and 2b clinical trials for tenapanor;
- the receipt, if any, of milestone payments from one or more of our collaboration partners;
- whether we exercise our right to co-fund the Phase 3 clinical development program for tenapanor and at what financial level;
- whether we exercise our right to co-promote tenapanor and/or a NaP2b inhibitor under our agreements with our collaboration partners;
- the size, scope and timing of any nonclinical or clinical trials that we may decide to pursue; and
- the number and scope of any discovery programs and research and development activities that we may undertake.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in interest-bearing, investment-grade securities, certificates of deposit or government securities.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Capitalization

The following table sets forth our capitalization as of March 31, 2014:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the conversion of all outstanding shares of our convertible preferred stock pursuant to a stockholder vote under our amended and restated certificate of incorporation into an aggregate of 11,517,222 shares of common stock immediately prior to the consummation of this offering;
  - the net exercise, based on the initial public offering price, of all of our Series B warrants into 571,244 shares of our common stock at an exercise price of $0.09 per share, and the related reclassification of our convertible preferred stock warrant liability to additional paid-in capital; and
  - the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering; and
- on a pro forma as adjusted basis to give further effect to the sale of 4,286,000 shares of common stock in this offering at the initial public offering price, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this information together with our audited financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the headings "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of March 31, 2014		
	Actual	Pro Forma	Pro Forma As Adjusted
	(unaudited)		
	(in thousands, except per share data)		
Cash and cash equivalents	$ 33,221	$ 33,221	$ 85,625
Convertible preferred stock warrant liability	9,059	—	—
Convertible preferred stock, $0.0001 par value per share, 108,829,748 shares authorized; 11,517,222 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted	56,155	—	—
Stockholders' (deficit) equity:			
Preferred stock, par value of $0.0001 per share, no shares authorized, issued or outstanding, actual; 5,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, $0.0001 par value per share, 130,360,121 shares authorized; 1,272,278 shares issued and outstanding, actual; 300,000,000 shares authorized, 13,360,744 shares issued and outstanding, pro forma and 17,646,744 shares issued and outstanding, pro forma as adjusted	—	1	2
Additional paid-in capital	5,266	70,479	122,882
Accumulated deficit	(71,724)	(71,724)	(71,724)
Total stockholders' (deficit) equity	(66,458)	(1,244)	51,160
Total capitalization	$ (1,244)	$ (1,244)	$ 51,160

The outstanding share information in the table above excludes the following:

- 880,497 shares of common stock issuable upon the exercise of outstanding stock options as of March 31, 2014 having a weighted-average exercise price of $1.23 per share (which includes 239,423 shares of early exercised stock options subject to a repurchase right as of March 31, 2014);
- 26 shares of common stock reserved for issuance pursuant to future awards under our 2008 Stock Incentive Plan, as amended, as of March 31, 2014, which will become available for issuance under our 2014 Equity Incentive Award Plan after consummation of this offering;
- 1,419,328 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the consummation of this offering; and
- 202,762 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan.

Dilution

If you invest in our common stock in this offering, your interest will be immediately diluted to the extent of the difference between the initial public offering price per share of our common stock in this offering and the net tangible book value per share of our common stock after this offering. As of March 31, 2014, we had a historical net tangible book value of $(67.0) million, or $(52.64) per share of common stock. Our net tangible book value represents total tangible assets less total liabilities and convertible preferred stock, all divided by the number of shares of common stock outstanding on March 31, 2014. Our pro forma net tangible book value at March 31, 2014, before giving effect to this offering, was $(1.8) million, or $(0.13) per share of our common stock. Pro forma net tangible book value, before the issuance and sale of shares in this offering, gives effect to:

- the conversion of all outstanding shares of our convertible preferred stock pursuant to a stockholder vote under our amended and restated certificate of incorporation into an aggregate of 11,517,222 shares of common stock immediately prior to the consummation of this offering;
- the net exercise, based on the initial public offering price, of all of our Series B warrants into 571,244 shares of our common stock at an exercise price of $0.09 per share, and the related reclassification of our convertible preferred stock warrant liability to additional paid-in capital; and
- the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the consummation of this offering.

After giving effect to the sale of shares of common stock in this offering at the initial public offering price and after deducting the underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value at March 31, 2014 would have been approximately $50.6 million, or $2.87 per share. This represents an immediate increase in pro forma as adjusted net tangible book value of $3.00 per share to existing stockholders and an immediate dilution of $11.13 per share to new investors. The following table illustrates this per share dilution:

Initial public offering price per share		$ 14.00
Historical net tangible book value per share as of March 31, 2014	$ (52.64)	
Pro forma increase in net tangible book value per share	52.51	
Pro forma net tangible book value per share as of March 31, 2014	(0.13)	
Increase in pro forma net tangible book value per share attributable to new investors	3.00	
Pro forma as adjusted net tangible book value per share after this offering		2.87
Dilution per share to new investors participating in this offering		$ 11.13

If the underwriters fully exercise their option to purchase additional shares, pro forma as adjusted net tangible book value after this offering would increase to approximately $3.23 per share, and there would be an immediate dilution of approximately $10.77 per share to new investors.

To the extent that outstanding options with an exercise price per share that is less than the pro forma as adjusted net tangible book value per share, before giving effect to the issuance and sale of shares in this offering, are exercised, new investors will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

The following table shows, as of March 31, 2014, on a pro forma as adjusted basis, after giving effect to the pro forma adjustments described above, the number of shares of common stock purchased from us, the total consideration paid to us and the average price paid per share by existing stockholders and by new investors purchasing common stock in this offering at the initial public offering price, before deducting the underwriting discounts and commissions and estimated offering expenses payable by us (in thousands, except share and per share amounts and percentages):

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	13,360,744	76%	$ 56,554	49%	$ 4.23
Investors participating in this offering	4,286,000	24%	60,004	51%	$14.00
Total	17,646,744	100%	$116,558	100%	$ 6.61

The number of shares of common stock to be outstanding after this offering is based on the number of shares outstanding as of March 31, 2014 and excludes the following:

- 880,497 shares of common stock issuable upon the exercise of outstanding stock options as of March 31, 2014 having a weighted-average exercise price of $1.23 per share (which includes 239,423 shares of early exercised stock options subject to a repurchase right as of March 31, 2014);
- 26 shares of common stock reserved for issuance pursuant to future awards under our 2008 Stock Incentive Plan, as amended, as of March 31, 2014, which will become available for issuance under our 2014 Equity Incentive Award Plan after consummation of this offering;
- 1,419,328 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan, which will become effective immediately prior to the consummation of this offering; and
- 202,762 shares of common stock reserved for future issuance under our Employee Stock Purchase Plan, as well as any automatic increases in the number of shares of our common stock reserved for future issuance under this plan.

Selected Financial Data

The selected statements of operations data for the years ended December 31, 2012 and 2013 and the selected balance sheet data as of December 31, 2012 and 2013 are derived from our audited financial statements included elsewhere in this prospectus. The selected statements of operations data for the three months ended March 31, 2013 and 2014 and the selected balance sheet data as of March 31, 2014 are derived from our unaudited financial statements included elsewhere in this prospectus. The unaudited interim financial information has been prepared on the same basis as the annual financial information and, in the opinion of management, reflects all adjustments, consisting only of normal recurring adjustments, that we consider necessary for a fair presentation of the financial information set forth in those statements.

Our historical results are not necessarily indicative of the results to be expected in the future, and our interim unaudited results are not necessarily indicative of the results to be expected for the full year. You should read the following selected financial data together with the section of this prospectus entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes included in this prospectus.

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
	(in thousands, except per share data)			
			(unaudited)	
Statements of Operations Data:				
Revenue:				
Licensing revenue	$ 3,182	$ 8,063	$ 1,989	$ 3,236
Collaborative development revenue	2,228	20,865	4,567	5,314
Total revenue	5,410	28,928	6,556	8,550
Operating expenses:				
Research and development[1]	10,184	28,093	5,939	7,637
General and administrative[1]	4,031	3,700	1,027	1,377
Total operating expenses	14,215	31,793	6,966	9,014
Loss from operations	(8,805)	(2,865)	(410)	(464)
Other expense, net	(30)	(52)	(25)	(4)
Change in fair value of preferred stock warrant liability	(950)	(3,506)	—	(2,603)
Loss before provision for income taxes	(9,785)	(6,423)	(435)	(3,071)
Provision for income taxes	—	(141)	(35)	—
Net loss	$ (9,785)	$ (6,564)	$ (470)	$ (3,071)
Net loss per common share, basic and diluted[2]	$ (11.32)	$ (5.82)	$ (0.45)	$ (2.44)
Shares used to compute net loss per common share, basic and diluted[2]	864,020	1,127,948	1,042,675	1,256,245
Pro forma net loss per common share, basic and diluted (unaudited)[2]		$ (0.23)		$ (0.04)
Shares used to compute pro forma net loss per common share, basic and diluted (unaudited)[2]		13,216,414		13,344,711

(1) Included in the statement of operations data above are the following stock-based compensation expenses (in thousands):

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
			(unaudited)	
Research and development	$ 221	$ 200	$ 48	$ 37
General and administrative	252	152	59	27
Total stock-based compensation	$ 473	$ 352	$ 107	$ 64

(2) See Notes 2 and 12 to our audited financial statements and Note 5 to our unaudited financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per common share, pro forma net loss per common share, and the weighted-average number of shares used in the computation of the per share amounts.

	As of December 31,		As of March 31,
	2012	2013	2014
		(in thousands)	(unaudited)
Balance Sheet Data:			
Cash and cash equivalents	$ 32,903	$ 34,435	$ 33,221
Working capital	20,069	24,697	20,347
Total assets	37,884	42,904	40,548
Convertible preferred stock warrant liability	2,950	6,456	9,059
Convertible preferred stock	56,155	56,155	56,155
Accumulated deficit	(62,089)	(68,653)	(71,724)
Total stockholders' deficit	(57,392)	(63,479)	(66,458)

Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion and analysis of our financial condition and results of operations together with the section entitled "Selected Financial Data" and our financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as our plans, objectives, expectations, intentions and beliefs. 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 identified below and those discussed in the section entitled "Risk Factors" included elsewhere in this prospectus.

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the gastrointestinal, or GI, tract to treat cardio-renal, GI and metabolic diseases. We have developed a proprietary drug discovery and design platform enabling us, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing our platform, we discovered and designed our lead product candidate, tenapanor, which in preclinical and clinical studies has consistently demonstrated the ability to reduce the absorption of dietary sodium and phosphorus, both of which are key factors in the progression of kidney disease. To enhance our proprietary drug discovery and design platform, we have developed a cell-culture system to simulate gut tissues called the Ardelyx Primary Enterocyte and Colonocyte Culture System, or APECCS. We have also identified over 3,800 proteins on the inner surface of the gut, many of which we believe may be drug targets. In addition to tenapanor, we are evaluating small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in end stage renal disease, or ESRD, a program we have licensed to Sanofi S.A., or Sanofi. We are also independently advancing three other discovery and lead development programs focused in cardio-renal, GI and metabolic diseases.

In October 2012, we entered into a collaboration partnership with AstraZeneca AB, or AstraZeneca, for the worldwide development and commercialization of tenapanor. AstraZeneca is responsible for all of the development and commercialization costs for tenapanor, and we have retained an option to co-promote in the United States. Together with AstraZeneca, we are evaluating tenapanor in three Phase 2 clinical trials in patients with ESRD, late-stage CKD, and constipation-predominant irritable bowel syndrome, or IBS-C. If we exercise our right to co-fund the first Phase 3 clinical development program for tenapanor, we may invest $20.0 million, $30.0 million or $40.0 million to acquire an increase of 1%, 2% or 3%, respectively, in the royalties payable to us by AstraZeneca on net sales of tenapanor. In December 2013, we entered into an amendment to the license agreement to acknowledge the intention of AstraZeneca to commence development of tenapanor for the treatment of hyperphosphatemia in ESRD patients and to provide additional clarification for certain payments. There was no change in the total consideration that we could receive under the agreement.

Through our participation with AstraZeneca on a development collaboration committee, we are involved in the management and oversight of the development of tenapanor and participation will continue until all of Phase 2 clinical trials with tenapanor have been completed. In addition, we are directly responsible for the conduct of certain specified clinical trials being conducted with tenapanor. AstraZeneca reimburses us for our internal and external costs related to those development efforts, and any other development efforts that may be assigned to us by the development collaboration committee. We are initially responsible for supplying tenapanor for use in development. The agreement also obligates us to transfer the technology and other necessary information such that AstraZeneca will be able to assume the responsibility for the supply of the drug product for use in later-stage clinical trials.

Under the terms of the agreement with AstraZeneca, we received a $35.0 million upfront payment and we are eligible to receive up to $237.5 million in development milestones, of which we have received $40.0 million.

The $40.0 million in development milestones consists of a payment of $15.0 million that we received in January 2014 and a payment of $25.0 million that we received in May 2014 as a result of the dosing of the first patient in the Phase 2b ESRD clinical trial in hyperphosphatemia in April 2014. In addition to the $237.5 million in total development milestones, we are also eligible to receive up to $597.5 million in sales and launch milestones. Through March 31, 2014, we also received $24.5 million in reimbursement for our development efforts provided under the agreement. We are also eligible to receive incremental tiered royalties based on aggregate annual net sales of each licensed product starting in the high single digits and increasing to high teen percentages as annual net sales increase, subject to an increase related to our co-fund election, if we decide to make such an election.

We have identified the deliverables within the arrangement as a license to the technology, the initial supply of the compound of the licensed product for use in development, and ongoing development activities through completion of all Phase 2 clinical trials to be conducted with tenapanor, which are accounted for as a single unit of accounting. We have concluded that the license is not a separate unit of accounting. It does not have stand-alone value to AstraZeneca, separable from the development services to be performed pursuant to the agreement, as AstraZeneca is unable to use the license for its intended purpose without our performance of the development services, which includes the initial supply of the compound of the licensed product. As a result, we recognize revenue from the $35.0 million up-front payment on a straight-line basis over the period from the effective date of the agreement through the completion of all Phase 2 clinical trials to be conducted with tenapanor, which we currently estimate to be December 2016, and we recognize revenue from the $15.0 million development milestone payment on a straight-line basis over the period from the amendment date through the same estimated completion date of all Phase 2 clinical trials. We will recognize revenue from the $25.0 million development milestone payment on a straight-line basis through the same estimated completion date of all Phase 2 clinical trials.

In 2014, we entered into an option and license agreement with Sanofi under which we granted Sanofi an exclusive worldwide license to conduct research utilizing our small molecule NaP2b inhibitors. In addition, Sanofi has the option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors. Sanofi is advancing this program towards first-in-human clinical trials. Under our arrangement, Sanofi is responsible for all of the costs and expenses for research and preclinical activities and, should it exercise its option, for the development and commercialization efforts under the program. Under the license option and license agreement, we received an upfront payment of $1.25 million and are responsible for up to $175,000 of patent costs, at which point any additional patent costs will be fully reimbursed to us by Sanofi. We have the potential to earn future development, regulatory and commercial milestone payments of up to $196.75 million if Sanofi continues to advance the program into development and through commercialization. If a NaP2b inhibitor is commercialized by Sanofi as a result of this program, we will receive tiered royalties ranging from the mid-single digits into the low double digits. As part of our agreement with Sanofi, we retain an option to co-promote licensed products in the United States. The upfront payment was recognized as deferred revenue as we have not provided all deliverables as of March 31, 2014.

Our revenue to date has been generated from collaboration and license revenue pursuant to our license agreements with AstraZeneca, and Sanofi. We have not generated any commercial product revenue. As of March 31, 2014, we had accumulated deficit of $71.7 million. We have incurred significant losses in the past and may continue to incur significant losses in the future as we advance our unpartnered preclinical programs. The significance of future losses will be dependent in part on whether AstraZeneca continues to develop and advance tenapanor, and whether Sanofi exercises its option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors, which in either case would result in milestone payments to us. There can be no assurance that we will receive additional collaboration revenue in the future.

Financial Operations Overview

Revenue

Our revenue to date has been generated from non-refundable license payments and reimbursements for research and development expenses under our license agreements. We recognize revenue from upfront payments

ratably over the term of our estimated period of performance under the agreement which we consider to be licensing revenue. In addition to receiving upfront payments, we may also be entitled to milestone and other contingent payments upon achieving predefined objectives. Such payments are recorded as revenue when we achieve the underlying milestone if it is deemed to be a substantive milestone at the date the arrangement is entered into. To the extent that non-substantive milestones are achieved and we have remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance. Reimbursements from AstraZeneca for development costs incurred under our license and collaboration agreement with them are classified as collaborative development revenue.

We expect that any revenue we generate will fluctuate from year to year as a result of the timing and amount of milestones and other payments from our collaboration partnerships with AstraZeneca, Sanofi, and any future collaboration partners, and as a result of the fluctuations in the research and development expenses we incur in the performance of assigned activities under our license agreement with AstraZeneca.

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our unpartnered product candidates, as well as the development of product candidates pursuant to our license agreement with AstraZeneca. We recognize all research and development costs as they are incurred.

Research and development expenses consist of the following:

- external research and development expenses incurred under agreements with consultants, third-party contract research organizations, or CROs, and investigative sites where a substantial portion of our clinical studies are conducted, and with contract manufacturing organizations, or CMOs, where our clinical supplies are produced;
- employee-related expenses, which include salaries, benefits and stock-based compensation; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

Prior to the execution of our license agreement with AstraZeneca in October 2012, we incurred $18.0 million in research and development expenses related to tenapanor. Following the execution of the license agreement and through March 31, 2014, we incurred $27.5 million in research and development expenses related to tenapanor, all of which are reimbursed by AstraZeneca under the license agreement. The reimbursements are recognized in collaborative development revenue in the Statement of Operations and Comprehensive Loss.

The following table summarizes our research and development expenses during the years ended December 31, 2012 and 2013 and the three months ended March 31, 2013 and 2014.

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
	(in thousands)			
			(unaudited)	
Discovery research expense	$ 6,311	$ 7,746	$ 1,727	$ 2,360
Clinical development expense—tenapanor	1,961	—	—	—
Total non-collaboration expense	8,272	7,746	1,727	2,360
AstraZeneca collaboration development expense	1,912	20,347	4,212	5,277
Total research and development expenses	$10,184	$28,093	$ 5,939	$ 7,637

We expect our unpartnered research and development expenses will increase in the future as we progress our internal product candidates, advance our discovery research projects 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 or our collaboration partners may never succeed in achieving marketing approval for any of our product candidates. The probability of success of each of the product candidates may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability.

Most of our product development programs are at an early stage; therefore, the successful development of our product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each product candidate and are difficult to predict. Given the uncertainty associated with clinical trial enrollment and the risks inherent in the development process, we are unable to determine the duration and completion costs of current or future clinical trials of our product candidates or if and to what extent we will generate revenues from the commercialization and sale of any of our product candidates. We anticipate that we and our collaboration partners 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, as well as an ongoing assessment as to each product candidate's commercial potential. We will need to raise additional capital or may seek additional collaboration partnerships in the future in order to complete the development and commercialization of our product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, travel expenses and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, bonus, benefits and stock-based compensation. We expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administration and professional services.

Change in Fair Value of Convertible Preferred Stock Warrant Liability

Change in fair value of convertible preferred stock warrant liability is the fair value remeasurement of our liability related to our convertible preferred stock warrants. We will continue to record adjustments to the estimated fair value of the convertible preferred stock warrants until they are exercised or expire. In connection with our initial public offering, our outstanding warrants will automatically net exercise and the convertible preferred stock warrant liability will be reclassified to additional paid-in capital.

Provision for Income Taxes

Provision for income taxes for the 2013 periods consists of California state income taxes as we were required to pay the Alternative Minimum Tax for the $35.0 million upfront payment received from AstraZeneca in 2012.

Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with United States generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the

accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

Revenue from research activities made under collaboration partnership agreements are recognized as the services are provided and when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue generated from research and license agreements typically includes up-front signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments, and royalties on future licensees' product sales.

For revenue agreements with multiple-element arrangements, such as license and development agreements, we allocate revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, we determine the selling price for each deliverable using vendor-specific objective evidence or third-party evidence. If neither exists, we use the best estimate of selling price for that deliverable. Revenue allocated is then recognized when the four basic revenue recognition criteria are met for each element. Our obligations under the agreements may include the transfer of intellectual property rights in the form of licenses, obligations to provide research and development services and obligations to participate on certain development committees with the collaboration partner. We make judgments that affect the period over which we recognize revenue. On a quarterly basis, we review our estimated period of performance for our license revenue based on the progress under the arrangement and account for the impact of any changes in estimated periods of performance on a prospective basis.

We recognize cost reimbursement revenue under collaboration partnership agreements as the related research and development costs for services are rendered. Deferred revenue represents the portion of research or license payments received that have not been earned.

A milestone is considered substantive when the consideration earned from the achievement of the milestone (i) is commensurate with either our performance to achieve the milestone or the enhancement of value of the item delivered as a result of a specific outcome resulting from our performance to achieve the milestone, (ii) relates solely to past performance and (iii) is reasonable relative to all deliverables and payment terms in the arrangement. Such payments that are contingent upon the achievement of a substantive milestone are recognized entirely as revenue in the period in which the milestone is achieved. To the extent that non-substantive milestones are achieved and we have remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance. If there were no remaining performance obligations, we recognize the revenue in the period it is earned.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. Stock-based compensation expense was $473,000, $352,000, $107,000 and $64,000 for the years ended December 31, 2012 and 2013 and the three months ended March 31, 2013 and 2014, respectively.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected Term—The expected term represents the period that stock-based awards are expected to be outstanding. We used the simplified method to determine the expected term, which is calculated as the average of the time-to-vesting and the contractual life of the options.

Expected Volatility—Since we are privately held and do not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which we based our expected stock price volatility, we selected companies with comparable characteristics to us, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

In addition to the Black-Scholes assumptions, we estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior, and other factors. The impact from any forfeiture rate adjustment would be recognized in full in the period of adjustment and if the actual number of future forfeitures differs from our estimates, we might be required to record adjustments to stock-based compensation in future periods.

Historically, for all periods prior to this initial public offering, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

In determining a fair value for our common stock, we estimated the enterprise value of our business using the income approach and the market approach. The income approach estimates the fair value of a company based on the present value of the company's future estimated cash flows. These future cash flows are discounted to their present values using an appropriate discount rate, to reflect the risks inherent in the company achieving these estimated cash flows. The discount rate used in our third-party valuations was based primarily on benchmark venture capital studies of discount rates for other companies in similar stages of development. The market approach estimates the fair value of a company by including an estimation of the value of a business based on estimating a future value under an initial public offering scenario based on recent biopharmaceutical initial public offerings and an estimate of value under a merger and acquisition scenario. The estimated enterprise value is then allocated to the common stock using the Option Pricing Method, or OPM, and the Probability Weighted Expected Return Method, or PWERM, or the hybrid method. The hybrid method applied the PWERM utilizing the probability of two exit scenarios, going public or being acquired, and the OPM was utilized in the remaining private scenario.

For valuations after the completion of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant.

The intrinsic value of all outstanding options as of March 31, 2014 was $11.2 million based on the initial public offering price of our common stock set forth on the cover page of this prospectus.

Estimated Fair Value of Convertible Preferred Stock Warrants

Freestanding warrants for shares that are contingently redeemable are classified as a liability on the balance sheet at their estimated fair value. At the end of each reporting period, the change in estimated fair value during the period is recorded in change in fair value of convertible preferred stock warrant liability in the statement of operations and comprehensive loss. We will continue to adjust the carrying value of the warrants until the earlier of the exercise or expiration of the warrants. We estimated the fair values of these warrants using their intrinsic value in 2012 given their low exercise price. Beginning in 2013, we have estimated the fair value of the warrant liability using a hybrid of the OPM, and the PWERM. The hybrid method applied the PWERM utilizing the probability of two exit scenarios, going public or being acquired, and the OPM was utilized in the remaining private scenario. The scenarios were weighted based on our estimate of the assigned probability.

Income Taxes

We account for income taxes under an asset and liability approach for deferred income taxes, which require recognition of deferred income tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements, but have not been reflected in taxable income. Estimates and judgments occur in the calculation of certain tax liabilities and in the determination of the recoverability of certain deferred income tax assets, which arise from temporary differences and carryforwards. Deferred income tax assets and liabilities are measured using the currently enacted tax rates that apply to taxable income in effect for the years in which those tax assets are expected to be realized or settled. We regularly assess the likelihood that deferred income tax assets will be realized based on historical levels of taxable income, projections for future taxable income, and tax planning strategies. To the extent that we believe any amounts are not more likely than not to be realized, we record a valuation allowance to reduce the deferred income tax assets. We regularly assess the need for the valuation allowance on its deferred tax assets, and to the extent that we determine that an adjustment is needed, such adjustment will be recorded in the period that the determination is made.

We regularly review our tax positions and benefits to be realized. We recognize tax liabilities based upon estimate of whether, and the extent to which, additional taxes will be due when such estimates are more likely than not to be sustained. An uncertain income tax position will be recognized if it has a more likely than not of being sustained. We recognize interest and penalties related to income tax matters in the income tax provision in the statements of operations and comprehensive loss appearing elsewhere in this prospectus. We have not incurred any interest or penalties associated with unrecognized tax benefits for any periods presented.

Results of Operations

Comparison of the three months ended March 31, 2013 and 2014

	Three Months Ended March 31,		Dollar Change
	2013	2014	
	(in thousands)		
Revenue:			
Licensing revenue	$1,989	$ 3,236	$ 1,247
Collaborative development revenue	4,567	5,314	747
Total revenue	6,556	8,550	1,994
Operating expenses:			
Research and development	5,939	7,637	1,698
General and administrative	1,027	1,377	350
Total operating expenses	6,966	9,014	2,048
Loss from operations	(410)	(464)	(54)
Other expense, net	(25)	(4)	21
Change in fair value of preferred stock warrant liability	—	(2,603)	(2,603)
Loss before provision for income taxes	(435)	(3,071)	(2,636)
Provision for income taxes	(35)	—	35
Net loss	$ (470)	$(3,071)	$(2,601)

Revenues

Licensing revenue for the three months ended March 31, 2014 was $3.2 million, an increase of $1.2 million, or 63%, compared to $2.0 million for the three months ended March 31, 2013. The increase was due to the $15.0 million we received in December 2013 related to the amendment to the AstraZeneca agreement which is being amortized over our expected period of performance under the agreement. The estimated period of performance is based on the completion of all of the Phase 2 clinical trials for tenapanor. We estimate that the end of all Phase 2 clinical trials will be December 2016. The expected period of performance is reviewed quarterly and adjusted, as needed, to reflect the progress of clinical studies.

Collaborative development revenue consists of our development expenses that are reimbursable to us by AstraZeneca as part of our license agreement. Collaborative development revenue for the three months ended March 31, 2014 was $5.3 million, an increase of $0.7 million, or 16%, compared to $4.6 million for the three months ended March 31, 2013. The increase was due to an increase in our development activities primarily related to the expansion of the clinical trials that are a part of the AstraZeneca agreement.

Research and Development

Research and development expenses were $7.6 million for the three months ended March 31, 2014, an increase of $1.7 million, or 29%, compared to $6.0 million for the three months ended March 31, 2013. The increase was primarily driven by a $1.1 million increase in development activities related to tenapanor as we expanded the clinical trial activities under our license agreement with AstraZeneca. Discovery research expenses increased by $0.6 million due to an increase in our research activities for non-partnered programs.

General and Administrative

General and administrative expenses were $1.4 million for the three months ended March 31, 2014, an increase of $0.4 million, or 34%, compared to $1.0 million for the three months ended March 31, 2013. The increase was primarily due to an increase in professional services fees of $0.3 million.

Change in fair value of preferred stock warrant liability

Change in fair value of preferred stock warrant liability was $2.6 million for the three months ended March 31, 2014, an increase of $2.6 million compared to zero for the three months ended March 31, 2013. The increase was due to an increase in the fair value of our convertible preferred stock.

Provision for Income Taxes

Provision for income taxes was zero during the three months ended March 31, 2014 compared to a provision for income taxes of $35,000 during the three months ended March 31, 2013. The provision for the three months ended March 31, 2013 was due to California state income taxes related to the Alternative Minimum Tax for the $35.0 million upfront payment received from AstraZeneca.

Comparison of the years ended December 31, 2012 and 2013

	Year Ended December 31,		
	2012	2013	Dollar Change
		(in thousands)	
Revenue:			
Licensing revenue	$ 3,182	$ 8,063	$ 4,881
Collaborative development revenue	2,228	20,865	18,637
Total revenue	5,410	28,928	23,518
Operating expenses:			
Research and development	10,184	28,093	17,909
General and administrative	4,031	3,700	(331)
Total operating expenses	14,215	31,793	17,578
Loss from operations	(8,805)	(2,865)	5,940
Other expense, net	(30)	(52)	(22)
Change in fair value of preferred stock warrant liability	(950)	(3,506)	(2,556)
Loss before provision for income taxes	(9,785)	(6,423)	3,362
Provision for income taxes	—	(141)	(141)
Net loss	$ (9,785)	$ (6,564)	$ 3,221

Revenue

Licensing revenue for the year ended December 31, 2013 was $8.1 million, an increase of $4.9 million, or 153%, compared to $3.2 million for the year ended December 31, 2012. The increase was due to a full year of amortization in 2013 of the AstraZeneca up-front license payment as compared to a partial period in 2012. In addition, we received an additional payment of $15.0 million in December 2013 related to the amendment to the AstraZeneca agreement which is also being amortized over the expected period of performance. The estimated period of performance is based on the completion of all of the Phase 2 clinical trials for tenapanor. We initially estimated the period of performance to be through June 2015. In connection with our process of evaluating the progress of clinical activities, we subsequently revised our estimate of the period of performance to be through December 2016.

Collaborative development revenue consists of our development expenses that are reimbursable to us by AstraZeneca as part of our license agreement. Collaborative development revenue for the year ended December 31, 2013 was $20.9 million, an increase of $18.6 million, compared to $2.2 million for the year ended December 31, 2012. The increase was due to a full year of development activities related to the AstraZeneca agreement.

Research and Development

Research and development expenses were $28.1 million for the year ended December 31, 2013, an increase of $17.9 million, or 176%, compared to $10.2 million for the year ended December 31, 2012. The increase was primarily driven by increased development activities, including our ongoing Phase 2 clinical trials, as part of our license agreement with AstraZeneca for the research, development, and commercialization of tenapanor. AstraZeneca reimburses us for our internal and external development-related costs associated with our license agreement. These development-related costs are mainly comprised of external research and development expenses incurred under agreements with consultants and third-party contract research organizations.

General and Administrative

General and administrative expenses were $3.7 million for the year ended December 31, 2013, a decrease of $0.3 million, or 8%, compared to $4.0 million for the year ended December 31, 2012. The decrease was primarily due to a decrease in consulting and legal fees of $0.5 million related to negotiation costs incurred in 2012 in connection with the AstraZeneca agreement, partially offset by an increase in salary expenses as a result of increased headcount in 2013.

Change in Fair Value of Preferred Stock Warrant Liability

Change in fair value of preferred stock warrant liability was $3.5 million for the year ended December 31, 2013, an increase of $2.6 million compared to $1.0 million for the year ended December 31, 2012. The increase was due to an increase in the fair value of our convertible preferred stock.

Provision for Income Taxes

Provision for income taxes was $0.1 million for the year ended December 31, 2013 compared to zero for the year ended December 31, 2012. The provision in 2013 was due to California state income taxes as we were required to pay the Alternative Minimum Tax in 2013 for the $35.0 million upfront payment received from AstraZeneca.

Liquidity and Capital Resources

Liquidity and Capital Expenditures

Since inception, as of March 31, 2014, our operations have been financed primarily by net proceeds of $56.2 million from the sales of shares of our convertible preferred stock and $51.3 million from payments received from our collaboration partners AstraZeneca and Sanofi. As of March 31, 2014, we had $33.2 million of cash and cash equivalents. In May 2014, we received a $25.0 million development milestone payment from AstraZeneca as a result of the dosing of the first patient in the Phase 2b ESRD clinical trial in hyperphosphatemia in April 2014.

Our primary uses of cash are to fund operating expenses, primarily research and development expenditures. 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 will be sufficient to meet our projected operating requirements for at least the next 12 months. 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. Further, our operating plan may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development expenditures. We currently have no credit facility or committed sources of capital other than potential milestones receivable under our current collaboration partnership. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates and the extent to which we may enter into additional collaboration partnerships with third parties to participate in their development and commercialization, we are unable to

estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical studies. Our future funding requirements will depend on many factors, including the following:

- our decision whether or not to exercise our right to co-fund the first Phase 3 clinical development program for tenapanor, in which we may invest $20.0 million, $30.0 million or $40.0 million to acquire an increase of 1%, 2% or 3%, respectively, in the royalties payable to us by AstraZeneca on net sales of tenapanor;
- the achievement of development and regulatory milestones resulting in the payment to us from our collaboration partners of contractual milestone payments and the timing of the receipt of such payments, if any;
- the progress, timing, scope, results and costs of our preclinical studies and clinical trials for our product candidates that have not been licensed, including the ability to enroll patients in a timely manner for clinical trials;
- the time and cost necessary to obtain regulatory approvals for our product candidates that have not been licensed and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability and the ability of our collaboration partners to successfully commercialize and/or co-promote our product candidates;
- the manufacturing, selling and marketing costs associated with product candidates, including the cost and timing of building our sales and marketing capabilities;
- our ability to establish and maintain collaboration partnerships, in-license/out-license or other similar arrangements and the financial terms of such agreements;
- the timing, receipt, and amount of sales of, or royalties on, our future products, if any;
- the sales price and the availability of adequate third-party reimbursement for our product candidates;
- 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;
- the time and cost necessary to respond to technological and market developments; and
- 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 our product candidates.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical studies, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, collaboration partnerships, licensing arrangements and other marketing and distribution arrangements. To the extent that we raise additional capital through marketing and distribution arrangements or other collaboration partnerships or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

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

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
			(unaudited)	
Cash provided by (used in) operating activities	$ 21,980	$ 1,811	$ (4,125)	$ (1,120)
Cash used in investing activities	(128)	(278)	(70)	(94)
Cash provided by (used in) financing activities	270	(1)	—	—

Cash Flows from Operating Activities

Cash used in operating activities for the three months ended March 31, 2014 was $1.1 million, consisting of a net loss of $3.1 million, which was offset by non-cash charges of $64,000 for stock-based compensation, $73,000 for depreciation and amortization expense, and $2.6 million for the change in the fair value remeasurement of our convertible preferred stock warrant liability. The change in our net operating assets and liabilities was due primarily to a $2.4 million decrease in deferred revenue which was mainly driven by the amortization of the $35.0 million up-front payment and $15.0 million additional payment received in connection with our agreement with AstraZeneca, and a $1.5 million decrease in our accounts receivable due to the timing of payments received from AstraZeneca for reimbursable costs incurred under our licensing agreement.

Cash used in operating activities for the three months ended March 31, 2013 was $4.1 million, consisting of a net loss of $0.5 million, and non-cash charges of $0.1 million for stock-based compensation, and $0.2 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to a $2.4 million decrease in deferred revenue which was mainly driven by the amortization of the $35.0 million up-front payment received in connection with our agreement with AstraZeneca, and a $1.3 million decrease in our accounts receivable due to the timing of payments received from AstraZeneca for reimbursable costs incurred under our licensing agreement, and a $0.6 million increase in our accrued compensation and benefits as a result of 2012 bonus accruals that were paid in the beginning of 2013.

Cash provided by operating activities for the year ended December 31, 2013 was $1.8 million, consisting of a net loss of $6.6 million, which was offset by non-cash charges of $0.4 million for stock-based compensation, $0.6 million for depreciation and amortization expense, and $3.5 million for the change in the fair value remeasurement of our convertible preferred stock warrant liability. The change in our net operating assets and liabilities was due primarily to a $7.6 million increase in deferred revenue as a result of the $15.0 million payment received in 2013 under our license agreement with AstraZeneca, offset by $8.1 million in amortization of revenue and a $1.1 million increase in our accounts payable due to the timing of payments. Our accounts receivable increased by $3.4 million due to the timing of payments received from AstraZeneca for reimbursable costs incurred under our license agreement.

Cash provided by operating activities for the year ended December 31, 2012 was $22.0 million, consisting of a net loss of $9.8 million which was offset by non-cash charges of $0.5 million for stock-based compensation, $0.7 million for depreciation and amortization expense, and $1.0 million for the change in the fair value remeasurement of our convertible preferred stock warrant liability. The change in our net operating assets and liabilities was due primarily to a $32.7 million increase in deferred revenue which was mainly driven by the $35.0 million up-front payment received in connection with our agreement with AstraZeneca, net of the amortization to revenue of $3.2 million. The remaining difference was an increase in reimbursable expenses included in deferred revenue of $0.9 million that related to reimbursements received for prepaid development expenses. Our accounts receivable increased by $3.1 million due to the recognition of reimbursable development costs and related timing of payments received from AstraZeneca.

Cash Flows from Investing Activities

Cash used in investing activities for the three months ended March 31, 2013 and 2014 was related to our acquisition of property and equipment of $70,000 and $94,000. Purchases of property and equipment are primarily related to the expansion of our laboratory and research activities.

Cash used in investing activities for the years ended December 31, 2012 and 2013 was related to our acquisition of property and equipment of $0.1 million and $0.3 million. Purchases of property and equipment are primarily related to expansion of our laboratory and related equipment.

Cash Flows from Financing Activities

There were no cash flows from financing activities for the three months ended March 31, 2013 and 2014.

Cash provided by financing activities for the years ended December 31, 2012 and 2013 was related to proceeds from the issuance of common stock upon the exercise of stock options of $0.3 million and $1,000, respectively, offset by repurchase of unvested common stock that was early exercised of $20,000 and $2,000, respectively.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2013:

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More Than 5 Years**	**Total**
			(in thousands)		
Operating lease obligations	$ 569	$ 999	$ —	$ —	$1,568
Total contractual obligations[1]	$ 569	$ 999	$ —	$ —	$1,568

(1) We had unrecognized tax benefits in the amount of $1.4 million as of December 31, 2013 related to uncertain tax positions. However, there is uncertainty regarding when these liabilities will require settlement so these amounts were not included in the contractual obligations table above.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities**.** We had cash and cash equivalents of $33.2 million as of March 31, 2014, which consist of bank deposits and money market funds. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. We had no outstanding debt as of March 31, 2014.

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, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Recent Accounting Pronouncements

In July 2013, the Financial Accounting Standards Board, or FASB, issued ASU 2013-11, *Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists*. ASU 2013-11 concludes an unrecognized tax benefit should be presented as a reduction of a deferred tax asset when settlement in this manner is available under the law. We will adopt this amendment as of January 2014. The result of adoption may be to reclassify certain long term liabilities to long term deferred tax assets, and the adoption will not result in a change to the tax provision. We do not believe that the impact on the balance sheet will be significant.

Business

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the gastrointestinal, or GI, tract to treat cardio-renal, GI and metabolic diseases. We have developed a proprietary drug discovery and design platform enabling us, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing our platform, we discovered and designed our lead product candidate, tenapanor, which in preclinical and clinical studies has consistently demonstrated the ability to reduce the absorption of dietary sodium and phosphorus, both of which are key factors in the progression of kidney disease. In 2012, we entered into a collaboration partnership with AstraZeneca for the worldwide development and commercialization of tenapanor. AstraZeneca is responsible for all of the development and commercialization costs for tenapanor, and we have retained an option to co-promote in the United States. Together with AstraZeneca AB, or AstraZeneca, we are evaluating tenapanor in three Phase 2 clinical trials in patients with end stage renal disease, or ESRD, late-stage chronic kidney disease, or CKD, and constipation-predominant irritable bowel syndrome, or IBS-C. To enhance our proprietary drug discovery and design platform, we have developed a cell-culture system to simulate gut tissues called Ardelyx Primary Enterocyte and Colonocyte Culture System, or APECCS. We have also identified over 3,800 proteins on the inner surface of the gut, many of which we believe may be drug targets. In addition to tenapanor, we are evaluating small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in ESRD, a program we have licensed to Sanofi S.A., or Sanofi. We are also independently advancing three other discovery and lead development programs focused in cardio-renal, GI and metabolic diseases.

Tenapanor is a small molecule, orally administered inhibitor of NHE3, a transporter of sodium in the GI tract. We and AstraZeneca have evaluated tenapanor in eight human clinical studies in over 765 individuals. In Phase 1 and Phase 2 clinical trials, tenapanor has generally been well-tolerated and has shown the ability to divert dietary sodium into the stool in both healthy adult subjects and patients with ESRD. In Phase 1 clinical trials in healthy adults, we observed that tenapanor has a significant effect on the diversion of dietary phosphorus into the stool. Additionally, tenapanor has demonstrated activity consistent with an IBS-C drug by increasing the frequency of bowel movements in IBS-C patients in a Phase 2a clinical trial. We and AstraZeneca are continuing development in ongoing Phase 2a and Phase 2b clinical trials in three different indications:

- ESRD patients on hemodialysis to treat hyperphosphatemia: Phase 2b randomized, double-blind, placebo-controlled clinical trial in 150 patients to evaluate the effects of tenapanor on serum phosphorus. Enrollment is ongoing and the results of this trial are expected in the first half of 2015.
- Stage 3 CKD patients with type 2 diabetes mellitus, albuminuria and high blood pressure: Phase 2a randomized, double-blind, placebo-controlled clinical trial in 140 patients to evaluate the effects of tenapanor on kidney function and fluid overload. Enrollment is ongoing and the results of this clinical trial are expected in the second half of 2015.
- IBS-C patients: Phase 2b randomized, double-blind, placebo-controlled clinical trial in 371 patients to evaluate the effect of tenapanor on the frequency of bowel movements versus placebo. Enrollment is completed and the results of this clinical trial are expected in the fourth quarter of 2014.

We believe the market opportunity for tenapanor for these three potential patient populations is significant. We estimate, based on phosphate binder utilization, the only approved therapies for hyperphosphatemia, that there are about 270,000 ESRD patients with hyperphosphatemia in the United States. The worldwide market for phosphate binders in 2011 was reported to be $1.5 billion and is projected to reach $2.3 billion by 2015. We believe there are approximately 1.8 million patients in the United States that have late-stage, or stage 3b or stage 4 CKD with type 2 diabetes, and approximately 4.4 million individuals in the United States with IBS-C.

In addition to tenapanor, we have discovered novel NaP2b inhibitors for the treatment of hyperphosphatemia in ESRD patients by inhibiting the active absorption of phosphorus. In February 2014, we

entered into an option and license agreement with Sanofi under which we granted Sanofi an exclusive worldwide license to conduct research utilizing our small molecule NaP2b inhibitors. Sanofi is advancing this program towards first-in-human clinical trials. In addition, Sanofi has the option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors. Under our arrangement, Sanofi is responsible for all of the costs and expenses for research and preclinical activities and, should it exercise its option, for the development and commercialization efforts under the program, while we retain an option to co-promote licensed products in the United States.

Utilizing our proprietary drug discovery and design platform, we are pursuing other internal discovery and lead-development programs that are currently in the research phase. While we have identified molecules that exhibit certain of the activity we are seeking in each of the following programs, we have not yet selected a lead molecule in these programs.

- RDX009 Program: Our focus is the discovery and development of non-systemic TGR5 agonists that stimulate GLP-2 and GLP-1 and have the potential when used in combination with a DPP4 inhibitor to heal the intestines and reduce inflammation in inflammatory bowel disease, or IBD;
- RDX013 Program: Our focus is the discovery and development of drug candidates to treat hyperkalemia, or elevated serum potassium, also commonly seen in CKD and ESRD patients; and
- RDX020 Program: Our focus is the discovery and development of drug candidates that provide alternate ways to manage fluid overload and kidney function by inhibiting chloride transport in CKD patients, particularly those who also experience acid-base disorders due to their disease.

Our executive management team has extensive experience in the discovery, development and commercialization of products in the renal field. As the Senior Vice President and General Manager of Renagel at Genzyme Corporation, or Genzyme, a Sanofi company, our President and Chief Executive Officer, Michael Raab, launched and oversaw the sales growth of sevelamer, the leading phosphate binder for the treatment of hyperphosphatemia with over $1.0 billion in worldwide sales in 2013. Mr. Raab was also instrumental in the worldwide launch of both Ceredase and Cerezyme, Genzyme's $1.0 billion therapies for Gaucher disease. Other members of our executive team have discovered or developed important products in the cardio-renal, GI and metabolic fields, including Renagel, patiromer and Welchol, among other products, in key roles in leading biopharmaceutical companies such as Ilypsa, Inc., MedImmune, LLC, a subsidiary of AstraZeneca Plc, GelTex Pharmaceuticals, Inc., Genzyme and PDL BioPharma, Inc.

Our operations to date have been funded by $56.2 million in equity investments primarily from leading venture capital investment firms and $76.3 million in upfront and development milestone payments from our collaboration partners AstraZeneca and Sanofi, which includes a development milestone payment of $25.0 million that we received in May 2014. Based on the current development plan for tenapanor, and assuming AstraZeneca's decision to proceed with development in accordance with those plans, we expect to receive a $20.0 million development milestone payment in the first half of 2015 and, assuming positive results in the ongoing Phase 2b clinical trial of tenapanor for the treatment of hyperphosphatemia, along with a decision by AstraZeneca to move forward into a Phase 3 clinical trial, we expect that we would receive an additional $50.0 million development milestone payment by the second half of 2015.

Our Proprietary Drug Discovery and Design Platform

Our platform, comprised of proprietary know-how and drug discovery and design tools such as APECCS, provides us with a competitive advantage in drug development. This platform enables us, in a rapid and cost-efficient manner, to discover and design novel drug candidates that work exclusively in the GI tract to treat cardio-renal, GI and metabolic diseases. By targeting receptors and transporters localized in the GI tract, we can modulate important functions of the gut, such as absorption of specific nutrients and minerals, or the gut's various hormonal functions, to treat and prevent diseases while avoiding systemic toxicities.

Benefits of our Platform versus Traditional Drug Discovery

Traditional small molecule drug discovery and design focuses on drugs that are rapidly absorbed in the GI tract. Once absorbed, those molecules typically need to survive the first-pass metabolism that occurs in the liver in order to arrive at the targeted cells or tissues and provide the desired benefit or effect. Compared to the traditional approach employed by the pharmaceutical industry to develop systemic drugs, we believe our proprietary drug discovery and design platform has several key benefits:

- Exploits the natural functions of the gut to affect disease. The gut is not a passive organ. It is lined with a variety of cell types that actively control the absorption of nutrients and minerals from the diet and serves to assist in the balance of those in the body. The gut also functions as an endocrine gland, causing the release of hormones in response to various stimuli. Additionally, the gut has multiple ways to communicate with the immune system and central nervous system. Our platform allows us to design drugs to modulate these active functions of the gut in order to prevent and treat disease. With our drug candidates, we can stimulate receptors in the gut to increase the release of endogenous hormones to take advantage of their natural effect on diseases and conditions. We have identified over 3,800 proteins on the inner surface of the gut, many of which we believe may be drug targets.
- Results in drug candidates with a superior safety profile that remain non-systemic. Traditional approaches to drug development, require the design of molecules to elicit an effect in a particular area or tissue of the body. To do this, those molecules must be absorbed into the bloodstream thereby exposing many or all tissues to the drug and potentially to the drug's metabolites. Drug and metabolite exposure in tissues not relevant to treating the intended disease or condition increases the chance of unwanted side effects. We avoid this systemic exposure by limiting the penetration of our drug candidates through the gut and into the bloodstream. We believe that our approach minimizes the possibility that our drugs may bind to or affect unintended targets in the body, reducing the potential for unwanted side effects.
- Reduces discovery time. Because our drug candidates are designed to be non-systemic and work locally, we avoid the time that is dedicated in traditional drug discovery to designing molecules to achieve adequate bioavailability and avoid undesirable off-target side effects, while still providing the desired pharmacologic response. When animal studies confirm that one of our drug candidates is non-systemic and we observe minimal metabolism of the candidate in the gut with the use of our discovery platform tools, we have a high degree of certainty that the drug candidate will reach our intended target on the surface of the gut when administered orally.
- Promotes efficient phenotypic screens. Our platform, particularly as enhanced with APECCS, allows us to conduct efficient phenotypic screening as the cell lines used for screening are a better representation of the GI. The *in vitro* activity of selected hits is believed to be more predictive of *in vivo* activity compared to more traditional approaches.

How our Proprietary Drug Discovery and Design Platform Works

Our platform allows us to identify and design novel non-systemic drug candidates to treat cardio-renal, GI and metabolic diseases.

- Identify: We identify and evaluate receptors and transporters on the epithelia of the GI tract that may impact diseases and we use a suite of techniques to characterize cell functions such as protein imaging and pharmacological probes in order to confirm that such targets are found on cells of the lumen, or inside surface, of the intestines. Using our scientific expertise and specialized know-how, along with traditional screening methodologies, we identify starting chemistries that have the potential to engage actively with the targeted receptor or transporter. These starting tool compounds are often absorbed into the bloodstream and have undesirable properties but serve the purpose of confirming the presence of the target we are pursuing. We use medicinal chemistry techniques to optimize potency and target engagement to eliminate or limit off-target activity and improve various drug properties of the compound.

- Non-Systemic: We use our medicinal chemistry expertise, together with a suite of tools and capabilities we have developed to test and monitor the non-systemic qualities of our drugs. We then transform the optimized tool compounds into pre-lead drug candidates that have low systemic availability, low gastric and intestinal metabolism, favorable drug properties such as solubility and stability, and that affect the desired biological response in animals. These pre-lead molecules are then optimized in all respects to create lead molecules that can enter IND-enabling studies.
- APECCS: APECCS, our novel cell-based system, involves the biopsy of various segments of the gut and the growth of those cells under proprietary conditions to maintain, to the extent possible, the integrity and functionality of the various cell types and substructures. We have developed this into a miniaturized format that allows us to utilize it for cell based drug screening. In addition to using APPECS in the design of our small molecule drug candidates, we use the APECCS technology to measure epithelial transport of ions and nutrients and to screen compounds to identify potential disease modulators such as inhibitors or activators using phenotypic screening. APECCS has the potential to allow us to identify novel targets, mechanisms of action and physiology as well as provide us an early understanding of how identified compounds may interact with specific gut tissues. In addition, we believe that APECCS may also provide us a clear path to translate cell-based observations into *in vivo* rodent models and ultimately into human clinical studies. We expect to use a portion of the proceeds from this offering to continue to enhance the capabilities of our APECCS cell-culture system by acquiring equipment to monitor, miniaturize and automate the APECCS cell culture and screening processes; developing the conditions to grow intestinal cells in the APECCS format from multiple segments of the intestine and multiple species including human, mouse, and rat; developing APECCS cultures from intestinal tissues derived from humans with various diseases and conditions; developing assays with the APECCS system that allow us to screen for drugs that affect various functional attributes of intestinal cells, and acquiring or in-licensing technologies, if necessary, to broaden the scope of APECCS capabilities.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the GI tract to treat cardio-renal, GI and metabolic diseases. Our strategy involves the following:

Advance tenapanor into late-stage and pivotal clinical trials in collaboration with AstraZeneca. We are actively involved with AstraZeneca in the development efforts for tenapanor, including overseeing and conducting, on AstraZeneca's behalf, two of the three ongoing Phase 2 clinical trials, for which AstraZeneca is solely responsible for all development costs. We participate in the strategic and operational management of the global tenapanor program and are focused on rapidly and efficiently advancing this program. With successful completion of the ongoing Phase 2 clinical trials and assuming AstraZeneca's decision to move forward with these programs, we expect that in the second half of 2015, AstraZeneca would initiate a Phase 3 pivotal clinical trial for hyperphosphatemia in ESRD, along with a Phase 2b clinical trial in CKD patients.

Use non-dilutive financing from our existing collaboration partnerships and the proceeds of this offering to expand our product pipeline and advance our earlier-stage product candidates into clinical trials. To date, we have received $76.3 million in non-dilutive funding from our collaboration partners, AstraZeneca and Sanofi, which includes the $25.0 million development milestone payment that we received in May 2014. If we achieve our milestones in these agreements, we would receive additional significant non-dilutive funding. We plan to use these payments, together with the proceeds of the offering, to continue our discovery and development efforts for our preclinical product candidates, which include our RDX009, RDX013 and RDX020 programs, and expand our product pipeline, including through the potential acquisition or in-license of other products. In addition, we will continue to evaluate new collaboration partnerships to enhance the discovery, development or commercialization of other product candidates in our product pipeline.

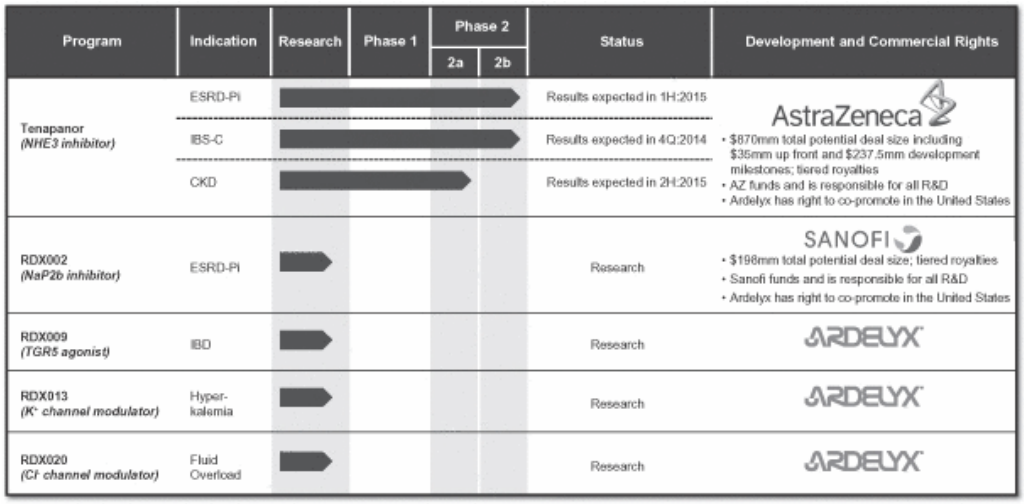
Leverage our technological capabilities and drug discovery and design platform to expand our product pipeline. We have developed a unique approach to discover and develop new agents to treat diseases involving the exploitation of receptors and targets on the epithelia of the GI tract that affect related biology to treat disease. We have built a suite of tools, knowledge and capabilities around this approach and have leveraged such tools for the discovery of NHE3 inhibitors such as tenapanor, NaP2b inhibitors, TGR5 agonists and other drug candidates in our pipeline. We have developed APECCS to augment and help streamline the approach. We have identified over 3,800 proteins on the inner surface of the gut, many of which we believe may be drug targets amenable to our approach. We plan to leverage these tools, capabilities and know-how to discover, develop and commercialize new first-in-class drugs that treat cardio-renal, GI and metabolic diseases.

Develop commercial capabilities. We expect to develop U.S. commercial capabilities, initially focusing on the renal field and targeting nephrologists or other specialty physicians. Our executive management team, and in particular our President and Chief Executive Officer, Michael Raab, has extensive experience in developing and commercializing therapeutic drugs for the CKD and ESRD markets. Upon receipt of positive Phase 3 results, we expect to exercise our right to co-promote one of our drug candidates with AstraZeneca or Sanofi, either of which would provide financial support that would assist us in building a specialty sales and marketing team for this purpose. We also may develop additional commercial capabilities in connection with other opportunities we choose to pursue.

Leverage our management team's drug development and commercialization expertise to identify and secure complementary in-licensing opportunities. Our management team has significant experience in the development and commercialization of products in the cardio-renal, GI and metabolic fields in which we operate. We intend to leverage this expertise to pursue in-licensing opportunities that expand our product pipeline within relevant therapeutic fields.

Our Product Pipeline

With AstraZeneca, we are evaluating the safety and efficacy of tenapanor in three ongoing Phase 2 clinical trials for three different indications. Through our collaboration partner, Sanofi, we are continuing discovery efforts with our NaP2b inhibitors. We also have three internal on-going discovery efforts aimed at non-systemic agents to treat IBD and hyperkalemia and to modulate chloride transport. The following table summarizes key information about our product candidates:



Tenapanor

Summary of tenapanor

Tenapanor has consistently demonstrated the ability to reduce the absorption of dietary sodium and phosphorus, both of which are widely recognized as key factors in the progression of kidney disease. Our lead indication is the treatment of hyperphosphatemia in ESRD patients. We and AstraZeneca are also evaluating the potential for tenapanor's long-term benefit in the treatment of patients with CKD. Trials are underway to understand the potential impact tenapanor may have on markers of kidney disease and fluid status in CKD patients. We and AstraZeneca are also evaluating the use of tenapanor for the treatment of IBS-C.

Tenapanor is a non-systemic small molecule inhibitor of NHE3, a sodium transporter present on the epithelia of the GI tract. *In vitro* studies have shown that tenapanor is potent against human NHE3 and specific for NHE3 versus other similar transporters such as NHE1, NHE2 and NaP2b. When radiolabeled tenapanor was administered orally to rats, we demonstrated that approximately 98% of the administered dose was detected, unchanged, in feces, indicating that no substantial metabolism occurred and that the drug was non-systemic. In human studies of orally-administered tenapanor, the drug was detected in the blood in only 0.7% of more than 2,000 collected serum samples, and even in those, at very low levels (< 1.5 ng/mL). Tenapanor is stable at room temperature and has been formulated into small tablets ranging from 1 mg to 50 mg.

We have administered tenapanor to over 765 subjects to date including 291 healthy volunteers, 410 IBS-C subjects and 65 patients with CKD and ESRD. Tenapanor has been administered in a single dose of up to 900 mg and for a period of up to 3 months at 100 mg/day. Tenapanor has generally been observed to be well-tolerated in clinical studies. All findings were consistent with findings for non-systemic drugs, where dose-limiting side effects are due to the exaggerated pharmacology of the drug and, in the case of tenapanor, such side effects were related to gastrointestinal symptoms. All serious adverse events reported thus far have been assessed as unrelated to tenapanor by the study investigators, by us and by AstraZeneca.

In animal studies and Phase 1 studies in healthy adult volunteers where fecal sodium was measured, we observed that tenapanor has a significant effect on the diversion of dietary sodium into the stool. In addition, in IBS-C patients, we saw that tenapanor elicited the expected pharmacological effect of increased fecal fluid that results from the inhibition of sodium absorption. The sodium effect of tenapanor is related to its interaction with NHE3. NHE3 is a sodium-proton exchanger located on the epithelia or surface of the intestinal lumen. NHE3 is also located on absorptive cells of the nephrons (structural units of the kidney that filter the blood). Its role is to absorb sodium into the body from the intestine or, alternately, re-absorb it from the filtered plasma in the kidney in order to maintain sodium balance in the body. The net flow of sodium (and chloride through other means) from the intestines also results in the complementary absorption of intestinal water to maintain a constant blood sodium concentration.

In preclinical studies with tenapanor, we observed that, in addition to diverting sodium into the stool, tenapanor also inhibited the absorption of phosphorus, and in Phase 1 studies in healthy adults, we observed that tenapanor has a significant effect on the diversion of dietary phosphorus into the stool. In *in vitro* studies we determined that tenapanor does not directly inhibit NaP2b or PiT1, both of which are phosphorus transporters in the gut. AstraZeneca continues to evaluate the mechanism for tenapanor's phosphorus effect. Based on results from preclinical and Phase 1 studies, we and AstraZeneca determined that developing tenapanor to treat hyperphosphatemia in ESRD patients offered the most expeditious path to approval and commercialization.

We and AstraZeneca have submitted the following three INDs to the FDA in connection with the development of tenapanor: we submitted IND 108,732 for the treatment of constipation-related diseases in October 2010 and IND 115,992 for the treatment of sodium and fluid overload diseases in December 2012, and AstraZeneca submitted IND 120,566 for the treatment of hyperphosphatemia in ESRD patients on dialysis in December 2013.

Tenapanor for treating hyperphosphatemia in ESRD patients on hemodialysis

The treatment of hyperphosphatemia in ESRD patients by reducing the absorption of dietary phosphorus is the lead indication for tenapanor. We and AstraZeneca have undertaken a Phase 2b clinical trial in this indication.

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 either changes in life-style 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 three- to five-hour session, significantly reducing quality of life.

Hyperphosphatemia in ESRD

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 kidney and excreted in urine. In adults with functioning kidneys, normal serum phosphorus levels are 2.6 to 3.8 mg/dL. With kidney failure, elevated phosphorus becomes a toxin and is diagnosed as hyperphosphatemia when serum phosphorus levels are greater than 5.0 mg/dL. Although patients with ESRD rely on dialysis to eliminate toxins, phosphorus is not readily removed by the procedure and other means of managing phosphorus levels must be employed.

In ESRD, 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 serum endocrine hormone that regulates phosphorus metabolism, and elevated parathyroid hormone, also known as secondary hyperparathyroidism. These endocrine changes in ESRD patients are a concern as elevated parathyroid hormone leads to the development of renal osteodystrophy, a condition of abnormal bone growth characterized by brittle bones. Elevated levels of FGF-23 are strongly associated with an increased risk of cardiovascular mortality. With concurrent elevated calcium levels common in these patients, particularly when calcium is used as a means of controlling phosphorus, deposits containing calcium and phosphate develop in arteries, joints, skin, soft tissue and other organs. Increased coronary artery calcification is associated with an increased risk of heart disease, stroke and death.

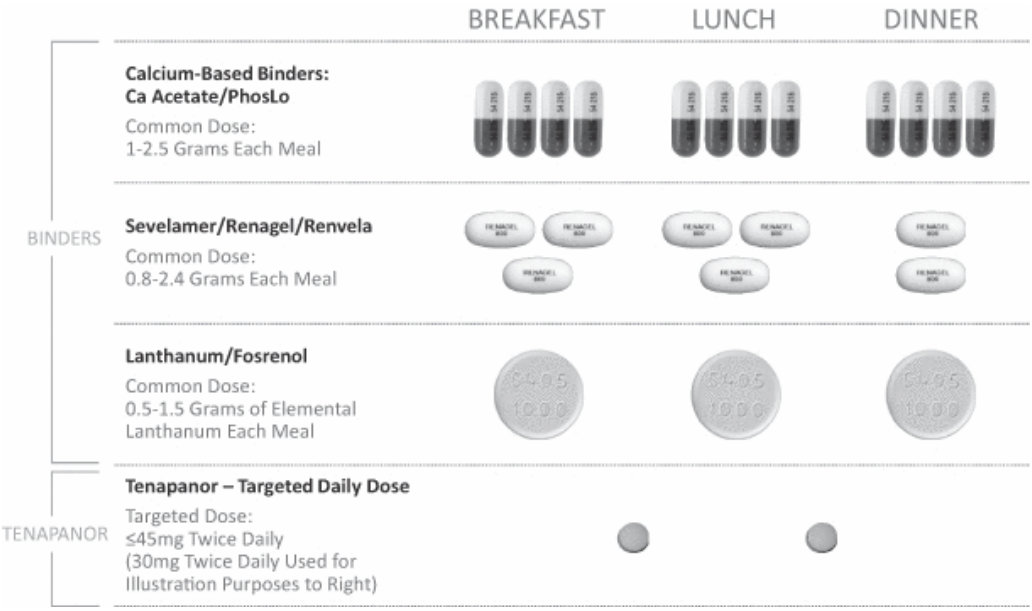
Limitations of current products for hyperphosphatemia

Since dialysis is unable to efficiently eliminate excess phosphorus, ESRD patients are put on restrictive low phosphorus diets and are prescribed medications called phosphate binders, the only pharmacologic interventions currently marketed for the treatment of hyperphosphatemia. Binders are a collection of drugs whose function is to bind, or absorb, dietary phosphorus and are taken in conjunction with meals and snacks. They include calcium or lanthanum, a rare-earth metal, which bind to and precipitate with dietary phosphate in the GI tract. The goal is for patients to excrete the precipitated phosphorus in their stool. A limitation of this approach is the systemic absorption of calcium or lanthanum, resulting in side effects and other unintended consequence for ESRD patients. In an effort to eliminate these unwanted side effects, non-absorbed exchange resins, such as sevelamer were developed to bind to phosphate in the GI tract and to be eliminated in stool.

Safety and tolerability have been significant concerns with many approved phosphate binders. The more common side effects of approved phosphate binders include long-term vascular calcification, nausea and vomiting, ileus or disruption of the normal propulsive ability of the GI tract.

ESRD patients take on average 10-14 oral medications each day, and they are severely restricted in their fluid intake. In addition, to control their serum phosphorus, their phosphate binder-related pill burden is significant, typically consisting of nine or more pills a day. The amount of phosphate a binder can remove is limited by its binding capacity, and therefore, increasing the dose, and the pill burden, of the binder is the only way to increase the amount of phosphate being bound and excreted. As a result, prescribed binder doses are intolerable for many patients.

The effectiveness of current treatment with phosphate binders is limited. For example, in a 2012 study conducted by Amgen in 1,430 ESRD patients on hemodialysis in the United States in which 89% of the patients in the study had previously been prescribed phosphate binders, the average baseline serum phosphorus level was 6.4 mg/dL, significantly above the target for dialysis patients of 5.5 mg/dL and far above normal serum phosphorus levels of 2.6 to 3.8 mg/dL. Other studies suggest that this lack of efficacy is due primarily to poor patient compliance associated with significant pill burden and other tolerability issues.



The above graph does not reflect actual size but is to scale.

Size of the hyperphosphatemia market

According to the most recent data available from the U.S. Renal Data System, in 2011 there were 395,656 patients on hemodialysis in the United States. Additionally, according to the European ERA-EDTA Registry 2011 Annual Report and a study in 2010 by the Japanese Society for Dialysis Therapy, there were approximately 270,000 patients on hemodialysis in Europe and about 250,000 in Japan. We estimate, based on phosphate binder utilization, the only approved therapies for hyperphosphatemia, that there are approximately 270,000, 215,000 and 220,000 ESRD patients with hyperphosphatemia in the United States, Europe and Japan, respectively. The worldwide market for phosphate binders in 2011 was reported to be approximately $1.5 billion and is projected to reach $2.3 billion by 2015. Although phosphate binders are not approved by the U.S. Food and Drug Administration, or FDA, for the treatment of hyperphosphatemia in CKD patients, in other major markets such as Europe and Japan, phosphate binders are approved for the treatment of hyperphosphatemia in Stages 3 and 4 CKD patients.

Preclinical and clinical data supporting tenapanor in hyperphosphatemia

Several preclinical and clinical studies have shown tenapanor's ability to inhibit the absorption of dietary phosphorus while maintaining an attractive safety and tolerability profile. In rats with normal renal function, tenapanor administered orally was able to significantly reduce urinary phosphorus. In a rat model of CKD, tenapanor reduced urinary and serum phosphorus and improved blood uremic markers indicative of improved renal status. Additionally in this model, tenapanor significantly improved survival, reduced aortic and gastric calcification, and reduced blood levels of FGF23, an important serum endocrine hormone that regulates phosphorus metabolism.

In four separate clinical trials tenapanor has consistently demonstrated the ability to inhibit the absorption of dietary phosphorus as measured by a decrease of urinary phosphorus and/or an increase of fecal phosphorus. The fecal phosphorus results in the studies described below were similar to those from a Phase 1 study in healthy adult volunteers published in 1997 by GelTex, where sevelamer was dosed at 5g three times daily, about 500 times the dose of tenapanor used in our studies.

- RDX5791-101: In this first-in-man clinical trial of tenapanor in healthy adults, doses of 3 to 100 mg administered once daily for 7 days produced increased fecal phosphorus as compared to placebo, suggesting that dietary phosphorus was diverted to the feces.
- RDX5791-102: In this Phase 1b study in healthy adults, tenapanor administered once, twice or three times daily for 7 days at various total daily doses of 30 to 120 mg consistently increased fecal phosphorus as compared to placebo.
- D5611C00002: In this Phase 1 clinical trial, designed to evaluate different formulations, 15 mg of tenapanor was administered twice daily to healthy adults. Tenapanor reduced urinary phosphorus compared to baseline.
- D5611C00006: In this Phase 1 clinical trial to evaluate drug-drug interactions, tenapanor alone, versus baseline, increased fecal phosphorus and decreased urinary phosphorus.

We and AstraZeneca are encouraged by the consistency of these data and as a result have commenced a Phase 2b clinical trial designed to evaluate tenapanor's ability to lower serum phosphorus in dialysis patients.

Development plans for tenapanor in hyperphosphatemia

We and AstraZeneca have initiated a Phase 2b clinical trial to evaluate the effects of tenapanor on serum phosphorus in hemodialysis patients with hyperphosphatemia. The study is designed to evaluate several doses and dosing schedules, including once and twice daily dosing schedules, in a wide range of doses designed to find the minimum effective dose. We expect to receive results for this trial in the first half of 2015.

Based on the results of this study and AstraZeneca's decision to seek concurrence by the FDA, this study may be accepted for use as a pivotal Phase 3 trial. Additionally, upon successful completion of the Phase 2b trial, we expect that AstraZeneca would initiate either one or two pivotal Phase 3 studies in the second half of 2015 for hyperphosphatemia.

Tenapanor's competitive advantage in hyperphosphatemia

Given that the objective is to lower serum phosphorus levels to below 5.5 mg/dL in dialysis patients, and that many of these patients are unable to accomplish this goal with currently marketed phosphate binders, there is a clear medical need for new treatments for hyperphosphatemia. We believe that there is a significant opportunity for new agents with 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 among any of the marketed hyperphosphatemia drugs, with milligram rather than gram quantities dosed once or twice daily. In addition, we and AstraZeneca may evaluate 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.

Tenapanor for treating CKD: potential long-term benefit from sodium control

In an ongoing Phase 2a trial, we and AstraZeneca are exploring the potential benefit of tenapanor in treating patients with CKD who still have some renal function and are not yet on dialysis. In order to explore the benefits of tenapanor in this population, we are initially evaluating tenapanor for its effect on markers of kidney disease and fluid status.

The decline in renal function in patients with CKD is initially asymptomatic and the rate of disease progression varies based on genetics, ethnicity, the underlying cause, such as cardiovascular disease, diabetes, and many other factors. As the disease progresses, signs and symptoms of CKD become more apparent and include fluid overload, hyperkalemia, metabolic acidosis, hypertension, anemia, and mineral and bone disorders. Therapy to delay progression of the disease focuses on blood pressure control and reduction in urinary protein excretion.

If the results of the ongoing Phase 2a study demonstrate that tenapanor offers a benefit by decreasing elevated urine albumin to creatinine ratio, or UACR (a measure that roughly correlates with kidney disease severity and which has a significant component that may be independent of any blood pressure effect), we believe this may give us insight into the potential long-term benefit of tenapanor on delaying the progression of kidney disease.

CKD is defined as abnormalities of kidney structure or function, present for more than three months, and is categorized by five general stages of progression (stages 1-5), according to estimated glomerular filtration rate, or eGFR. Stage 3b and beyond are generally considered to be late-stage CKD.

Sodium and fluid overload in CKD

In CKD patients, failing kidneys are less efficient at blood filtration and sodium elimination resulting in fluid and sodium overload. This fluid overload correlates with the rapid decline of kidney function and the eventual requirement for renal replacement therapy including hemodialysis. The effects of fluid overload include high blood pressure, worsening kidney and heart disease, fluid in the lungs (edema) causing dyspnea (shortness of breath) and ultimately poor survival. Fluid overload has been shown to be an independent predictor of mortality in both hemodialysis patients and in CKD patients.

In a study of CKD patients where sodium intake was restricted, the investigators demonstrated that by merely decreasing sodium intake that they were able to reduce blood pressure and albuminuria in those patients. Those two measures alone are indicators that kidney function may be improving. Although generally acknowledged that excess sodium intake should be curtailed in this population, it is also recognized that the majority of people who are told to restrict sodium intake are non-compliant. We believe that the pharmacologic approach we are taking with tenapanor may have the same impact.

We believe that, if we are successful in demonstrating an improvement in UACR, our ongoing Phase 2a clinical trial of tenapanor in CKD patients will provide data to allow for further investment in larger trials evaluating tenapanor's ability to delay disease progression. We expect to receive results from the ongoing Phase 2a study in the second half of 2015.

Limitations of current approaches to delay CKD progression

In an effort to preserve renal function, physicians often suggest a number of interventions and life-style modifications; however, most of them are quite cumbersome and lead to poor patient compliance. Although low sodium diets are generally required for all CKD patients, most patients are generally poorly compliant for a variety of reasons, including cost, lack of availability of low sodium foods and the inability to change eating habits.

Most CKD patients are also treated with a combination of therapies designed to delay progression of kidney disease by controlling diabetes, blood pressure and decreasing fluid retention. Diuretics are often prescribed to inhibit sodium re-uptake in the kidney and increase urinary sodium and water excretion. However, diuretics lose efficacy as kidney function declines, and are known to cause electrolyte disorders such as hypokalemia (low potassium) and metabolic alkalosis (high bicarbonate level in the blood). Hypertension medications referred to as ACE inhibitors, ARBs and mineral corticoid receptor blockers also reduce blood pressure associated with fluid overload, which in turn can delay the rate of progression of CKD. In addition, these agents, particularly mineral corticoid receptor blockers, can result in hyperkalemia (high potassium), preventing their widespread use in CKD patients.

Size of late-stage CKD market

Worldwide, there are about 64.6 million patients with stage 3 or 4 CKD all of which are at significant risk of kidney disease progression, heart disease caused by vascular calcification and premature death. There are approximately 3.6 million patients in the United States with stage 3b and 4 CKD. There are about 8.5 million and 2.3 million patients with stage 3b or 4 CKD in Europe and Japan, respectively. Of these, there are about 1.8 million, 1.7 million and 0.6 million patients in the United States, Europe and Japan, respectively, that have both CKD and type 2 diabetes, the patient population currently studied in the ongoing Phase 2a CKD clinical trial.

Preclinical and clinical data supporting tenapanor for CKD

In preclinical models rats with CKD that were fed a high salt diet and exhibited hypervolemia, cardiac hypertrophy and arterial stiffening, had improved measures of cardio-renal function including a dose-dependent reduction of extracellular fluid volume, left ventricular hypertrophy, albuminuria, and blood pressure in a dose-dependent manner with administration of tenapanor. We observed these effects whether tenapanor was administered prophylactically or after disease was established. In these studies, tenapanor also prevented increases in glomerular area and urinary KIM-1, both markers of renal injury. In addition, rats dosed with a combination of tenapanor and the blood pressure medication enalapril showed improvement in cardiac diastolic dysfunction and arterial pulse wave velocity relative to those animals dosed with enalapril alone.

In human studies, tenapanor reduced urinary sodium excretion by 20 to 50 mmol/day and led to an increase of similar magnitude in stool sodium.

The results of these preclinical and clinical studies suggest that therapeutic alteration of sodium transport with tenapanor in the gastrointestinal tract could lead to improvements in CKD and has informed the design of our development plan.

Development plans for tenapanor in CKD

We and AstraZeneca have commenced an Phase 2a, randomized, double-blind, placebo-controlled, parallel design study to evaluate the safety, tolerability, and pharmacodynamics of tenapanor in CKD patients with type 2 diabetes, albuminuria and high blood pressure.

With positive results from this Phase 2a study, we expect that AstraZeneca would commence a Phase 2b clinical program to evaluate the long-term benefit of sodium and fluid reduction in the CKD patient population. If the Phase 2b clinical program is successful, and should AstraZeneca decide to move forward with the development of tenapanor in the CKD patient population, we believe the Phase 3 clinical program could include endpoints such as the delay of the progression of kidney disease as measured by eGFR percentage of patients who progress to ESRD, cardiovascular events and survival.

Tenapanor for treating IBS-C

Tenapanor is being evaluated in a randomized Phase 2b, double-blind, placebo-controlled clinical trial in 371 IBS-C patients to evaluate the effect of tenapanor on the frequency of bowel movements versus placebo.

Enrollment is completed and the results of this clinical trial are expected in the fourth quarter of 2014. IBS-C is a GI disorder in which abdominal pain or discomfort is associated with constipation, which significantly affects the health and quality of life of affected patients. It is unknown what causes IBS-C. There is no specific test or biomarker for IBS-C and therefore, its presence is diagnosed by symptoms and by eliminating other disorders. IBS-C is very similar to chronic constipation and it is clinically distinguished by a significant pain component.

Limitations of current products for IBS-C

Numerous treatments exist for the constipation component of IBS-C, many of which are over-the-counter. We are aware of two prescription products marketed for IBS-C, Linzess (linaclotide) marketed by Ironwood Pharmaceuticals and Forest Laboratories and Amitiza (lubiprostone) marketed by Sucampo and Takeda. In Phase 3 clinical trials of Linzess in IBS-C patients, up to 20% more patients receiving Linzess than placebo reached the primary endpoint, indicating a significant response during 6 out of 12 weeks of treatment. In these studies, Linzess caused diarrhea in up to 17% more patients than placebo. Amitiza also causes significant levels of nausea and diarrhea.

Preclinical and clinical data supporting tenapanor in IBS-C

Prior to initiating our IBS-C clinical program, we generated a variety of evidence from animal studies which suggested that tenapanor would be effective in treating constipation disorders and IBS-C in particular. Rats treated with tenapanor exhibited a dose-dependent increase in both fecal water content and fecal form score in which higher scores mean looser stools. Similar results were observed in mouse, rabbit, dog, and non-human primates. In animal studies, we also showed that tenapanor transiently increases water content and transit rate in all segments of the intestinal tract, which is consistent with reported expression patterns of tenapanor's target, NHE3. In a rat model of visceral hypersensitivity, tenapanor reduced or abolished stress-induced hypersensitivity to colorectal distention at two different doses without affecting the overall tone or relaxation effect in the relevant tissue.

Results from two separate Phase 1 clinical trials were supportive of pursuing applications of tenapanor in constipation indications. For example, tenapanor administration reduced the median time to first post-treatment bowel movement, increased a measure of stool consistency (the Bristol Stool Form Scale), and increased average stool weight. Twice-daily dosing was shown to increase the pharmacodynamic response of tenapanor. On the basis of the Phase 1 results, we initiated and completed a Phase 2a study to evaluate complete spontaneous bowel movements in subjects with IBS-C. Although this primary endpoint was not met, we determined that the 100 mg once daily dose demonstrated activity consistent with an IBS-C drug with an incidence of diarrhea that was no different than placebo. In this randomized, placebo-controlled study, tenapanor was generally well-tolerated when administered once daily for 4 weeks at doses of 10 mg, 30 mg and 100 mg (n=46-47/group). The results from these studies provided support for the design and initiation of a Phase 2b clinical trial evaluating twice daily dosing.

Tenapanor's competitive advantage in IBS-C

We believe that tenapanor may offer a significant benefit over currently marketed drugs like Amitiza and Linzess, due in part, to the potential to adjust the dose and/or dose frequency of tenapanor in order to optimize its efficacy. The data we have generated in both animal and human studies have suggested that the effect of tenapanor for the treatment of IBS-C can be modulated by adjusting its dose and dose frequency.

In our Phase 1 clinical trials in healthy adults, we observed a consistent increase of fecal sodium when the once daily dose was increased from 3 mg to 100 mg, and we observed an approximate doubling of fecal sodium when the frequency of dosing was increased to twice daily. In all of our studies, we have seen that stool form change correlates with the amount of sodium diverted. In our Phase 2a clinical trial in IBS-C patients, we dosed up to 100 mg once daily and observed activity consistent with an IBS-C drug and an incidence of diarrhea, a significant limitation of other IBS-C drugs, that was similar to placebo. Our fully enrolled Phase 2b clinical trial is designed to explore the effect of twice daily dosing at various dose levels to determine if greater diversion of sodium equates to a greater effect and a larger percentage of patients meeting the primary endpoint.

We will require large clinical trials in IBS-C patients to confirm this titration effect of tenapanor and its effect on efficacy and safety.

Size of the IBS-C market

Based on reports in the literature regarding the prevalence of IBS in the U.S. population and the percentage of individuals who have IBS-C as opposed to other forms of IBS, we estimate that approximately 1.4% of the U.S. population has IBS-C, or about 4.4 million individuals. Of those, approximately 1.0 million patients have been diagnosed with IBS-C. Additionally, there are about 6.6 million IBS-C patients in Europe and about 3.4 million in Japan. The per-patient economic burden of IBS-C is estimated to be $1,500 to $7,500 per year in direct costs and $800 to $7,700 per year in indirect costs, implying the total burden in the United States is $2 billion to $15 billion.

Development plans for tenapanor in IBS-C

We and AstraZeneca have completed enrollment of a 12-week randomized, placebo-controlled Phase 2b study of tenapanor in a population of IBS-C patients that is substantially similar to that studied in the four-week Phase 2a study. We expect to receive results from this study in the fourth quarter of 2014. If this study is successful and AstraZeneca decides to move forward with the development of tenapanor in IBS-C, we expect that the Phase 3 pivotal studies would be similar to those conducted in the development of Linzess.

Tenapanor clinical program

Safety and tolerability

Tenapanor has been administered to over 765 subjects to date including 291 healthy volunteers, 410 IBS-C subjects and 65 subjects with CKD and ESRD. Tenapanor has been administered in a single dose of up to 900 mg and for a period of up to 3 months at 100 mg/day. We have seen little to no absorption of tenapanor into the blood with less than 0.7% of all tested serum samples having any detectable levels of tenapanor. Tenapanor has been observed to be generally well-tolerated in clinical studies. All findings were consistent with findings for non-systemic drugs, where dose-limiting side effects are due to the exaggerated pharmacology of the drug and, in the case of tenapanor, such side effects include diarrhea, nausea, flatulence, abdominal discomfort, abdominal pain, and abdominal distention. All serious adverse events reported thus far have been assessed as unrelated to tenapanor by the study investigators, by us and by AstraZeneca.

Summary of clinical results

Tenapanor has been observed to inhibit the absorption of both dietary sodium and phosphate in healthy volunteers. These findings have been confirmed in ESRD patients on hemodialysis in a Phase 2a proof-of-concept study. Based on these observations from early clinical studies, a number of clinical development programs are ongoing to fully evaluate the utility of tenapanor in treating different disease conditions. Based on the ability of tenapanor to inhibit the absorption of dietary sodium, a Phase 2a study in CKD patients with type 2 diabetes mellitus, albuminuria and elevated systolic blood pressure is ongoing to examine the ability of tenapanor to decrease albuminuria, a measure that roughly correlates with decline in kidney function. A Phase 2b clinical trial is also ongoing in IBS-C patients to examine the ability of tenapanor to increase the number of weekly bowel movements and reduce abdominal pain. Based on its ability to inhibit the absorption of dietary phosphorus, a Phase 2b clinical trial is ongoing in ESRD patients with hyperphosphatemia to examine the ability of tenapanor to reduce serum phosphorus levels. The following chart provides a general overview of our clinical program to date for tenapanor:

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Trial (Conducted by)	Subjects (active/ placebo)	Objectives	Indication (Status)	Dose Levels(1)	Conclusions
Phase 1 Trials					
RDX5791-101 (Ardelyx)	80 (62/18)	Safety, tolerability, pharmacodynamics and pharmacokinetics of single and multiple doses of tenapanor. Effects on urinary and stool sodium excretion	Healthy adults (completed)	10, 50, 150, 450, 900 mg –single dose 3, 10, 30, 100 mg QD for 7 days	• Tenapanor was well-tolerated • Tenapanor was pharmacodynamically active • Tenapanor was minimally systemically available
RDX5791-102 (Ardelyx)	105 (84/21)	Pharmacological activity, safety and tolerability of TID, BID and QD dosing of tenapanor	Healthy adults (completed)	15, 30, 60 mg BID 30 mg QD 30 mg TID for 7 days	• Tenapanor was well-tolerated • Tenapanor increased stool sodium excretion and reduced urinary sodium excretion • Tenapanor increased stool phosphorus excretion
D5611C00002 (Ardelyx)	18 (18/0)	Pharmacological activity of different formulations of tenapanor	Healthy adults (completed)	15 mg BID	• Tenapanor increased fecal phosphorus and reduced urine phosphorus
D5611C00003 (AstraZeneca)	37 (37/0)	Pharmacological activity of tenapanor with and without food (Part A) and pharmacological activity of free-base tenapanor with and without omeprazole (Part B)	Healthy adults (completed)	15 mg BID	• Trial results under evaluation and have not yet been released
D5611C00005 (Ardelyx)	83 (66/17)	Safety, tolerability, and pharmacokinetics of single and multiple doses of tenapanor in Japanese subjects	Healthy adults (completed)	180 mg – single dose 15, 30, 60, 90 mg BID	• Trial results under evaluation and have not yet been released
D5611C00006 (Ardelyx)	16 (16/0)	Pharmacological activity of tenapanor when administered with Renvela	Healthy adults (completed)	15 mg BID	• Tenapanor activity was similar with and without administration with Renvela for both the increase of fecal sodium and phosphorus
D5611C00007 (AstraZeneca)	8 (8/0)	The absorption, distribution, metabolism and excretion (ADME) of a single oral dose of ^{14}C-labelled tenapanor in healthy male volunteers	Healthy adults (ongoing)	15 mg QD	Pre-specified primary analysis: • To characterise the metabolism, excretion and pharmacokinetics of a single oral dose of (^{14}C)-tenapanor in healthy male subjects
Phase 2a Trials					
RDX5791-201 (Ardelyx)	186 (139/47)	Safety, tolerability, and pharmacodynamics of tenapanor for the treatment of constipation-predominant irritable bowel syndrome (IBS-C)	IBS-C (completed)	10, 30, 100 mg QD	• Tenapanor was well-tolerated • The results of this study provide preliminary evidence of the ability of tenapanor to alleviate symptoms associated with IBS-C
D5610C00001 (Ardelyx)	140 (70/70)	Safety, tolerability, and pharmacodynamics of tenapanor in CKD patients with type 2 diabetes mellitus and albuminuria	CKD – Na & Fluid (ongoing)	5, 15, 30, 60 mg BID titration	Pre-specified primary analysis: • To compare the effect of tenapanor versus placebo on the changes in urine albumin-to-creatinine ratio (UACR) from baseline to week 12
D5611C00001 (Ardelyx)	88 (45/43)	Safety, tolerability, and pharmacodynamics of tenapanor in ESRD-HD patients with elevated interdialytic weight gain (IDWG)	ESRD-Fluid (completed)	Dose between 5 and 90 mgs	• Tenapanor was well-tolerated • No effect on IDWG • Increase in stool sodium excretion • Minimal to no systemic exposure

Trial (Conducted by)	Subjects (active/ placebo)	Objectives	Indication (Status)	Dose Levels(1)	Selected Results
Phase 2b Trials					
D5612C00001 (Ardelyx)	360 expected (270/90); 371 enrolled	Efficacy and safety of tenapanor for the treatment of constipation-predominant irritable bowel syndrome (IBS-C) Determination of Phase 3 dose(s)	IBS-C (ongoing; enrollment completed)	5, 20, 50 mg BID	Pre-specified primary analysis: • Percent CSBM responders (weekly responders for 6/12 weeks; ≥1 CSBM from baseline) vs. placebo
D5613C00001 (AstraZeneca)	150 (125/25)	Efficacy and safety of tenapanor for the treatment of hyperphosphatemia in ESRD-HD patients Determination of Phase 3 dose(s)	ESRD-hyperphosphatemia (ongoing)	3, 30 mg QD 1, 3, 10, 30 mg BID	Pre-specified primary analysis: • The change in serum phosphate levels from the end of wash out (pre randomization value) to end of treatment

(1) For purposes of this prospectus, QD means once a day, BID means twice a day and TID means three times a day.

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% chance that the observed change was purely due to chance). Generally, a p-value less than 0.05 is considered statistically significant. Certain of the trial results discussed below were evaluated using an analysis method referred to as "least square means." Least square means is a mean estimated from a linear model and is adjusted for other variables that may affect the experimental value.

Phase 1 trials

- **RDX5791-101 (completed):** In this first-in-human clinical trial, healthy volunteers received either a fixed dose of tenapanor or placebo once daily for either 1 day or 7 consecutive days. The objectives of this trial were:
  - Primary: To evaluate the safety of tenapanor capsules
  - Secondary: To determine the pharmacokinetics of tenapanor capsules
  - Secondary: To determine the pharmacodynamics of tenapanor capsules as assessed by bowel movement timing, consistency, and frequency, and by urine sodium excretion

  This trial demonstrated that single doses up to 900 mg and multiple doses up to 100 mg for 7 consecutive days of tenapanor were well-tolerated. In the multiple-dose phase, only 2 of 576 plasma samples had any detectable tenapanor (< 1 ng/mL), confirming that tenapanor is minimally systemically available. Administration of multiple doses of tenapanor resulted in a decrease in urinary sodium excretion ($p < 0.05$ at scattered time points). Time to first bowel movement was slightly reduced with tenapanor (not statistically significant), and consistency was generally greater (not statistically significant). As expected for individuals with normal renal function, there was no change in serum sodium levels. In addition, in *post hoc* analysis we observed a significant, dose-dependent, increase in fecal sodium excretion at doses of 10 to 100 mg/day compared with placebo ($p < 0.05$), and an increase in stool phosphorus excretion ($p < 0.05$) as compared to placebo.
- **RDX5791-102 (completed)**: In this second completed Phase 1 trial, healthy volunteers were administered a daily dose of 30-120 mg/day of tenapanor either once, twice or three times a day. The objectives of this trial were:
  - Primary: To evaluate the safety of different dosing regimens of tenapanor capsules
  - Secondary: To determine the pharmacodynamics of different dosing regimens of tenapanor capsules as assessed by bowel movement timing, consistency, frequency, and by urine and stool sodium excretion.

Tenapanor was well-tolerated in this study. Least square means with 95% confidence intervals were used to evaluate responses; no p-values were calculated. In all cohorts receiving tenapanor, an increase in 24-hour stool sodium with a concomitant decrease in 24-hour urine sodium was observed. The magnitude of the response appeared to be dose-dependent with those cohorts receiving the highest doses of tenapanor showing greater changes from baseline than subjects receiving placebo. Twice daily dosing appeared to be more effective in reducing urine sodium as compared with once daily dosing. Tenapanor increased the frequency of bowel movements and stool weight. In *post hoc* analysis, tenapanor (15 mg, 30 mg, 60 mg BID, 30 mg TID), also caused an increase in 24-hour stool phosphorus.

- **D5611C00002 (completed)**: This Phase 1 trial was an open-label, three-way cross-over trial designed to evaluate the pharmacological activity of three different formulations (capsules versus tablets) of tenapanor. The objectives of this trial were:
  - Primary: To evaluate the pharmacodynamics for a tenapanor HCl capsule, a tenapanor HCl tablet and a tenapanor free base tablet
  - Secondary: To evaluate the safety and pharmacokinetics of tenapanor

  Least square means with 90% confidence intervals were used to evaluate responses; no p-values were calculated. The results demonstrated a similar increase in fecal sodium and phosphorus excretion and a concomitant decrease in urinary sodium and phosphorus excretion using the tablet formulation. The results demonstrated that the pharmacological activity of tenapanor in a tablet formulation was similar to previous results. Tenapanor was well-tolerated in this study and minimal systemic availability was confirmed.
- **D5611C00003 (completed)**: This Phase 1 trial was an open-label, three-way cross-over trial designed to determine whether food intake affects the pharmacodynamics activity of tenapanor. Subjects received tenapanor 5-10 minutes before breakfast and dinner, 30 minutes after breakfast and dinner, or in a fasted state. Trial results are under evaluation and have not yet been released.
- **D5611C00005 (completed)**: This Phase 1 trial was a double-blind, placebo-controlled study to assess the safety, tolerability, pharmacokinetics and pharmacodynamic effects in healthy male and female Japanese subjects. Doses up to 180 mg for 7 consecutive days of tenapanor were administered. Trial results are under evaluation and have not yet been released.
- **D5611C00006 (completed)**: This Phase 1 trial was a single-center, randomized, open-label study to evaluate the effect of Renvela on the pharmacological activity of tenapanor administered twice a day for 4 days in healthy male and female subjects. The objectives of this trial were:
  - Primary: To evaluate the effect of Renvela on the pharmacodynamic activity of tenapanor
  - Secondary: To evaluate the safety and pharmacokinetics of tenapanor

  Least square means with 90% confidence intervals were used to evaluate responses; no p-values were calculated. The effect on stool and urine sodium was comparable for the two treatments (tenapanor alone and tenapanor with Renvela). The effect on stool and urine phosphorus, and urine potassium and creatinine was similar for the two treatments (tenapanor alone and tenapanor with Renvela). No tenapanor was detected in blood plasma (all samples were below the limit of quantification). Tenapanor administered with or without Renvela was well-tolerated in this study. Since Renvela is the most commonly used phosphate binder and it could have potentially interfered with the activity of tenapanor, this study was performed to support the Phase 2a study in ESRD patients. The results demonstrated that Renvela had no effect on the pharmacological activity of tenapanor.
- **D5611C00007, ClinicalTrials.gov Identifier NCT02063386 (ongoing)**: This is an open-label, single dose study in 8 healthy male subjects to characterize the metabolism, excretion and pharmacokinetics of a single oral dose of 15 mg (14C)-tenapanor in healthy male subjects. The study is designed to measure the concentration of total radioactivity in blood and its ratio to the concentration of total

radioactivity in plasma. The percentage of the administered radioactivity recovered in urine and feces and the percentage of radioactive dose recovered overall will be measured. Determination of the presence of metabolites in plasma, urine and feces will also be measured, if possible. This study is being performed to support the regulatory dossier of tenapanor as a minimally absorbed drug.

Phase 2a trials

- **IBS-C Phase 2a, RDX5791-201, ClinicalTrials.gov Identifier NCT01340053 (completed)**: This was a multi-center, randomized, double-blind, placebo-controlled Phase 2a study in subjects with IBS-C. 186 subjects were randomized, including 46 subjects in both the 10 mg and 100 mg groups and 47 subjects in both the 30 mg and placebo groups. This 8-week study included a 2-week treatment-free screening period, a 4-week blinded treatment period, and a 2-week treatment-free follow-up period. The primary objective of this study was to evaluate the safety of tenapanor and the secondary objective was to evaluate the efficacy of tenapanor. The endpoints evaluated in this study were:
  - Primary: Change in weekly complete spontaneous bowel movement, or CSBM, frequency from the 14 day pretreatment baseline period to the end of the 4 week treatment period.
  - Secondary: Daily/weekly assessments of other bowel habits including spontaneous bowel movement, or SBM, frequency, stool consistency, degree of straining, degree of bloating, degree of abdominal pain, rescue medication usage, IBS severity, IBS-QOL, adequate relief of IBS symptoms, global relief of IBS symptoms, and treatment satisfaction. Percentage of patients reporting > 3 weekly CSBMs, an increase over baseline of > 1 weekly CSBMs, and a decrease in abdominal pain of >30% and an increase in > 1 weekly CSBMs from baseline for each week of the study.

  The mean changes from baseline in the 30 mg and 100 mg tenapanor groups were greater than in the placebo group, but the overall test of equality of the 3 treatment arms was not statistically significant. A significant difference in mean change from baseline for weekly CSBM frequency was noted between placebo and the 30 mg and 100 mg tenapanor groups at Week 1 ($p < 0.05$). Subjects who received 100 mg tenapanor were twice as likely to have >3 CSBM frequency rates in comparison to subjects in the placebo group at this time point. Further, the proportion of subjects with weekly CSBM frequency >1 was higher in the active treatment groups compared with the placebo group for all on-treatment assessments, although the differences were not statistically significant.

  The difference in mean changes in SBMs from baseline between the placebo group and the 30 mg and 100 mg tenapanor groups was significant at Weeks 1 and 4. The differences in mean changes from baseline for stool consistency scores between the placebo group and the tenapanor 30 mg and 100 mg groups were statistically significant ($p < 0.05$) at all study weeks. There were significant differences ($p < 0.05$) in mean changes from baseline from Weeks 2 to 4 between the straining scores reported by subjects in the placebo group in comparison to subjects who received tenapanor 30 mg or 100 mg.

  The proportion of subjects reporting a >30% decrease from baseline in the average weekly degree of abdominal pain score was generally higher for subjects in the 100 mg tenapanor group throughout the treatment period; however, a significant difference between subjects in the placebo group and subjects who received 30 mg and 100 mg of was reported only at Week 2 ($p < 0.05$). Although we were under powered (too few subjects) to demonstrate statistical significance, in order to plan for our Phase 2b and Phase 3 trials, we examined the current approval endpoints for IBS-C. There was a significant difference ($p< 0.05$) at Week 2 with subjects in the tenapanor 100 mg group approximately 1.5 times more likely to have a >30% decrease from baseline in average weekly degree of abdominal pain and >1 increase from baseline in weekly CSBM frequency as subjects in the placebo group.

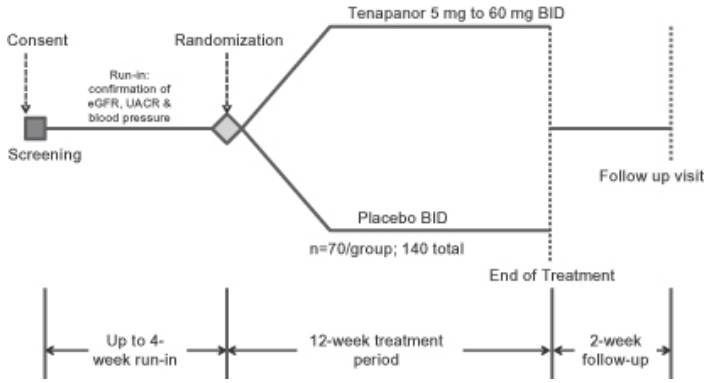
  Improvements were noted for subjects who received tenapanor in the degree of bloating, average degree of abdominal pain, relief of IBS symptoms, IBS severity, and IBS quality of life measurements; however, the differences between active treatment and placebo were not statistically significant. The

proportion of subjects who reported they were quite or very satisfied with treatment was 36%, 36% and 41% in the 10 mg, 30 mg, and 100 mg RDX5791 groups, respectively, compared with 26% in the placebo group, which was not statistically significant. These data demonstrated consistent effects of tenapanor in multiple endpoints and supported the design of a Phase 2b clinical trial in IBS-C patients.

- **ESRD-Fluid Phase 2a, D5611C00001 ClinicalTrials.gov Identifier, NCT01764854 (completed)**: This Phase 2a study was a randomized, double-blind, placebo-controlled, parallel design study to evaluate the pharmacodynamics, safety, and tolerability of tenapanor in ESRD patients with fluid overload. Trial results are still under evaluation; preliminary results are available. The objectives of this study were:
  - Primary: To compare the effect of tenapanor versus placebo on the reduction of interdialytic weight gain, or IDWG.
  - Secondary: To evaluate the safety and tolerability of tenapanor
  - Secondary: To evaluate the effect of tenapanor on stool sodium content during Week 1 in clinic
  - Secondary: To evaluate the effect of tenapanor versus placebo on the reduction of IDWG after weekly intervals of treatment
  - Secondary: To evaluate plasma concentrations of tenapanor

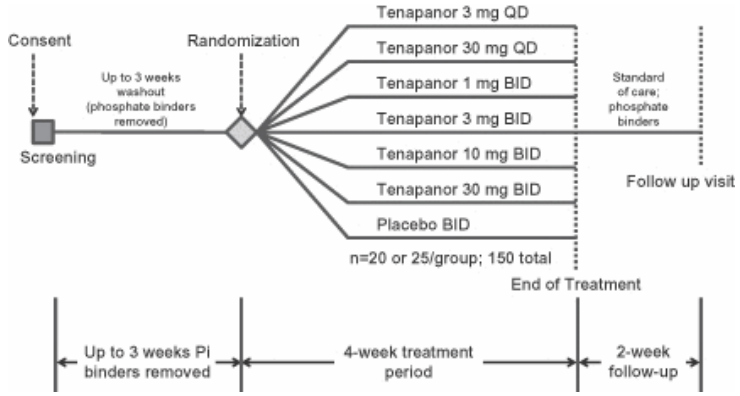
  There was no statistically significant difference between tenapanor and placebo in change of IDWG from baseline to week 4, the primary endpoint. We used this endpoint because interdialytic weight gain is driven by fluid intake which is usually driven by sodium intake; however, we believe that this result was due to dialysis practice in the US, where patients are dialyzed with and administered intravenous sodium concentrations higher than an individual patient's serum sodium level, thus offsetting the therapeutic benefit every 2 to 3 days. Additionally, we and AstraZeneca are evaluating the possibility, consistent with recent reports in the literature, that sodium may be stored short-term at high levels in the skin, muscles and vasculature, before affecting thirst and fluid retention. The pharmacological activity of tenapanor was confirmed by the increase in fecal sodium in the tenapanor group versus placebo. Tenapanor was well-tolerated and continued to display the non-systemic properties seen in previous studies.
- **CKD Phase 2a, D5610C00001, ClinicalTrials.gov Identifier NCT01847092 (ongoing)**: This is an exploratory Phase 2a, randomized, double-blind, placebo- controlled study to evaluate pharmacodynamics of tenapanor in 140 patients with stage 3 CKD, type 2 diabetes mellitus with albuminuria and elevated systolic blood pressure. The study consists of a 4-week run-in period, 12 weeks of blinded treatment with tenapanor 5, 15, 30, or 60 mg BID or placebo, and a 2-week follow-up period.

Pharmacodynamic assessments, or assessments of biological effects of tenapanor, include the following measures: Urine albumin-to-creatinine ratio (UACR) and eGFR (s-creatinine, and s-cystatin-c) which are indications of kidney function, blood pressure, bioimpedance a measure of excess body fluid, mean weekly stool consistency and stool frequency and urinary and blood markers associated with kidney disease. Safety assessments are performed at regular intervals and include physical examinations, vital signs, body weights, electrocardiograms, and laboratory results from blood and urine tests.



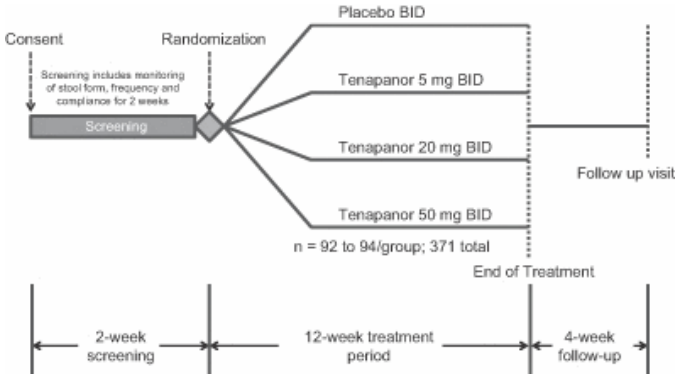
Phase 2b trials

- **ESRD-Phosphorus Phase 2b, D5613C00001, ClinicalTrials.gov Identifier NCT02081534 (ongoing)**: This is a randomized, double blind, placebo-controlled, parallel group, multicenter dose finding study to evaluate the efficacy, safety and tolerability of tenapanor to treat hyperphosphatemia in ESRD patients on hemodialysis. The study consists of a wash out period of up to 3 weeks where existing phosphorus lowering medication is withheld, a 4-week treatment period, and a follow-up period of 2 weeks. A total of 150 patients (20-25/group) are given tenapanor doses of either 1 mg, 3 mg, 10 mg or 30 mg twice a day or 3 mg and 30 mg once a day or matching placebo. To be randomized, patients must have a serum phosphorus level of at least 6.0 mg/dL (1.94 mmol/L) and have had an increase of at least 1.5 mg/dL (0.48 mmol/L) vs. pre wash out level. The primary objective of this study is to show effect of tenapanor versus placebo on the change in serum phosphorus levels from the end of wash out to end of treatment in hyperphosphatemic ESRD patients.



- **IBS-C Phase 2b, D5612C00001, ClinicalTrials.gov Identifier NCT01923428 (ongoing)**: This is a multi-center, Phase 2b, randomized, double-blind, placebo controlled study of tenapanor in subjects with IBS-C. The study consists of a 2-week screening period, a 12-week treatment period, and a 4-week follow-up period. Eligible subjects have been randomized 1:1 into one of four treatment groups (approximately 93 patients/group) for a total of 371 patients) at doses of 5 mg, 20 mg, or 50 mg of tenapanor or placebo, twice a day.

  The primary endpoint for this study is the percent complete spontaneous bowel movement (CSBM) responders; a CSBM is a bowel movement that feels complete and is not aided by the use of any other medication, like a laxative. In order to be a responder a patient needs to have an increase of at least one CSBM from baseline for 6 of the 12 treatment weeks.



RDX002 NaP2b Inhibitor for Hyperphosphatemia

Overview

RDX002 refers to our program aimed at discovering and evaluating small molecule inhibitors of the intestinal phosphate transporter NaP2b (also known as NaPi2b, Npt2b and SLC34A2). Our RDX002 program includes a portfolio of non-systemic NaP2b inhibitors in the discovery and preclinical stage of development. We have licensed this program to Sanofi, and under the terms of the agreement, Sanofi is responsible for completing discovery and preclinical work and, if it exercises its option, developing and commercializing at least one NaP2b inhibitor resulting from the program.

NaP2b is an intestinal phosphate transporter whose activity is believed to account for a significant portion of dietary phosphate absorption in humans. We believe the inhibition of NaP2b would provide utility for the treatment of hyperphosphatemia in ESRD patients.

We have identified several NaP2b inhibitors that showed activity *in vitro* and in animal models. In rats with normal renal function certain NaP2b compounds were able to reduce urinary excretion of phosphorus better than commercial phosphate binders such as sevelamer or colestilan, even when these compounds were dosed at approximately 1/10th of the dose of the commercial binders. In addition, our NaP2b compounds had additive effects when administered with sevelamer or colestilan. In a rat model designed to emulate CKD (5/6^{ths} nephrectomized rats where one full kidney and 2/3^{rds} of the second kidney are removed) one of our NaP2b inhibitors significantly reduced serum phosphorus and was additive or synergistic with sevelamer. This agent also significantly improved animal survival in the same model.

Rationale for product differentiation

Our identified NaP2b inhibitors work through a mechanism distinct from those employed by binders. Our NaP2b inhibitors are designed to inhibit NaP2b, one of the primary phosphate transporters in the gut. We have shown that our inhibitors are able to inhibit phosphate regardless of the amount of phosphate in the diet. We believe this mechanism would have a significant advantage over phosphate binders, and may allow us to significantly decrease pill burden while retaining a similar phosphorus effect. Additionally, we believe that the use of a NaP2b inhibitor in combination with a phosphate binder may allow the dose of the phosphate binder to be reduced. We cannot predict whether or not these effects will be seen until the appropriate clinical trials are conducted.

Other Development Programs

Utilizing our proprietary drug discovery and design platform, we are pursuing other internal discovery and lead-development programs that are currently in the research phase, which include our RDX009, RDX013 and RDX020 programs. While we have identified molecules that exhibit certain of the activity we are seeking in each of these programs, we have not yet selected a lead molecule in these programs.

RDX009 TGR5 agonists for IBD

Our RDX009 program is aimed at discovering and evaluating small molecule, orally-administered drug candidates that stimulate TGR5. We are initially focused on the treatment of IBD for proof-of-concept, but believe the stimulation of TGR5 may have utility in several other conditions, including short bowel syndrome.

TGR5 is a receptor present on the membrane of certain cells within the GI tract that responds to bile acids secreted in response to food. In the normal physiological response, binding of bile acids to TGR5 stimulates the production of hormones such as glucagon-like peptides 1 and 2 (GLP-1 and GLP-2). GLP-2 is involved in maintenance of the structural integrity of the gut as well as its growth. GLP-2 also communicates with immune cells including macrophages and is believed to serve a role in the reduction of the inflammation response.

We believe that endogenous and local secretion of GLP-2 triggered by the stimulation of TGR5 receptors may have significant therapeutic potential for the treatment of IBD. An injectable, stabilized form of GLP-2, called teduglutide (Gattex), is marketed for short bowel syndrome and has been studied in Crohn's disease. GLP-2 is hypothesized to work in IBD such as Crohn's disease and ulcerative colitis, or UC, by stimulating the repair of the gut and improving the structural integrity of gut wall that is damaged in patients with IBD. Additionally, the anti-inflammatory effects of GLP-2 may help reduce the inflammation present in IBD. Together these properties would represent a unique approach to treating IBD. We are therefore working to identify and optimize TGR5 agonists that can stimulate GLP-2 in rodent models of IBD.

Historically one of the limitations for the development of TGR5 agonists has been the observation with systemic compounds that stimulation of TGR5 in the gallbladder results in excess gallbladder filling, potentially increasing the risk of gallstones. Utilizing our approach to design small molecules, we have created novel TGR5 agonist candidates that have extremely low systemic exposure and we have shown that these agents do not result in excess gallbladder filling in preclinical animal models.

Recently, we have demonstrated that our TGR5 agonists are significantly more active in animal models of IBD if they are combined with an inhibitor of DPP4. This effect may be due to the mechanisms of DPP4 inhibitors, which prevent the degradation of GLP-2 in the body. Without a DPP4 inhibitor present, GLP-2 would rapidly degrade and disappear from the blood. DPP4 inhibitors lengthen the half-life of GLP-2. In animal models of colonic inflammation, the combination of our TGR5 agonists and a DPP4 inhibitor, both orally administered, have been able to significantly reduce various measures of disease severity. We continue to test our TGR5 agonists to determine a lead product that would be appropriate for beginning IND-enabling studies.

Inflammatory bowel disease primarily comprises UC and Crohn's disease. In UC, the first line of treatment involves mesalamine and related drugs, followed by corticosteroids and finally immune modulators such as cyclosporine and TNF inhibitors that are injectable. A last approach would be removal of the colon, or colectomy, which requires use of a removable bag to collect solid waste. About 30-50% of patients are treatment failures at each therapeutic stage. There are about 31,000 hospitalizations in the United States per year due to UC as a first-listed diagnosis and about 15% of UC patients progress to colectomy over a period of 20 years. There are about 400,000 patients in the United States with UC. In Crohn's disease, similar therapeutic agents are used; however, about 60% of Crohn's patients will progress over time and eventually require surgery to remove a portion of the most affected segment of the intestine. There are about 435,000 patients in the United States with Crohn's disease and about 73,000 hospitalizations in the United States per year due to Crohn's as a first-listed diagnosis.

The goal of therapies in IBD is to induce full healing of the intestinal tissue. Most agents do not focus on tissue healing, but instead focus on anti-inflammatory effects. TNF inhibitors, for example, are believed to work by reducing the inflammation associated with IBD to reduce progression and pain. We believe our oral TGR5 agonists may have the potential to induce healing of intestinal tissue in IBD as a result of the dual anti-inflammatory and tissue rebuilding properties of GLP-2. We believe a significant opportunity may exist in the IBD market for a safe and effective, orally administered, disease modifying agent that offers a dual effect of anti-inflammation and tissue healing.

RDX013 for hyperkalemia

Our RDX013 program is aimed at discovering and evaluating small molecule, orally-administered drug candidates that modulate the transport of potassium in the GI tract.

Our agents will be designed to enhance potassium secretion in the colon and correct hyperkalemia disorders in CKD patients. We believe that specific potassium transporters in the intestines may serve as useful targets for our program. We are also using APECCS to identify novel pathways to activate potassium flux from the interior of the GI epithelium cells to the GI lumen. We believe that such agents may be used as stand-alone agents or used in combination with potassium binders boost efficacy or to reduce the pill burden of the potassium binders.

RDX020 for inhibition of chloride channels

Our RDX020 program is aimed at discovering and evaluating small molecule, orally administered drug candidates that modulate the transport of chloride in the GI tract.

We are targeting transporters responsible for the movement of chloride from the lumen of the gut to within the mucosa while secreting bicarbonate ions in the opposite direction. Our discovery platform is designed to find transporters and targets on the surface of the intestines and to identify small molecules that interfere with the activity of such targets. The objective of this program is to obtain non-systemic agents that would limit dietary chloride uptake and limit the loss of bicarbonate (or enhance fecal acid excretion).

We believe that an agent that prevents the absorption of dietary chloride could reduce fluid overload and improve acidosis in CKD patients.

Collaboration Partnerships

Collaboration partnership with AstraZeneca

Overview

In October 2012, we entered into a collaboration partnership with AstraZeneca for the development and commercialization of our small molecule NHE3 inhibitors, including tenapanor as well as to back-up

compounds. Additionally, as part of the collaboration partnership, we agreed to provide development support related to the licensed compounds subject to reimbursement by AstraZeneca for our internal and external expenses incurred in providing such efforts, subject to an agreed upon cap on AstraZeneca's obligation to reimburse our costs for the Phase 2b clinical trial of tenapanor for IBS-C.

Under the terms of the agreement, we received a $35.0 million upfront payment and we are eligible to receive up to $237.5 million in development milestones, of which we have received $40.0 million. The $40.0 million in development milestones consists of a payment of $15.0 million that we received in January 2014 and a payment of $25.0 million that we received in May 2014 as a result of the dosing of the first patient in the Phase 2b ESRD clinical trial in hyperphosphatemia in April 2014. In addition to the $237.5 million in total development milestones, we are also eligible to receive up to $597.5 million in sales and launch milestones which, when combined with the $35.0 million upfront payment, provides for potential payments of up to $870.0 million. Through March 31, 2014, we also received $24.5 million in reimbursement for our development efforts provided under the agreement. We are also eligible to receive incremental tiered royalties based on aggregate annual net sales of each licensed product starting in the high single digits and increasing to high teen percentages as annual net sales increase. If we exercise our right to co-fund the first Phase 3 development program for tenapanor, we could acquire an increase in our royalties by 1%, 2% or 3%, as described below under the heading "—Right to co-fund/royalty buy-up."

AstraZeneca solely funds all development and commercialization costs for licensed compounds and licensed products, except for costs that we elect to undertake if we exercise our right to co-fund certain development efforts in exchange for an increase in the royalty percentage, as described below under the heading "—Right to co-fund/royalty buy-up."

AstraZeneca may choose to develop tenapanor for any indication. Provided that it is pursuing development for at least one indication, AstraZeneca may choose not to develop tenapanor for any other indications. AstraZeneca must use commercially reasonable efforts to develop, manufacture, seek regulatory approval for and commercialize a licensed product in each of certain specified major markets.

Right to co-fund/royalty buy-up

We may elect to participate in the funding of the first Phase 3 development program for the first indication for the first licensed product by paying a co-funding amount of $20.0 million, $30.0 million or $40.0 million. We may exercise this right within a specified time period after the decision to proceed to Phase 3 clinical development for the first indication for the first licensed product. If we elect to co-fund the Phase 3 development program for the specific indication for the relevant licensed product, we will receive either a 1%, 2% or 3% increase in the royalty payable on net sales of the licensed product for all indications, depending upon the level of co-funding that we elect. We may exercise this right only for a period of 60 days following AstraZeneca's determination to proceed to the first Phase 3 clinical development program for tenapanor for a specific indication. An election to participate in the co-fund will be based, in part, on our analysis as to the likelihood of success of the Phase 3 clinical development program and the potential for regulatory approval to commercialize tenapanor. The selected co-funding amount would be paid quarterly over the estimated period of the Phase 3 clinical development program.

Right to co-promote in the United States

We may elect to co-promote in the United States the first licensed product for the first indication for which Phase 3 clinical development is completed. If we make such an election, we may also elect to co-promote the same licensed product for additional indications for which Phase 3 clinical development is completed in the specified period. After we make a co-promotion election, we must enter into a separate co-promotion agreement on terms and conditions set out in our agreement with AstraZeneca, which includes, among other rights and obligations, a requirement for Ardelyx to provide a trained sales force for promoting the licensed product, which may not also promote products that compete with the licensed product or other products then promoted by AstraZeneca or its affiliates and AstraZeneca must reimburse us for our agreed-upon co-promotion efforts other than for general training of our sales force.

Other terms

We are initially responsible for supplying tenapanor for use in development. AstraZeneca must reimburse our costs of providing such supply. AstraZeneca must use commercially reasonable efforts to assume responsibility for manufacturing and supplying all licensed compounds and licensed products for development and commercialization beginning with supplies required for Phase 2b and Phase 3 clinical trials, although AstraZeneca may choose to assume such supply responsibilities earlier.

For periods specified in the agreement, neither we nor AstraZeneca can research, develop or commercialize NHE3 inhibitors, other than pursuant to the agreement.

The agreement will expire in its entirety upon the expiration of all applicable royalty terms for all licensed products in all countries, and the satisfaction or expiration of all other payment obligations under the agreement. The royalty term for each licensed product in each country is the period commencing with the first commercial sale of the applicable licensed product in the applicable country and ending on the later of expiration of specified patent coverage or 10 years after the first commercial sale in the applicable country. AstraZeneca has the right to terminate the agreement at any time in its entirety, upon specified prior written notice to us, and is deemed to have so terminated the agreement if it ceases all exploitation of licensed products for a specified continuous time period and does not provide a plan to recommence such exploitation within a particular time period thereafter. AstraZeneca may also terminate the agreement on a country by country basis upon a specified prior written notice if there are third party patents that may be infringed in particular countries by the development, manufacture or commercialization of licensed products, subject to certain conditions. The agreement may also be terminated by us in the event that AstraZeneca actively assists in a legal challenge of any of the patents exclusively licensed to AstraZeneca under the agreement, and it may be terminated by us or by AstraZeneca for a material breach by or insolvency of the other party.

Collaboration partnership with Sanofi

Overview

In February 2014, we entered into a license option and license agreement with Sanofi under which we granted Sanofi an exclusive worldwide license to conduct research utilizing our small molecule NaP2b inhibitors solely for the purpose of completing activities under a preclinical development plan. Under the terms of this agreement, Sanofi has the option to obtain an exclusive license to develop, manufacture and commercialize our NaP2b inhibitors. Sanofi may exercise this option at any time following the effective date of the agreement and ending 45 days after the filing of an IND, subject to certain exceptions, and if Sanofi does not file an IND on or before the 40th month anniversary at the completion of the technology transfer phase, the agreement will terminate. Sanofi is responsible for conducting and funding all research, development and commercialization of licensed products under the agreement. If Sanofi exercises its option, it must use commercially reasonable efforts to develop, seek regulatory approval for, manufacture and commercialize a licensed product for any indication in each of certain specified major markets.

We received a $1.25 million upfront payment, and we are eligible to receive up to $196.75 in development and regulatory milestone payments. We are also eligible to receive incremental tiered royalties based on aggregate annual net sales of any licensed product starting in the mid-single digits and increasing to low teen percentages as annual net sales increase, subject to reduction in specified circumstances.

Right to co-promote in the United States

We may elect to co-promote in the United States for each licensed product for which Phase 3 clinical development is completed. We may elect to provide a level of co-promotion support within a range specified in our agreement with Sanofi. If we make such an election to co-promote, we have additional rights to elect to co-promote other licensed products under this agreement. After we make a co-promotion election, we must enter

into a separate co-promotion agreement on terms and conditions set out in our agreement with Sanofi. Such co-promotion agreement must provide reasonable terms and conditions under which we will co-promote the relevant licensed products, and will require Sanofi to compensate us for performing our co-promotion obligations.

Other terms

During the term of the agreement, and in certain circumstances for a specified period following termination of the agreement, neither we nor Sanofi can, subject to certain exceptions described in the agreement, research, develop or commercialize a NaP2b inhibitor other than pursuant to the agreement.

The agreement will expire if Sanofi does not exercise its option by the earlier of (i) 45 days after the filing of an IND for a NaP2b inhibitor (subject to certain extensions for regulatory actions) and (ii) the expiration or termination of the agreement. If Sanofi does exercise its option, the agreement will expire in its entirety upon the expiration of all applicable royalty terms for all licensed products in all countries, and the satisfaction or expiration of all other payment obligations under the agreement. The royalty term for each licensed product in each country is the period commencing with the first commercial sale of the applicable licensed product in the applicable country and ending on the later of expiration of specified patent coverage or 10 years after the first commercial sale in the applicable country. Sanofi has the right to terminate the agreement at any time in its entirety or on a country-by-country basis upon specified prior written notice to us, and is deemed to have so terminated the agreement if it has not filed an IND for a licensed compound within a specified period of time, if it fails to exercise its option within a specified period of time, or if, after exercising its option, it ceases all exploitation of licensed products for a specified continuous time period and does not provide a plan to recommence such exploitation within a particular time period thereafter. The agreement may also be terminated by us in the event that Sanofi actively assists in a legal challenge of one of the patents exclusively licensed to Sanofi under the agreement, and it may be terminated by us or by Sanofi for a material breach by or insolvency of the other party.

Commercialization of our Products

We retain co-promotion rights with our collaboration partners, AstraZeneca and Sanofi, in the United States, and under the terms of our agreements, our commercialization costs will be funded by the collaboration partner. We expect, subject to certain conditions set forth in the AstraZeneca agreement, to take advantage of these opportunities to co-promote our licensed products. We intend to build a focused, specialized sales force in the United States to effectively support the commercialization of these and future products. If we co-promote our licensed products, we would develop a sales capability to target key prescribing physicians in nephrology, endocrinology and cardiology. We currently do not have any sales or marketing activities or personnel. Within the time required under our agreements with AstraZeneca and Sanofi, if we exercise our co-promotion right we will establish the required capabilities in advance of any product approval and commencement of commercialization to prepare for product launch. If we are not able to establish these sales and marketing capabilities, either on our own or through collaboration with AstraZeneca and Sanofi, any revenue from our future products that we commercialize may be materially adversely affected.

Competition

Competition for hyperphosphatemia

Phosphate binders are the only pharmacologic interventions currently marketed for the treatment of hyperphosphatemia. Calcium-based binders are the least expensive option to treat hyperphosphatemia. In hemodialysis patients, sevelamer has a 36% patient share versus 51% for calcium-based binders and 18% for lanthanum. 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 marketed by Shire)

- Sevelamer hydrochloride (Renagel, marketed by Sanofi; new generic competition is also expected to enter the market in early 2014 after expiration of Sanofi's patent)
- Sevelamer carbonate (Renvela, marketed by Sanofi)
- Sucroferric oxyhydroxide (Velphoro, marketed by Vifor Fresenius)

Each of these agents has certain limitations. Calcium carbonate and calcium acetate can cause long term vascular calcification. Lanthanum carbonate (Fosrenol) entered the market in 2004 as an alternative to calcium and aluminum based agents, but nephrologists' concerns about the long term toxicity from the absorption of metals such as lanthanum and its GI side effect profile have limited its market penetration. Sevelamer hydrochloride (Renagel) is an acidic formulation of sevelamer that has been linked with worsening of metabolic acidosis in patients. Sevelamer carbonate (Renvela) was developed as an improved formulation of sevelamer to reduce incidence of acidosis. The active ingredient of both products, sevelamer, is associated long-term with vomiting (22%), nausea (20%), diarrhea (19%), dyspepsia (16%), abdominal pain (9%), and flatulence (8%). When nephrologists have been asked to name the most important feature of a new phosphate management drug, they have mentioned tolerability more than any other attribute including safety and efficacy.

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. Renvela is currently priced in the United States at a cost of approximately $7,600 per patient per course of therapy, Fosrenol (lanthanum carbonate) is comparably priced at about $7,500 and calcium-based binders are approximately $900. Despite its higher price, sevelamer has become the leading phosphate binder product in the hemodialysis market with 36% patient share (versus 51% split among several calcium-based binders). Sanofi booked €750 million ($1.0 billion) in worldwide sales of sevelamer during 2013. The U.S. patents for sevelamer expired in February 2014 and generic launch was allowed in March 2014. Impax Laboratories, Inc. launched a generic version of sevelamer carbonate in April 2014 and is expected to launch a generic version of sevelamer hydrochloride in September 2014.

In addition to the currently marketed phosphate binders, we are aware of several other binders in development such as ferric citrate (Zerenex), an iron-based binder in Phase 3 being developed in the United States by Keryx Biopharmaceuticals Inc. and approved in Japan, fermagate (Alpharen), an iron-based binder in Phase 2 being developed by Opko Health, Inc., and sucroferric oxyhydroxide (Velphoro), an iron-based binder with an average dose of one 500 mg pill per meal (versus three or more pills for other binders).

Competition for long-term management of CKD

There are no treatments for CKD that have been proven to reverse the disease. Additionally, various interventions, such as improved diet, blood pressure control, and blood glucose control have had only moderate success in delaying the progression of the disease. CKD patients are currently treated with a combination of diuretics and inhibitors of the renin-angiotensin aldosterone system, or RAAS, to decrease fluid retention and improve hypertension.

We are aware of one agent, CLP-1001, being developed by Sorbent Therapeutics, Inc. which is an orally administered, non-absorbed exchange resin that binds both sodium and potassium ions as well as protons that showed positive effects in CKD patients with heart failure in a Phase 2a clinical trial and which demonstrated the ability to increase fecal sodium at doses of up to 15g/day. We believe this agent may be competitive with tenapanor to treat CKD patients.

There are several dozen generic and branded products that interfere with the RAAS pathway, or act as diuretics. Some of these agents, such as furosemide and thiazide diuretics, were first used in the late 1950s. We are aware of a few new products being developed for treatment of hypertension such as Novartis AG's LCZ696, a dual inhibitor of angiotensin ll receptor and neutral endopeptidase that is in Phase 3, and Palatin Technology, Inc.'s PL-3994, a long-acting natriuretic peptide receptor A agonist in Phase 2.

We are aware of certain investigational drugs that were being developed for delaying kidney decline as measured by eGFR. Among other products, Concert Pharmaceuticals, Inc. is developing CTP-499 which showed protective effects on kidney function at 48 weeks in a Phase 2 clinical trial in patients with CKD and type 2 diabetes. Bardoxolone, an anti-inflammation drug, was being developed by Reata Pharmaceuticals, Inc. and Abbott Laboratories and was examined in CKD patients with type 2 diabetes for its ability to reduce progression to ESRD and cardiovascular death rates, as well as delay the decline of eGFR; however, the Phase 3 clinical trial of bardoxolone was stopped in 2012 because of safety issues, and we are unaware of any additional development of the molecule in CKD. We are aware of several drugs in Phase 2 clinical trials being evaluated for diabetic nephropathy (excluding drugs for blood pressure) including ChemoCentrix, Inc.'s CCR antagonist CCX140, Eli Lilly and Company's TGF-beta monoclonal antibody LY2382770, Genkyotex S.A.'s dual NOX1/NOX4 inhibitor GKT137831, Fibrogen, Inc.'s CTGF inhibitor FG-3019, Pfizer, Inc.'s long-acting PDE5 inhibitor PF-489791, and Noxxon Pharma AG's aptamer inhibitor of MCP-1/CCR2 NOX-E36. None of these drugs to our knowledge has clinical data showing a delay in the progression of CKD.

Competition for management 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 relieve temporary constipation.

We are aware of two prescription drugs currently on the U.S. market that are approved to treat IBS-C:

- Linzess (linaclotide): Linzess is a drug developed by Ironwood Pharmaceuticals, Inc., approved in 2012 and 2013 for IBS-C and chronic constipation in both the United States and in Europe. Linzess is based on the heat stable enterotoxin produced in *E. coli* that causes traveler's diarrhea. Linzess targets guanylate cyclase C in the intestines and, by doing so, induces intestinal chloride and fluid secretion, which results in the outpouring of water into the intestine. Linzess in a meta-analysis was deemed "moderately effective compared with placebo for improving typical symptoms of IBS-C" and had a risk-adjusted effect on 13% to 21% of patients in various measures of IBS-C compared to the placebo effect. The most common side effect was diarrhea (mostly during the first two weeks of treatment), reported in about 11% to 17% more patients than placebo, and requiring discontinuation in about 4% of patients more than placebo.
- Amitiza (lubiprostone): Amitiza was first approved in the United States in 2006 and is currently marketed by Sucampo Pharmaceuticals, Inc. and Takeda Pharmaceutical Company Limited for treatment of chronic idiopathic constipation, or CIC, IBS-C and OIC. Amitiza binds selectively to and activates the type-2 chloride channel in the intestine releasing chloride and water into the intestine. Amitiza overall responders were about 6% greater than placebo. The primary adverse events are nausea and/or diarrhea which occur in about 7% to as many as 37% of patients.

Relistor (methylnaltrexone) is approved to treat OIC and is marketed by Salix Pharmaceuticals, Inc. Resolor (prucalopride), also a 5-HT4 receptor agonist has not been launched in the United States but is marketed in Europe by Shire plc.

We are aware of several products in development targeting IBS-C and/or CIC. These include Ferring Pharmaceuticals, Inc./Albireo AB's elobixibat, an IBAT inhibitor in Phase 3 for CIC and in Phase 2 for IBS-C and Synergy Pharmaceuticals, Inc.'s plecanatide, a GC-C agonist similar to linaclotide in Phase 3 for CIC and in Phase 2 for CIC and OIC (as well, Synergy Pharmaceuticals, Inc. has SP-333 in Phase 2 for OIC).

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 proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on 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.

As a normal course of business, we pursue composition-of-matter and method-of-use patents for our product candidates in key therapeutic areas. We also seek patent protection for broader structural and functional attributes of our product candidates that enable a non-or-minimally systemic profile.

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, or our collaboration partners, 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 or our collaboration partners, 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. With respect to tenapanor, our collaboration partner, AstraZeneca, and with respect to our NaP2b portfolio, under certain circumstances, our collaboration partner, Sanofi, will be responsible for and have the right to control, with input from us, the selection of the appropriate issued patent for filing to obtain any patent term extension that may be available under applicable laws.

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.

NHE3 patents

Our NHE3 patent portfolio is wholly owned by us and exclusively licensed to AstraZeneca. This portfolio includes one issued U.S. patent, U.S. Patent No. 8,541,448, covering the composition of tenapanor, and one issued Japanese patent, Japanese Patent No. 5502106 covering the composition of tenapanor. Both of these issued patents are predicted to expire in 2029. Two additional patent applications are pending in the United States covering the composition of or methods of using tenapanor. 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 to expire in 2029. Additional pending composition of matter and method of use patent applications in this portfolio include three PCT applications that are eligible for worldwide filing, and we expect that AstraZeneca will file national patent applications in Europe, Japan, China, India, Israel and a number of other countries at the time when the PCT is converted to national filings.

NaP2b

Our NaP2b portfolio is wholly owned by us, exclusively licensed to Sanofi, and includes five pending U.S. patent applications covering the composition of or methods of using our NaP2b inhibitor compounds. If issued, these pending applications are predicted to expire in 2031. Related national patent applications are pending in Europe and Japan. Any patents resulting from these patent applications, if issued, are also predicted to expire in 2031.

TGR5 agonists

Our TGR5 agonist portfolio is wholly owned by us, and includes one PCT application covering the composition and methods of using our TGR5 agonist compounds that is eligible for worldwide filing. We expect to file national patent applications in Europe, Japan, China and a number of other countries at the time the PCT is converted to national filings.

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 tenapanor used as clinical trial material. Under our agreement with AstraZeneca, we are in the final stages of transferring the process for the manufacture of tenapanor drug substance and drug product to AstraZeneca. The clinical trial material being utilized in the ongoing clinical trials with tenapanor has been manufactured by our CMOs, but AstraZeneca will be responsible for the manufacture of all future clinical trial and commercial supplies of tenapanor.

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;
- 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 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.

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

The FDA, the IRB or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the study. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

New drug applications

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

Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs 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 GCP 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, plan 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. For many proposed post-approval changes to an NDA, but excluding efficacy supplements to an NDA, the FDA has up to 180 days to review the application. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

Other regulatory requirements

Any drugs manufactured or distributed by us or our collaboration partners pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the drug. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic announced and unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our third party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning 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.

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 Sunshine Payment 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, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute and federal criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. Moreover, 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 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 $5,500 and $11,000 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 $150,000 per year (or up to an aggregate of $1 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. The period between August 1, 2013 and December 31, 2013 was the first reporting period and manufacturers were required to report aggregate payment data by March 31, 2014, and will be required to report detailed payment data and submit legal attestation to the accuracy of such data during Phase 2 of the program (which begins in May 2014 and extends for at least 30 days). Thereafter, 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 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.

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, President Obama signed the Protecting Access to Medicare Act of 2014, which further extends this implementation date to January 1, 2024. As a result of the recent legislation, beginning in 2024, 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 bundling may have on the phosphate binder industry, the impact could potentially cause dramatic price reductions for tenapanor, if approved.

Healthcare reform

In March 2010, President Obama signed one of the most significant healthcare reform measures in decades. The Affordable Care Act substantially changes the way healthcare will be 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, which will impact existing government healthcare programs and will result 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;
- 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.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011 among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2 percent per fiscal year, which went into effect on April 1, 2013. In January 2013, the ATRA was enacted, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers. 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 March 31, 2014, we had 37 full-time employees, including a total of 14 employees with Ph.D. degrees. Within our workforce, 30 employees are engaged in research and development and the remaining 7 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.

Property and Facilities

Our headquarters is currently located in Fremont, California, and consists of approximately 27,620 square feet of leased office and laboratory space under a lease that expires on September 2016. We have the option to extend the termination date to September 2019. We expect that during the next year we will either increase the square footage available to us in our existing facility or obtain additional space in another location in order to accommodate our anticipated needs. We may also require additional space and facilities as our business expands.

Legal Proceedings

We are not currently subject to any material legal proceedings.

Management

Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors, as of June 6, 2014:

Name	Age	Position(s)
Executive Officers		
Michael Raab	49	President, Chief Executive Officer and Director
Dominique Charmot, Ph.D.	59	Chief Scientific Officer and Director
Mark Kaufmann	47	Chief Financial Officer
Jeffrey Jacobs, Ph.D.	51	Vice President, Chemistry
George Jue	62	Vice President, Finance and Operations
David Rosenbaum, Ph.D.	53	Vice President, Drug Development
Elizabeth Grammer, Esq.	50	Vice President, General Counsel
Non-Employee Directors		
David Mott(1)(2)	48	Chairman of the Board
Gordon Ringold, Ph.D.(1)(3)	63	Director
Richard Rodgers(1)(2)(3)	47	Director
Peter Schultz, Ph.D.(2)	57	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Michael Raab has served as our President and Chief Executive Officer and a director since March 2009. From 2002 to 2009, Mr. Raab was a partner at New Enterprise Associates, or NEA, a venture capital firm, specializing in healthcare investments focusing on the biotechnology and pharmaceutical sectors. Prior to joining NEA, Mr. Raab spent 15 years in commercial and operating leadership roles in the biotech and pharmaceutical industries. He was Senior Vice President, Therapeutics and General Manager of the Renal Division at Genzyme Corporation, a biotechnology company. Mr. Raab also spent two years with Genzyme's Diagnostic products and services division. Before Genzyme, Mr. Raab held business development and sales and marketing positions at Repligen Corporation, a life sciences company, and Bristol-Myers Squibb Company, a biopharmaceutical company. Mr. Raab received a B.A. from DePauw University.

Dominique Charmot, Ph.D., is our co-founder and has served as our Chief Scientific Officer and a director since October 2007. Dr. Charmot started his career in 1982 at Rhone-Poulenc SA, a chemical company. In 2000, Dr. Charmot joined Symyx Technologies Inc., a life sciences-based software company, where he was in charge of the development of integrated workflows in high throughput discovery targeted to specialty polymers. In 2003, Dr. Charmot co-founded Ilypsa Inc., a company developing polymeric drugs, and worked there until the acquisition of Ilypsa by Amgen Inc., a biopharmaceutical company, in 2007. Dr. Charmot received a M.S. in Chemical Engineering from Ecole Nationale Supérieure de Chimie de Paris and a Ph.D. in Polymer Chemistry from the Ecole Supérieure de Physique et Chimie Industrielle de Paris.

Mark Kaufmann has served as our Chief Financial Officer since May 2014 and formerly served as our Chief Business Officer from August 2011 until May 2014. Mr. Kaufmann has over twenty years of experience in the biopharmaceutical industry in both the U.S. and Canada in business and corporate development roles. From 2008 to 2010, Mr. Kaufmann was President and Chief Executive Officer of Allostera Pharma Inc., a preclinical company focused on autoimmune diseases. Prior to joining Allostera, Mr. Kaufmann was President and Chief Executive Officer of Celmed BioSciences, Inc., a biopharmaceutical company, and he started his career as Director of Strategic Planning and Investor Relations at MedImmune in 1994. Mr. Kaufmann received a B.A. in Biochemical Sciences from Harvard University and a M.B.A. from the University of Michigan School of Business.

Jeffrey Jacobs, Ph.D., has served as our Vice President, Chemistry since January 2011. Dr. Jacobs has spent his career in the discovery and development of new chemical entities for the treatment of unmet medical needs. Dr. Jacobs has held positions of increasing responsibility at Affymax, Inc., a biopharmaceutical company, Vicuron Pharmaceuticals, Inc., a biopharmaceutical company, and Sunesis Pharmaceuticals, Inc., a biopharmaceutical company, where he was most recently Senior Director of Development Chemistry. Dr. Jacobs received a B.S. in Chemistry, magna cum laude, from Gonzaga University and a Ph.D. in Bioorganic Chemistry at the University of California, Berkeley.

George Jue has served as our Vice President, Finance and Operations since June 2008. Prior to Ardelyx, Mr. Jue was Vice President of Finance and Controller at Hyperion Therapeutics, Inc., a biopharmaceutical company. Before Hyperion Therapeutics, Mr. Jue worked at VaxGen Inc., a biopharmaceutical company, as the Vice President of Finance. In addition, Mr. Jue previously served as Vice President of Finance and Principal Accounting Officer at PDL BioPharma, a biopharmaceutical company. Mr. Jue received a B.S. in Accounting from Bentley College and a M.B.A. from Golden Gate University.

David Rosenbaum, Ph.D., has served as our Vice President of Drug Development since January 2010. Dr. Rosenbaum has spent the past 20 years developing novel drugs for global registration. From 2003 to 2008, he was Vice President of Drug Development for Trine Pharmaceuticals, Inc., a biopharmaceutical company, where he was developing a novel non-systemic therapeutic for the treatment of IBS. In addition, Dr. Rosenbaum previously served as Vice President of Preclinical Research and Development at GelTex Pharmaceuticals, a biopharmaceutical company, where he was responsible for the preclinical development of Renagel and Welchol. He received a B.A. in Biology from the University of Pennsylvania, a M.S. in Toxicology from Albany Medical College and a Ph.D. in Pharmacology from Boston University School of Medicine.

Elizabeth Grammer, Esq., has served as our Vice President responsible for legal affairs since December 2012, after serving as an independent outside corporate counsel for Ardelyx for three years. In May 2014, Ms. Grammer was appointed as our Vice President, General Counsel. Ms. Grammer has over 20 years of experience representing privately held and publicly traded life sciences companies in structuring and negotiating strategic transactions, such as collaborations, joint ventures, and intellectual property licensing transactions. Prior to joining Ardelyx, from 2001 to 2006, Ms. Grammer served as Vice President and General Counsel of Trine Pharmaceuticals, Inc., a biopharmaceutical company. Ms. Grammer received a B.A. from Boston University and a J.D. from Stanford Law School.

Non-Employee Directors

David Mott has served on our board of directors since March 2009 and as chairman of the board of directors since March 2014. Mr. Mott joined NEA in September 2008 as a General Partner primarily focused on biopharmaceutical investments. Prior to joining NEA, he was President and Chief Executive Officer of MedImmune, LLC, a subsidiary of AstraZeneca Plc, and Executive Vice President of AstraZeneca. Mr. Mott joined MedImmune in 1992 and served in roles of increasing responsibility including Chief Operating Officer, Chief Financial Officer, President and from 2000, Chief Executive Officer. In 2002, Mr. Mott founded MedImmune Ventures and chaired its investment committee through his departure from MedImmune. Prior to joining MedImmune, he was a Vice President in the Health Care Investment Banking Group at Smith Barney, Harris Upham & Co. Inc. where he focused on public and private equity and debt financings as well as merger and acquisition work for biotechnology, healthcare services, and medical product and device companies. Mr. Mott is currently Chairman of TESARO, Inc., a biopharmaceutical company, and Prosensa Holding N.V., a biopharmaceutical company, and is a director of Epizyme, Inc., a biopharmaceutical company. Mr. Mott received a B.A. in Economics and Government from Dartmouth College. We believe that Mr. Mott is qualified to serve on our board of directors due to his investment experience, strategic leadership track record and service on other boards of directors of life sciences companies.

Gordon Ringold, Ph.D., was appointed to our board of directors in June 2014. From March 2000 to December 2013, Dr. Ringold served as Chairman and Chief Executive Officer of Alavita, Inc., a biotechnology

company. From March 1995 to February 2000, Dr. Ringold served as Chief Executive Officer and Scientific Director of Affymax Research Institute where he managed the development of novel technologies to accelerate the pace of drug discovery. Dr. Ringold is currently also a director of Alexza Pharmaceuticals, Inc., a pharmaceutical company, and 3V Biosciences, Inc., a biotechnology company. From 1997 to 2013, Dr. Ringold served as a member of the board of directors of Maxygen, Inc., a publicly-traded biopharmaceutical company, and was a member of the board of directors of Oxonica plc, a publicly-traded nanotechnology company, from 2005 to 2009. Dr. Ringold received a Ph.D. in microbiology from University of California, San Francisco, in the laboratory of Dr. Harold Varmus before joining the Stanford University School of Medicine, Department of Pharmacology. Dr. Ringold also received a B.S. in biology from the University of California, Santa Cruz. We believe that Dr. Ringold is qualified to serve on our board of directors due to his deep industry experience, including as a chief executive officer, and service on other boards of directors of publicly-traded life sciences companies.

Richard Rodgers has served on our board of directors since March 2014. From March 2010 until August 2013, Mr. Rodgers was co-founder, Executive Vice President, Chief Financial Officer, Secretary and Treasurer of TESARO, Inc., a biopharmaceutical company. Mr. Rodgers previously served as the Chief Financial Officer from June 2009 to February 2010 of Abraxis BioScience, Inc., a biotechnology company. Prior to that, Mr. Rodgers served as Senior Vice President, Controller and Chief Accounting Officer of MGI PHARMA, Inc., a biopharmaceutical company, from 2004 until its acquisition by Eisai Co. Ltd., a pharmaceutical company, in January 2008. Mr. Rodgers has held finance and accounting positions at several private and public companies, including Arthur Anderson & Co. Mr. Rodgers received a B.S. in Financial Accounting from St. Cloud State University and his M.B.A. in Finance from the University of Minnesota, Carlson School of Business. We believe that Mr. Rodgers is qualified to serve on our board of directors due to his financial background and deep industry experience.

Peter G. Schultz, Ph.D., is our co-founder and has served on our board of directors since April 2010. In 1985, after postdoctoral studies at the Massachusetts Institute of Technology, he joined the faculty of the University of California, Berkeley, where he was Professor of Chemistry, Principal Investigator at Lawrence Berkeley National Laboratory and an Investigator of the Howard Hughes Medical Institute. Dr. Schultz joined the faculty of Scripps in 1999, where he is currently the Scripps Professor of Chemistry. He founded and was the Institute Director of the Genomics Institute of the Novartis Research Foundation in San Diego, CA from 1999 to 2010. His awards include the Waterman Award of the National Science Foundation, membership in the National Academy of Sciences and National Institute of Medicine, the 1994 Wolf Prize in Chemistry, the 2003 Paul Ehrlich Prize, and the 2005 Arthur C. Cope Award of the American Chemical Society. Dr. Schultz received a B.S. in Chemistry and a Ph.D. in Organic Chemistry, both from the California Institute of Technology. We believe that Dr. Schultz is qualified to serve on our board of directors due to his extensive scientific background and deep industry experience.

Board Composition

Director Independence

Our board of directors currently consists of six members. Our board of directors has determined that all of our directors, other than Mr. Raab and Dr. Charmot, qualify as "independent" directors in accordance with the NASDAQ listing requirements. Mr. Raab and Dr. Charmot are not considered independent because they are both employees of Ardelyx. The NASDAQ independence definition includes a series of objective tests, such as that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by NASDAQ rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified Board of Directors

In accordance with our amended and restated certificate of incorporation to be in effect immediately prior to the consummation of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the consummation of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Drs. Charmot and Schultz, and their terms will expire at the annual meeting of stockholders to be held in 2015;
- the Class II directors will be Messrs. Raab and Mott, and their terms will expire at the annual meeting of stockholders to be held in 2016; and
- the Class III director will be Dr. Ringold and Mr. Rodgers, and his term will expire at the annual meeting of stockholders to be held in 2017.

Our amended and restated certificate of incorporation will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company.

Voting Arrangements

The election of the members of our board of directors is governed by the second amended and restated voting agreement that we entered into with certain holders of our common stock and certain holders of our convertible preferred stock and the related provisions of our amended and restated certificate of incorporation. Pursuant to the voting agreement and these provisions:

- the holders of our convertible preferred stock, voting separately as a single class, have the right to elect two (2) directors to our board of directors, which are designated as follows:
  - one (1) individual designated by New Enterprise Associates 12, Limited Partnership (together with its affiliated funds), for which Mr. Mott has been designated; and
  - one (1) individual designated by CMEA Ventures VII, L.P. (together with its affiliated funds), for which Dr. Ringold has been designated;
- the holders of our common stock, voting separately as a single class, have the right to elect two (2) directors, for which Drs. Charmot and Schultz have been designated; and
- the holders of our convertible preferred stock and common stock, voting together as a single class, have the right to elect the remaining two (2) directors, for which Messrs. Raab and Rodgers have been designated.

The holders of our common stock and convertible preferred stock who are parties to our voting agreement are obligated to vote for such designees indicated above. The provisions of this voting agreement will terminate upon the consummation of this offering and our certificate of incorporation will be amended and restated, after which there will be no further contractual obligations or charter provisions regarding the election of our directors. Our directors hold office until their successors have been elected and qualified or appointed, or the earlier of their death, resignation or removal.

Leadership Structure of the Board

Our bylaws and corporate governance guidelines provide our board of directors with flexibility to combine or separate the positions of chairman of the board of directors and Chief Executive Officer and/or the

implementation of a lead director in accordance with its determination that utilizing one or the other structure would be in the best interests of our company. Mr. Mott currently serves as the Chairman of our board of directors. In that role, Mr. Mott presides over the executive sessions of the board of directors in which Mr. Raab does not participate and serves as a liaison to Mr. Raab and management on behalf of the board of directors.

Our board of directors has concluded that our current leadership structure is appropriate at this time. However, our board of directors will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Role of Board in Risk Oversight Process

Risk assessment and oversight are an integral part of our governance and management processes. Our board of directors encourages management to promote a culture that incorporates risk management into our corporate strategy and day-to-day business operations. Management discusses strategic and operational risks at regular management meetings, and conducts specific strategic planning and review sessions during the year that include a focused discussion and analysis of the risks facing us. Throughout the year, senior management reviews these risks with the board of directors at regular board meetings as part of management presentations that focus on particular business functions, operations or strategies, and presents the steps taken by management to mitigate or eliminate such risks.

Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure, our audit committee is responsible for overseeing our major financial risk exposures and the steps our management has taken to monitor and control these exposures. The audit committee also monitors compliance with legal and regulatory requirements. Our nominating and governance committee monitors the effectiveness of our corporate governance guidelines and considers and approves or disapproves any related-persons transactions. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Board Committees

Audit Committee

Our audit committee oversees our corporate accounting and financial reporting process. Among other matters, the audit committee:

- appoints our independent registered public accounting firm;
- evaluates the independent registered public accounting firm's qualifications, independence and performance;
- determines the engagement of the independent registered public accounting firm;
- reviews and approves the scope of the annual audit and the audit fee;
- discusses with management and the independent registered public accounting firm the results of the annual audit and the review of our quarterly financial statements;
- approves the retention of the independent registered public accounting firm to perform any proposed permissible non-audit services;
- monitors the rotation of partners of the independent registered public accounting firm on our engagement team as required by law;
- is responsible for reviewing our financial statements and our management's discussion and analysis of financial condition and results of operations to be included in our annual and quarterly reports to be filed with the SEC;

- reviews our critical accounting policies and estimates; and
- annually reviews the audit committee charter and the committee's performance.

The current members of our audit committee are Messrs. Mott and Rodgers and Dr. Ringold. Mr. Rodgers serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our board of directors has determined that Mr. Rodgers is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable rules and regulations of NASDAQ. Under the rules of the SEC, members of the audit committee must also meet heightened independence standards. However, a minority of the members of the audit committee may be exempt from the heightened audit committee independence standards for one year from the date of effectiveness of the registration statement of which this prospectus forms a part. Our board of directors has determined that each of Messrs. Mott and Rodgers and Dr. Ringold are independent under the applicable rules of NASDAQ. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Compensation Committee

Our compensation committee reviews and recommends policies relating to compensation and benefits of our officers and employees. The compensation committee reviews and recommends corporate goals and objectives relevant to compensation of our Chief Executive Officer and other executive officers, evaluates the performance of these officers in light of those goals and objectives and recommends to our board of directors the compensation of these officers based on such evaluations. The compensation committee also recommends to our board of directors the issuance of stock options and other awards under our stock plans. The compensation committee will review and evaluate, at least annually, the performance of the compensation committee and its members, including compliance by the compensation committee with its charter. The current members of our compensation committee are Messrs. Mott and Rodgers and Dr. Schultz. Mr. Mott serves as the chairman of the committee. Each of the members of our compensation committee is independent under the applicable rules and regulations of The NASDAQ Global Market, is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act and is an "outside director" as that term is defined in Section 162(m) of the U.S. Internal Revenue Code of 1986, as amended, or Section 162(m). The compensation committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee is responsible for making recommendations to our board of directors regarding candidates for directorships and the size and composition of our board of directors. In addition, the nominating and corporate governance committee is responsible for overseeing our corporate governance policies and reporting and making recommendations to our board of directors concerning governance matters. The current members of our nominating and corporate governance committee are Dr. Ringold and Mr. Rodgers. Dr. Ringold serves as the chairman of the committee. Each of the members of our nominating and corporate governance committee is an independent director under the applicable rules and regulations of NASDAQ relating to nominating and corporate governance committee independence. The nominating and corporate governance committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Compensation Committee Interlocks and Insider Participation

During 2013, our compensation committee consisted of Drs. David Collier, Jean Frechet and Peter Schultz and Mr. Mott. Mr. Mott served as chairman of the compensation committee. In March 2014, Drs. Collier and Frechet resigned from our board of directors. None of the members of our compensation committee has at any time been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers on our board of directors or compensation committee.

Board Diversity

Upon consummation of this offering, our nominating and corporate governance committee will be responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- personal and professional integrity;
- ethics and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly held company;
- experience in the industries in which we compete;
- experience as a board member or executive officer of another publicly held company;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- conflicts of interest; and
- practical and mature business judgment.

Currently, our board of directors evaluates, and following the consummation of this offering will evaluate, each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the consummation of this offering, the code of business conduct and ethics will be available on our website at www.ardelyx.com. We expect that any amendments to the code, or any waivers of its requirements, will be disclosed on our website. The reference to our web address does not constitute incorporation by reference of the information contained at or available through our website.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately prior to the consummation of this offering, contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective immediately prior to the consummation of this offering, provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws also provide that we are obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage.

Director Compensation

In 2013, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of our non-employee members of our board of directors. We do not pay director fees to our directors who are employees. We reimburse our non-employee directors for travel and other necessary business expenses incurred in the performance of their services for us.

As of December 31, 2013, Mr. Schultz held 44,916 unvested restricted shares of our common stock pursuant to early exercised options. No other non-employee director held any restricted shares or any other equity award as of December 31, 2013.

Our board of directors has approved a compensation policy for our non-employee directors to be effective in connection with the consummation of this offering, or the Post-IPO Director Compensation Program. Pursuant to the Post-IPO Director Compensation Program, our non-employee directors will receive cash compensation, payable in a cash lump sum on the date of each annual meeting, as follows:

- Each non-employee director will receive an annual cash retainer in the amount of $35,000 per year.
- The Chairman will receive an additional annual cash retainer in the amount of $25,000 per year.
- The chairperson of the audit committee will receive additional annual cash compensation in the amount of $20,000 per year for such chairperson's service on the audit committee. Each non-chairperson member of the audit committee will receive additional annual cash compensation in the amount of $10,000 per year for such member's service on the audit committee.
- The chairperson of the compensation committee will receive additional annual cash compensation in the amount of $15,000 per year for such chairperson's service on the compensation committee. Each non-chairperson member of the compensation committee will receive additional annual cash compensation in the amount of $7,500 per year for such member's service on the compensation committee.
- The chairperson of the nominating and corporate governance committee will receive additional annual cash compensation in the amount of $8,000 per year for such chairperson's service on the nominating and corporate governance committee. Each non-chairperson member of the nominating and corporate

governance committee will receive additional annual cash compensation in the amount of $4,000 per year for such member's service on the nominating and corporate governance committee.

In lieu of a cash retainer, each non-employee director will also have the ability to elect to receive a number of fully vested stock options with a grant date fair value equal to such cash retainer.

Under the Post-IPO Director Compensation Program, each non-employee director will receive an option to purchase 25,000 shares of our common stock upon the director's initial appointment or election to our board of directors, referred to as the Initial Grant, and an annual option to purchase 15,000 shares of our common stock on the date of each annual stockholder's meeting thereafter, referred to as the Annual Grant. The Initial Grant will vest as to 1/36th of the shares subject to Initial Grant each month following the applicable grant date, subject to continued service through each applicable vesting date. The Annual Grant will vest as to 1/12th of the shares subject to the Annual Grant each month following the applicable grant date, which vesting will accelerate in full on the date of the next annual stockholder's meeting to the extent unvested as of such date, subject to continued service through each applicable vesting date.

Upon the pricing of this offering, each of Dr. Ringold and Mr. Rodgers received an option to purchase 30,000 shares of our common stock at an exercise price per share equal to the initial public offering price set forth on the cover of this prospectus, which option will vest as to 1/36th of the shares subject thereto each month following the date of the pricing of this offering, subject to continued service through each applicable vesting date.

Executive Compensation

The following is a discussion and analysis of compensation arrangements of our named executive officers, or NEOs. This discussion contains forward looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. Actual compensation programs that we adopt may differ materially from currently planned programs as summarized in this discussion. As an "emerging growth company" as defined in the JOBS Act, we are not required to include a Compensation Discussion and Analysis section and have elected to comply with the scaled disclosure requirements applicable to emerging growth companies.

We seek to ensure that the total compensation paid to our executive officers is reasonable and competitive. Compensation of our executives is structured around the achievement of individual performance and near-term corporate targets as well as long-term business objectives.

Our NEOs for fiscal year 2013 were as follows:

- Michael Raab, President and Chief Executive Officer;
- Dominique Charmot, Ph.D., Chief Scientific Officer; and
- David Rosenbaum, Ph.D., Vice President, Drug Development.

2013 Summary Compensation Table

The following table shows information regarding the compensation of our NEOs for services performed in the year ended December 31, 2013.

Name and Principal Position	Year	Salary ($)	Non-Equity Incentive Plan Compensation ($)(1)	Total ($)
Michael Raab *President and Chief Executive Officer*	2013	416,300	57,449	473,749
Dominique Charmot, Ph.D. *Chief Scientific Officer*	2013	310,000	33,325	343,325
David Rosenbaum, Ph.D. *Vice President, Drug Development*	2013	277,500	40,120	317,620

(1) The amounts reported in the Non-Equity Incentive Plan Compensation column represent the annual cash performance-based bonuses earned by our NEOs pursuant to the achievement of certain company and individual performance objectives. These amounts were paid to the named executive officers in February 2014. See the descriptions of the annual performance bonuses paid to our NEOs in "—Narrative to 2013 Summary Compensation Table and Outstanding Equity Awards at 2013 Fiscal Year End—Terms and Conditions of Annual Bonuses" below.

Outstanding Equity Awards at 2013 Fiscal Year End

The following table sets forth all outstanding equity awards held by each of the named executive officers as of December 31, 2013.

		Option Awards				Stock Awards	
Name	Vesting Commencement Date	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock That Have Not Vested (#)	Market Value of Shares or Units of Stock That Have Not Vested ($)(4)
Michael Raab	9/15/2010(1)	36,123	—	$ 1.08	10/26/2020		
	8/1/2011(1)	267,892	—	$ 0.54	8/11/2021		
Dominique Charmot, Ph.D.	9/15/2010(2)					2,919	27,847
	8/1/2011(2)					147,420	1,406,387
David Rosenbaum, Ph.D.	1/1/2010(3)					810	7,727
	9/15/2010(2)					1,921	18,326
	8/1/2011(2)					23,148	220,832

(1) The options are exercisable immediately, in whole or in part, conditioned upon the holder entering into a restricted stock purchase agreement with respect to any unvested shares. The shares subject to the options vest and/or are released from our repurchase option, as to 1/48th of the shares subject to such option on each monthly anniversary of the vesting commencement date, such that all shares will be vested on the fourth anniversary of the vesting commencement date, subject to the holder continuing to provide services to us through such vesting date.

(2) The shares are held pursuant to early exercised options and are released from our repurchase option as to 1/48th of the shares subject to such option on each monthly anniversary of the vesting commencement date, such that all shares will be vested on the fourth anniversary of the vesting commencement date, subject to the holder continuing to provide services to us through such vesting date.

(3) The shares are held pursuant to early exercised options and are released from our repurchase option as to 1/4th of the shares subject to the option on the first anniversary of the vesting commencement date, and thereafter as to 1/48th of the shares subject to such option on each monthly anniversary of the vesting commencement date, such that all shares will be vested on the four year anniversary of the vesting commencement date, subject to the holder continuing to provide services to us through such vesting date.

(4) Because our common stock was not traded on a public market on December 31, 2013, the market value has been determined based on a per-share common stock value of $9.54, which was the per share value of our common stock as of December 31, 2013 as determined by our board of directors.

Narrative to 2013 Summary Compensation Table and Outstanding Equity Awards at 2013 Fiscal Year End

Terms and Conditions of Employee Arrangements with our NEOs

We have entered into agreements with each of the NEOs in connection with his employment with us. These agreements set forth the terms and conditions of employment of each named executive officer, including base salary, initial equity award grants, and standard employee benefit plan participation. Our board of directors or the compensation committee reviews each NEO's base salary from time to time to ensure compensation adequately reflects the NEO's qualifications, experience, role and responsibilities. For fiscal year 2013, Mr. Raab's annual base salary was $416,300, Dr. Charmot's annual base salary was $310,000, and Dr. Rosenbaum's annual base salary was $265,000 through July 2013, and was increased to $295,000 effective August 1, 2013. In addition, for 2013, Mr. Raab, Dr. Charmot and Dr. Rosenbaum each had an annual bonus target of 30%, 25% and 20%, respectively, of base salary awarded based on the achievement of certain corporate and individual performance goals set by the board of directors.

In June 2014, we entered into an amended and restated employment agreement with Mr. Raab, which provides for an annual base salary of $426,708 and annual bonus targeted at 30% of base salary. We also entered into a change in control severance agreement with Dr. Charmot which supersedes his prior employment agreement with us, and an amended and restated change in control severance agreement with Dr. Rosenbaum.

Under Mr. Raab's amended and restated employment agreement, in the event Mr. Raab's employment with us is involuntarily terminated for reason other than "cause" or he resigns for "good reason" (each, as defined below), in each case more than three months prior to or more than 12 months after a change in control, then Mr. Raab will receive: (i) continued payment of his annual base salary as in effect immediately prior to such termination for a period of 12 months; (ii) payment of healthcare continuation costs for him and his eligible dependents for up to 12 months following the date of such termination; and (iii) 12 months of accelerated vesting of any outstanding equity awards, with any options remaining exercisable until 12 months following the date of termination or the original expiration date. In the event Mr. Raab's employment with us is involuntarily terminated for reason other than cause or he resigns for good reason, in each case within three months prior to and 12 months after a change in control, then Mr. Raab will receive: (i) a lump sum amount equal to 1.5 multiplied by the sum of his base salary as in effect immediately prior to such termination and his target annual bonus for the year of termination; (ii) payment of healthcare continuation costs for him and his eligible dependents for up to 18 months following the date of such termination; and (iii) full accelerated vesting of any outstanding equity awards, with any options remaining exercisable until 12 months following the date of termination or the original expiration date.

Under Dr. Charmot's change in control severance agreement, in the event Dr. Charmot's employment with us is involuntarily terminated for reason other than cause or he resigns for good reason, in each case more than three months prior to or more than 12 months after a change in control, then Dr. Charmot will receive: (i) continued payment of his annual base salary as in effect immediately prior to such termination for a period of nine months; (ii) payment of healthcare continuation costs for him and his eligible dependents for up to 12 months following the date of such termination; and (iii) accelerated vesting of 50% of his then outstanding and unvested shares subject to equity awards held as of the effective date of the change in control severance agreement. In the event Dr. Charmot's employment with us is involuntarily terminated for reason other than cause or he resigns for good reason, in each case within three months prior to and 12 months after a change in control, then Dr. Charmot will receive: (i) a lump sum amount equal to the sum of his base salary as in effect immediately prior to such termination and his target annual bonus for the year of termination; (ii) payment of healthcare continuation costs for him and his eligible dependents for up to 12 months following the date of such termination; and (iii) full accelerated vesting of any outstanding equity awards, with any options remaining exercisable until 12 months following the date of termination or the original expiration date.

Under Dr. Rosenbaum's amended and restated change in control severance agreement, in the event Dr. Rosenbaum's employment with us is involuntarily terminated for reason other than cause or he resigns for good reason, in each case more than three months prior to or more than 12 months after a change in control, then Dr. Rosenbaum will receive: (i) continued payment of his annual base salary as in effect immediately prior to such termination for a period of six months; and (ii) payment of healthcare continuation costs for him and his eligible dependents for up to six months following the date of such termination. In the event Dr. Rosenbaum's employment with us is involuntarily terminated for reason other than cause or he resigns for good reason, in each case within three months prior to and 12 months after a change in control, then Dr. Rosenbaum will receive: (i) a lump sum amount equal to 0.75 multiplied by the sum of his base salary as in effect immediately prior to such termination and his target annual bonus for the year of termination; (ii) payment of healthcare continuation costs for him and his eligible dependents for up to nine months following the date of such termination; and (iii) full accelerated vesting of any outstanding equity awards, with any options remaining exercisable until 12 months following the date of termination or the original expiration date.

For the purposes of Mr. Raab's amended and restated employment agreement, Dr. Charmot's change in control severance agreement, and Dr. Rosenbaum's amended and restated change in control severance

agreement, "cause" means (i) the NEO's theft, dishonesty or falsification of any employment or company records that is non-trivial in nature; (ii) malicious or reckless disclosure of our confidential or proprietary information or any material breach by the NEO of his obligations under his proprietary information and inventions assignment agreement with us; (iii) the conviction of the NEO of a felony (excluding motor vehicle violations) or the commission of gross negligence or willful misconduct, where a majority of the non-employee members of the board of directors reasonably determines that such act or misconduct has (A) seriously undermined the ability of the board of directors or management to entrust him with important matters or otherwise work effectively with him, (B) substantially contributed to our loss of significant revenues or business opportunities, or (C) significantly and detrimentally affected the business or reputation of our company or any of our subsidiaries; and/or (iv) the willful failure or refusal by the NEO to follow the reasonable and lawful directives of the board of directors, provided such willful failure or refusal continues after his receipt of reasonable notice in writing of such failure or refusal and a reasonable opportunity of not less than 30 days to correct the problem.

For the purposes of Mr. Raab's amended and restated employment agreement, Dr. Charmot's change in control severance agreement, and Dr. Rosenbaum's amended and restated change in control severance agreement, "good reason" means the occurrence of: (i) a material diminution in the NEO's authority, duties, or responsibilities, which substantially reduces the nature or character of his position; (ii) a reduction by us of his base salary as in effect immediately prior to such reduction; (iii) a relocation of his principal office to a location more than 50 miles from the location of our principal office as of immediately prior to such relocation, except for required travel by him on company business; or (iv) any material breach by us of any provision of the NEO's employment agreement or offer letter which we do not cure within 30 days following written notice from the NEO, provided that in order for "good reason" to exist, each of the following conditions must be met: (i) the foregoing good reason conditions must have occurred without the NEO's express written consent; (ii) the NEO must provide written notice to us of such condition within 30 days of the initial existence of the condition; (iii) the condition specified in such notice must remain uncorrected for 30 days after receipt of such notice; and (iv) the date of the NEO's resignation of employment must occur within 60 days after the initial existence of the condition specified in such notice.

Terms and Conditions of Annual Bonuses

For 2013, our NEOs were eligible for performance-based cash incentives pursuant to the achievement of certain corporate and individual performance objectives. The performance goals for these annual performance cash bonuses were reviewed and approved by the board of directors. The determination of the amount of bonuses paid to our NEOs generally reflects a number of considerations, including individual performance and financing and research goals.

Each NEO's target bonus opportunity is expressed as a percentage of base salary which can be achieved by meeting corporate and individual performance goals. Our board of directors or our compensation committee has historically reviewed these target percentages to ensure they are adequate, but does not follow a formula. Instead, our board of directors or our compensation committee has set these rates based on each participating executive's experience in her or his role with our company and the level of responsibility held by each executive, which the board of directors or our compensation committee believe directly correlates to her or his ability to influence corporate results. For fiscal year 2013, our board of directors used a guideline target bonus opportunity of 30% of base salary for Mr. Raab, 25% of base salary for Dr. Charmot, and 20% of base salary for Dr. Rosenbaum.

For determining performance bonus amounts for our NEOs for 2013, our board of directors set certain corporate performance goals. In setting these goals, our board of directors considered the status of our discovery programs, our financial status, and our role in certain critical activities being conducted under the collaboration partnership with AstraZeneca. Of the ten corporate goals, six were tied to the achievement of specific development milestones for tenapanor, two were aimed at advancing our internal discovery programs, and the remaining two addressed financing and business development objectives. While the board of directors did not specify specific goals for individuals, each individual's participation in the achievement of the corporate goals was assessed, as well as the executive's handling of unplanned events and opportunities. For 2013, the corporate

and individual components of the annual bonus were weighted at 80% and 20%, respectively, for Mr. Raab, 70% and 30%, respectively, for Dr. Charmot, and 60% and 40% for Dr. Rosenbaum. The board of directors determined that 40% of the corporate goals had been achieved, and that Mr. Raab, Dr. Charmot and Dr. Rosenbaum achieved 70%, 50% and 110% of their individual goals, respectively.

Following its review and determinations of corporate and individual achievements for 2013, the board of directors awarded cash bonuses to Mr. Raab, Dr. Charmot and Dr. Rosenbaum in amounts equal to 14%, 11% and 14% of each of their base salaries, respectively. The NEOs' 2013 bonuses are set forth in the "2013 Summary Compensation Table" above.

Terms and Conditions of Equity Award Grants

None of our NEOs received grants of equity awards in 2013. The table above entitled "Outstanding Equity Awards at 2013 Fiscal Year End" describes the material terms of other option awards made in past fiscal years to our NEOs.

Terms and Conditions of 401(k) Plan

Our U.S. eligible employees, including our NEOs, participate in our 401(k) plan. Enrollment in the 401(k) plan is automatic for employees who meet eligibility requirements unless they decline participation. The 401(k) plan is intended to qualify under Section 401(k) of the Internal Revenue Service Code of 1986, as amended, so that contributions to the 401(k) plan by employees or by us, and the investment earnings thereon, are not taxable to the employees until withdrawn from the 401(k) plan, and so that contributions by us, if any, will be deductible by us when made. Under the 401(k) plan, employees may elect to reduce their current compensation by between 1% and 90% of eligible pay, up to the statutorily prescribed annual limit and to have the amount of such reduction contributed to the 401(k) plan. We do not provide any matching contributions under the 401(k) plan.

Equity Compensation Plans

2014 Equity Incentive Award Plan

We have adopted the 2014 Equity Incentive Award Plan, or 2014 Plan, which will be effective on the closing of this offering. The principal purpose of the 2014 Plan is to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards and cash-based performance bonus awards. The material terms of the 2014 Plan, as it is currently contemplated, are summarized below. Our board of directors is still in the process of developing, approving and implementing the 2014 Plan and, accordingly, this summary is subject to change.

Share Reserve. Under the 2014 Plan, 1,419,328 shares of our common stock will be initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, stock appreciation rights, or SARs, restricted stock awards, restricted stock unit awards, deferred stock awards, deferred stock unit awards, dividend equivalent awards, stock payment awards and performance awards, plus the number of shares remaining available for future awards under the 2008 Stock Incentive Plan, as amended, or 2008 Stock Plan, as of the consummation of this offering. 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 our 2008 Stock Incentive Plan, as amended, that are forfeited or lapse unexercised and which following the effective date are not issued under our 2008 Stock Incentive Plan, as amended, and (ii), if approved by our board of directors or the compensation committee of our board of directors, an annual increase on the first day of each fiscal year beginning in 2015 and 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.

The following counting provisions will be in effect for the share reserve under the 2014 Plan:

- generally, to the extent that an award terminates, expires or lapses for any reason or an award is settled in cash without the delivery of shares or for which shares are forfeited or repurchased for the original purchase price thereof, any shares subject to the award at such time will be available for future grants under the 2014 Plan;
- shares tendered or withheld to satisfy the grant or exercise price or tax withholding obligation with respect to an award under the 2014 Plan and shares subject to a stock appreciation right that are not issued in connection with the stock settlement of the stock appreciation right on exercise thereof may again be available for future grants under the 2014 Plan;
- to the extent that shares of our common stock are repurchased by us prior to vesting so that shares are returned to us, such shares will be available for future grants under the 2014 Plan;
- the payment of dividend equivalents in cash in conjunction with any outstanding awards will not be counted against the shares available for issuance under the 2014 Plan; and
- to the extent permitted by applicable law or any exchange rule, shares issued in assumption of, or in substitution for, any outstanding awards of any entity acquired in any form of combination by us or any of our subsidiaries will not be counted against the shares available for issuance under the 2014 Plan.

In addition, the maximum number of shares underlying awards that may be granted to any non-employee director pursuant to the 2014 Plan during any calendar year is the greater of 100,000 shares or the number of shares such that the maximum aggregate value of awards granted to the non-employee director during such calendar year is $400,000.

Administration. The compensation committee of our board of directors is expected to administer the 2014 Plan unless our board of directors assumes authority for administration. Unless otherwise determined by our board of directors, the compensation committee will consist of at least two members of our board of directors, each of whom is intended to qualify as an "outside director," within the meaning of Section 162(m) of the Code, a "non-employee director" for purposes of Rule 16b-3 under the Exchange Act and an "independent director" within the meaning of the rules of the applicable stock exchange, or other principal securities market on which shares of our common stock are traded. The 2014 Plan provides that the board or compensation committee may delegate its authority to grant awards to employees other than executive officers and certain senior executives of our company to a committee consisting of one or more members of our board of directors or one or more of our officers, other than awards made to our non-employee directors, which must be approved by our full board of directors.

Subject to the terms and conditions of the 2014 Plan, the administrator has the authority to select the persons to whom awards are to be made, to determine the number of shares to be subject to awards and the terms and conditions of awards, and to make all other determinations and to take all other actions necessary or advisable for the administration of the 2014 Plan. The administrator is also authorized to adopt, amend or rescind rules relating to administration of the 2014 Plan. Our board of directors may at any time remove the compensation committee as the administrator and revest in itself the authority to administer the 2014 Plan. The full board of directors will administer the 2014 Plan with respect to awards to non-employee directors.

Eligibility. Options, SARs, restricted stock and all other stock-based and cash-based awards under the 2014 Plan may be granted to individuals who are then our officers, employees or consultants or are the officers, employees or consultants of certain of our affiliates. Such awards also may be granted to our directors. Only employees of our company or certain of our affiliates may be granted incentive stock options, or ISOs.

Awards. The 2014 Plan provides that the administrator may grant or issue stock options, SARs, restricted stock, restricted stock units, deferred stock, deferred stock units, dividend equivalents, performance awards, and

stock payments, or any combination thereof. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- *Nonstatutory Stock Options*, or NSOs, will provide for the right to purchase shares of our common stock at a specified price which may not be less than fair market value on the date of grant, and usually will become exercisable (at the discretion of the administrator) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of corporate performance targets and individual performance targets established by the administrator. NSOs may be granted for any term specified by the administrator that does not exceed ten years.
- *Incentive Stock Options*, or ISOs, will be designed in a manner intended to comply with the provisions of Section 422 of the Code and will be subject to specified restrictions contained in the Code. Among such restrictions, ISOs must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees, and must not be exercisable after a period of ten years measured from the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) at least 10% of the total combined voting power of all classes of our capital stock, the 2014 Plan provides that the exercise price must be at least 110% of the fair market value of a share of common stock on the date of grant and the ISO must not be exercisable after a period of five years measured from the date of grant.
- *Restricted Stock* may be granted to any eligible individual and made subject to such restrictions as may be determined by the administrator. Restricted stock, typically, may be forfeited for no consideration or repurchased by us at the original purchase price if the conditions or restrictions on vesting are not met. In general, restricted stock may not be sold or otherwise transferred until restrictions are removed or expire. Purchasers of restricted stock, unlike recipients of options, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse, however, extraordinary dividends will generally be placed in escrow, and will not be released until restrictions are removed or expire.
- *Restricted Stock Units* may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Like restricted stock, restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.
- *Deferred Stock Awards* represent the right to receive shares of our common stock on a future date. Deferred stock may not be sold or otherwise hypothecated or transferred until issued. Deferred stock will not be issued until the deferred stock award has vested, and recipients of deferred stock generally will have no voting or dividend rights prior to the time when the vesting conditions are satisfied and the shares are issued. Deferred stock awards generally will be forfeited, and the underlying shares of deferred stock will not be issued, if the applicable vesting conditions and other restrictions are not met.
- *Deferred Stock Units* are denominated in unit equivalent of shares of our common stock, and vest pursuant to a vesting schedule or performance criteria set by the administrator. The common stock underlying deferred stock units will not be issued until the deferred stock units have vested, and recipients of deferred stock units generally will have no voting rights prior to the time when vesting conditions are satisfied.
- *Stock Appreciation Rights*, or SARs, may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The exercise price of any SAR granted under the 2014 Plan must be at least 100% of the fair market value of a share of our common stock on the date of grant. Except as required by Section 162(m) of the Code with respect to a SAR intended to qualify as performance-based compensation as described in Section 162(m) of the Code, there are no restrictions specified in the 2014 Plan on the exercise of

SARs or the amount of gain realizable therefrom, although restrictions may be imposed by the administrator in the SAR agreements. SARs under the 2014 Plan will be settled in cash or shares of our common stock, or in a combination of both, at the election of the administrator.

- *Dividend Equivalents* represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the award. Dividend equivalents may be settled in cash or shares and at such times as determined by the compensation committee or board of directors, as applicable.
- *Performance Awards* may be granted by the administrator on an individual or group basis. Generally, these awards will be based upon specific performance targets and may be paid in cash or in common stock or in a combination of both. Performance awards may include "phantom" stock awards that provide for payments based upon the value of our common stock. Performance awards may also include bonuses that may be granted by the administrator on an individual or group basis and which may be payable in cash or in common stock or in a combination of both.
- *Stock Payments* may be authorized by the administrator in the form of common stock or an option or other right to purchase common stock as part of a deferred compensation or other arrangement in lieu of all or any part of compensation, including bonuses, that would otherwise be payable in cash to the employee, consultant or non-employee director.

Change in Control. In the event of a change in control where the acquiror does not assume or replace awards granted, prior to the consummation of such transaction, awards issued under the 2014 Plan, other than performance awards, will be subject to accelerated vesting such that 100% of such awards will become vested and exercisable or payable, as applicable. Performance awards will vest in accordance with the terms and conditions of the applicable award agreement. In addition, the administrator will also have complete discretion to structure one or more awards under the 2014 Plan to provide that such awards will become vested and exercisable or payable on an accelerated basis in the event such awards are assumed or replaced with equivalent awards but the individual's service with us or the acquiring entity is subsequently terminated within a designated period following the change in control event. The administrator may also make appropriate adjustments to awards under the 2014 Plan and is authorized to provide for the acceleration, cash-out, termination, assumption, substitution or conversion of such awards in the event of a change in control or certain other unusual or nonrecurring events or transactions. Under the 2014 Plan, a change in control is generally defined as:

- the transfer or exchange in a single transaction or series of related transactions by our stockholders of more than 50% of our voting stock to a person or group;
- a change in the composition of our board of directors over a two-year period such that the members of the board of directors who were approved by at least two-thirds of the directors who were directors at the beginning of the two year period or whose election or nomination was so approved cease to constitute a majority of the board of directors;
- a merger, consolidation, reorganization or business combination in which we are involved, directly or indirectly, other than a merger, consolidation, reorganization or business combination, sale or disposition of all or substantially all of our assets, or acquisition of assets or stock of another entity, in each case, other than a transaction that results in our outstanding voting securities immediately before the transaction continuing to represent a majority of the voting power of the acquiring company's outstanding voting securities and after which no person or group beneficially owns 50% or more of the outstanding voting securities of the surviving entity immediately after the transaction; or
- stockholder approval of our liquidation or dissolution.

Adjustments of Awards. In the event of a nonreciprocal transaction between our company and our stockholders such as any stock dividend, stock split, spin-off, recapitalization, distribution of our assets to stockholders (other than normal cash dividends) or any other corporate event affecting the number of outstanding

shares of our common stock or the share price of our common stock, the administrator will make appropriate, proportionate adjustments to:

- the aggregate number and type of shares subject to the 2014 Plan;
- the number and kind of shares subject to outstanding awards and terms and conditions of outstanding awards (including, without limitation, any applicable performance targets or criteria with respect to such awards); and
- the grant or exercise price per share of any outstanding awards under the 2014 Plan.

In the event of certain other corporate transactions, in order to prevent dilution or enlargement of the potential benefits intended to be made available under the 2014 Plan, the administrator has the discretion to make such equitable adjustments and may also:

- provide for the termination or replacement of an award in exchange for cash or other property;
- provide that any outstanding award cannot vest, be exercised or become payable after such event;
- provide that awards may be exercisable, payable or fully vested as to shares of common stock covered thereby; or
- provide that any surviving corporation will assume or substitute outstanding awards under the 2014 Plan.

Amendment and Termination. Our board of directors or the compensation committee (with board approval) may terminate, amend or modify the 2014 Plan at any time and from time to time. However, we must generally obtain stockholder approval:

- to increase the number of shares available under the 2014 Plan (other than in connection with certain corporate events, as described above);
- reduce the price per share of any outstanding option or stock appreciation right granted under the 2014 Plan; or
- cancel any option or stock appreciation right in exchange for cash or another award when the option or stock appreciation right price per share exceeds the fair market value of the underlying shares.

Termination. The board of directors may terminate the 2014 Plan at any time. No awards may be granted pursuant to the 2014 Plan after the tenth anniversary of the effective date of the 2014 Plan. Any award that is outstanding on the termination date of the 2014 Plan will remain in force according to the terms of the 2014 Plan and the applicable award agreement.

We intend to file with the SEC a registration statement on Form S-8 covering the shares of our common stock issuable under the 2014 Plan.

2008 Stock Incentive Plan

Our board of directors adopted, and our stockholders approved, the 2008 Stock Incentive Plan, or 2008 Stock Plan, effective as of February 12, 2008, which was subsequently amended on May 27, 2008, June 22, 2011, December 6, 2012 and May 23, 2014 to increase the number of shares available under the 2008 Stock Plan. The 2008 Stock Plan provided for the grant of ISOs, NSOs, SARs, restricted stock, restricted stock units, dividend equivalents and any other rights or benefits not inconsistent with the 2008 Stock Plan. As of March 31, 2014, options to purchase 880,497 shares of our common stock at a weighted-average exercise price per share of $1.23 remained outstanding under the 2008 Stock Plan. No other equity awards have been granted under the 2008 Stock Plan. As of March 31, 2014, 26 shares of our common stock were available for future issuance pursuant to awards granted under the 2008 Stock Plan. Following this offering and in connection with the effectiveness of our 2014 Plan, the 2008 Stock Plan will terminate and no further awards will be granted under the 2008 Stock Plan. However, all outstanding awards will continue to be governed by their existing terms.

Administration. Our board of directors, or a committee thereof appointed by our board of directors, has the authority to administer the 2008 Stock Plan and the awards granted under it, provided that after our common stock is sold to the public pursuant to a registration statement filed with the Securities and Exchange Commission, the 2008 Stock Plan will be administered by the board or a committee constituted in a manner to permit grants to be exempt from Section 16(b) of the Exchange Act with respect to grants of awards to directors. In addition, grants of awards to "covered employees" within the meaning of Section 162(m) of the Code may only be made by a committee comprised solely of two or more directors eligible to serve on a committee granting awards qualifying as "performance-based compensation" within the meaning of Section 162(m) of the Code. The administrator has the authority to select the employees to whom awards will be granted under the 2008 Stock Plan, the number of shares to be subject to those awards under the 2008 Stock Plan, and the terms and conditions of the awards granted. In addition, the administrator has the authority to construe and interpret the 2008 Stock Plan and to adopt rules for the administration, interpretation and application of the 2008 Stock Plan that are consistent with the terms of the 2008 Stock Plan.

Eligibility. Awards other than ISOs may be granted to any of our employees, consultants or directors or any employees, consultants or directors of a parent or subsidiary of our company. Only employees of our company and a parent or subsidiary of our company may be granted incentive stock options, or ISOs.

Awards. The 2008 Stock Plan provides that the administrator may grant or issue options, including ISOs and NSOs, SARs, restricted stock, restricted stock units, dividend equivalents and any other rights or benefits not inconsistent with the 2008 Stock Plan to eligible participants. Each award will be designated in an award agreement and in the case of an option, will be designated as either an ISO or NSO. The administrator will determine the provisions, terms and conditions of each award, including the vesting schedule, repurchase provisions, right of first refusal, forfeiture provisions, form of payment and any performance criteria. From time to time, the administrator may also establish one or more separate programs under the 2008 Stock Plan for the purpose of issuing particular forms of awards to one or more classes of grantees. No award may have a term of more than ten years from the date of grant, except that in the case of an ISO granted to an individual who owns stock representing more than 10% of the voting power of all classes of stock of our company or any parent or subsidiary of our company, the term of the ISO will be no more than five years from the date of grant.

- *Stock Options.* The 2008 Stock Plan provides for the grant of ISOs under the federal tax laws or NSOs. ISOs may be granted only to employees, and NSOs may be granted to employees, directors or consultants. The exercise price of options may not be less than 100% of the fair market value per share of our common stock on the date of grant, provided that the exercise price of ISOs granted to employees who at the time of grant own stock representing more than 10% of the voting power of all classes of our common stock may not be less than 110% of the fair market value per share of our common stock on the date of grant. Shares subject to options under the 2008 Stock Plan generally vest in a series of installments over an optionee's period of service.
- *Stock Appreciation Rights*. The 2008 Stock Plan provides that we may issue SARs. Each SAR will be governed by a stock appreciation right agreement and may be granted in connection with stock options or other awards, or separately. SARs typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The base appreciation amount of each SAR may not be less than 100% of the fair market value per share of our common stock on the date of grant.
- *Restricted Stock Awards.* The 2008 Stock Plan provides that we may issue restricted stock awards. Each restricted stock award will be governed by a restricted stock award agreement, which will detail the restrictions on transferability, risk of forfeiture and other restrictions the administrator approves. In general, restricted stock may not be sold, transferred, pledged, hypothecated, margined or otherwise encumbered until restrictions are removed or expire. Holders of restricted stock, unlike recipients of other equity awards, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse.
- *Restricted Stock Units.* The 2008 Stock Plan provides that we may issue restricted stock unit awards which may be settled in cash, common stock, other securities or a combination thereof. Each restricted

stock unit award will be governed by a restricted stock unit award agreement and may be awarded to any eligible individual, subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or, unless otherwise determined by the administrator, dividend rights prior to the time when vesting conditions are satisfied, except dividend equivalents may be credited in respect of shares of common stock.

- *Dividend Equivalents*. The 2008 Stock Plan provides that dividend equivalents may be awarded to employees, consultants or directors. Dividend equivalents represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the award. Dividend equivalents may be settled in cash, shares, other awards or other property equal in value to dividends paid and at such times as determined by the administrator.
- *Other Awards.* The 2008 Stock Plan also authorizes the administrator to award any type of arrangement to an employee, director or consultant that is not inconsistent with the provisions of the 2008 Stock Plan and by its terms involves or might involve the issuance of shares, cash, or right similar to an option or SAR, with an exercise or conversion privilege related to the passage of time, occurrence of one or more events or satisfaction of performance criteria or other conditions.

Exercisability. In the event of a termination of a participant's continuous service other than for disability or death, the participant may exercise the portion of participant's award that was vested at the date of termination (or such other portion as may be determined by the administrator) during such period of time as determined by the administrator. In the event of a termination of a participant's continuous service as a result of disability, the participant may exercise the vested portion of his or her award as of termination within 12 months from the date of termination (or such longer period specified in the award agreement, but in no event later than the original expiration date). In the event of a termination of a participant's continuous service as a result of death or in the event of participant's death during any post-termination exercise period, the participant's estate may exercise the vested portion of his or her award as of termination within 12 months from the date of termination (or such longer period specified in the award agreement, but in no event later than the original expiration date).

Transferability. ISOs may not be sold or otherwise transferred in any manner other than by will or the laws of descent and distribution and may be exercised only by the participant during the lifetime of the participant. Awards other than ISOs are transferable only by will and the laws of descent and distribution and during the lifetime of the participant, to the extent authorized by the administrator by gift or pursuant to a domestic relations order to members of the participant's immediate family. The participant may also designate one or more beneficiaries in the event of death on a designated form provided by the administrator.

Changes in Capitalization. In the event of certain corporate adjustments, including any stock split, stock dividend, combination or reclassification of shares, any other increase or decrease in the number of shares effected without receipt of consideration by our company, or any other transaction with respect to common stock including a merger, consolidation, reorganization or liquidation, the administrator will proportionately adjust the number of shares covered by each outstanding award, the number of shares authorized for issuance under the 2008 Stock Plan, the exercise or purchase price of each outstanding award, individual share limits under the 2008 Stock Plan, as well as any other terms the administrator determines requires adjustment. In connection with such adjustments, the administrator may, in its discretion, prohibit the exercise of awards or other issuance of shares, cash or other consideration pursuant to awards during certain periods of time.

Change in Control. In the event of certain mergers, sales of all or substantially all of our company's assets and the complete liquidation or dissolution of our company, or Corporate Transaction, outstanding awards may be assumed or substituted and to the extent not assumed or substituted, will termination upon the consummation of the Corporate Transaction. Except as otherwise provided in an individual award agreement, in the event of a Corporate Transaction or a change in control of our company, the vesting or exercisability of awards will not be accelerated.

Amendment; Termination. Our board of directors may amend or terminate the 2008 Stock Plan. We will obtain stockholder approval of any amendment to the extent necessary to comply with applicable law. No suspension or termination of the 2008 Stock Plan may adversely affect any rights under awards already granted to a participant. Following this offering and in connection with the effectiveness of our 2014 Plan, the 2008 Stock Plan will terminate and no further awards will be granted under the 2008 Stock Plan.

We intend to file with the SEC a registration statement on Form S-8 covering our shares of common stock issuable under the 2008 Stock Plan.

Employee Stock Purchase Plan

We have adopted an Employee Stock Purchase Plan, which we refer to as our ESPP, which will be effective upon the effectiveness of the registration statement to which this prospectus relates. The ESPP is designed to allow our eligible employees to purchase shares of our common stock, at semi-annual intervals, with their accumulated payroll deductions. The ESPP is intended to qualify under Section 423 of the Code.

Plan Administration. Subject to the terms and conditions of the ESPP, our compensation committee will administer the ESPP. Our compensation committee can delegate administrative tasks under the ESPP to the services of an agent and/or employees to assist in the administration of the ESPP. The administrator will have the discretionary authority to administer and interpret the ESPP. Interpretations and constructions of the administrator of any provision of the ESPP or of any rights thereunder will be conclusive and binding on all persons. We will bear all expenses and liabilities incurred by the ESPP administrator.

Shares Available Under ESPP. The maximum number of our shares of our common stock which will be authorized for sale under the ESPP is equal to the sum of (a) 202,762 shares of common stock and (b), if approved by our board of directors or the compensation committee of our board of directors, an annual increase on the first day of each year beginning in 2015 and ending in 2024, equal to the lesser of (i) one percent (1.0%) of the shares of common stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (ii) such number of shares of common stock as determined by our board of directors; provided, however, no more than 2,230,374 shares of our common stock may be issued under the ESPP. The shares made available for sale under the ESPP may be authorized but unissued shares or reacquired shares reserved for issuance under the ESPP.

Eligible Employees. Employees eligible to participate in the ESPP for a given offering period generally include employees who are employed by us or one of our subsidiaries on the first day of the offering period, or the enrollment date. Our employees and any employees of our subsidiaries who customarily work less than five months in a calendar year or are customarily scheduled to work less than 20 hours per week will not be eligible to participate in the ESPP. Finally, an employee who owns (or is deemed to own through attribution) 5% or more of the combined voting power or value of all our classes of stock or of one of our subsidiaries will not be allowed to participate in the ESPP.

Participation. Employees will enroll under the ESPP by completing a payroll deduction form permitting the deduction from their compensation of at least 1% of their compensation but not more than the lesser of 15% of their compensation and $25,000 per offering period. Such payroll deductions may be expressed as either a whole number percentage or a fixed dollar amount and the accumulated deductions will be applied to the purchase of shares on each semi-annual purchase date. However, a participant may not purchase more than 3,000 shares in each offering period, and may not subscribe for more than $25,000 in fair market value of shares our common stock (determined at the time the option is granted) during any calendar year. The ESPP administrator has the authority to change these limitations for any subsequent offering period.

Offering. Under the ESPP, participants are offered the option to purchase shares of our common stock at a discount during a series of successive offering periods, which will normally commence on March 1 and September 1 of each year. The initial offering period will commence and end on dates as determined by the ESPP

administrator. Unless otherwise determined by the ESPP administrator, each offering period will have a duration of six months. However, in no event may an offering period be longer than 27 months in length.

The option purchase price will be the lower of 85% of the closing trading price per share of our common stock on the first trading date of an offering period in which a participant is enrolled or 85% of the closing trading price per share on the semi-annual purchase date, which will occur on the last trading day of each offering period.

Unless a participant has previously canceled his or her participation in the ESPP before the purchase date, the participant will be deemed to have exercised his or her option in full as of each purchase date. Upon exercise, the participant will purchase the number of whole shares that his or her accumulated payroll deductions will buy at the option purchase price, subject to the participation limitations listed above.

A participant may cancel his or her payroll deduction authorization at any time prior to the end of the offering period. Upon cancellation, the participant will have the option to either (a) receive a refund of the participant's account balance in cash without interest or (b) exercise the participant's option for the current offering period for the maximum number of shares of common stock on the applicable purchase date, with the remaining account balance refunded in cash without interest. Following at least one payroll deduction, a participant may also decrease (but not increase) his or her payroll deduction authorization once during any offering period. If a participant wants to increase or decrease the rate of payroll withholding, he or she may do so effective for the next offering period by submitting a new form before the offering period for which such change is to be effective.

A participant may not assign, transfer, pledge or otherwise dispose of (other than by will or the laws of descent and distribution) payroll deductions credited to a participant's account or any rights to exercise an option or to receive shares of our common stock under the ESPP, and during a participant's lifetime, options in the ESPP shall be exercisable only by such participant. Any such attempt at assignment, transfer, pledge or other disposition will not be given effect.

Adjustments upon Changes in Recapitalization, Dissolution, Liquidation, Merger or Asset Sale. In the event of any increase or decrease in the number of issued shares of our common stock resulting from a stock split, reverse stock split, stock dividend, combination or reclassification of the common stock, or any other increase or decrease in the number of shares of common stock effected without receipt of consideration by us, we will proportionately adjust the aggregate number of shares of our common stock offered under the ESPP, the number and price of shares which any participant has elected to purchase pursuant under the ESPP and the maximum number of shares which a participant may elect to purchase in any single offering period.

If there is a proposal to dissolve or liquidate us, then the ESPP will terminate immediately prior to the consummation of such proposed dissolution or liquidation, and any offering period then in progress will be shortened by setting a new purchase date to take place before the date of our dissolution or liquidation. We will notify each participant of such change in writing at least ten business days prior to the new exercise date. If we undergo a merger with or into another corporation or sale of all or substantially all of our assets, each outstanding option will be assumed or an equivalent option substituted by the successor corporation or the parent or subsidiary of the successor corporation. If the successor corporation refuses to assume the outstanding options or substitute equivalent options, then any offering period then in progress will be shortened by setting a new purchase date to take place before the date of our proposed sale or merger. We will notify each participant of such change in writing at least ten business days prior to the new exercise date.

Amendment and Termination. Our board of directors may amend, suspend or terminate the ESPP at any time. However, the board of directors may not amend the ESPP without obtaining stockholder approval within 12 months before or after such amendment to the extent required by applicable laws.

We intend to file with the SEC a registration statement on Form S-8 covering our shares issuable under the ESPP.

Certain Relationships and Related Party Transactions

The following is a description of transactions since January 1, 2011 to which we have been a party, in which the amount involved exceeds $120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest.

Sales and Purchases of Securities

Series B Convertible Preferred Stock Financing

In June and August 2011, we issued an aggregate of 8,713,760 shares of our Series B convertible preferred stock at $3.4785 per share. 1,500,511 of those shares were issued in exchange for conversion of our notes payable on November 16, 2010 and 1,453,733 of those shares were issued in exchange for conversion of our notes payable on April 14, 2011, in both cases pursuant to our Secured Convertible Note and Warrant Purchase Agreement, dated November 16, 2010. Additionally, in connection with such issuances, we issued warrants to purchase an aggregate of 574,953 shares of our Series B convertible preferred stock at a price per share of $0.09, which we refer to as our Series B Financing Warrants. The Series B Financing Warrants automatically exercise in connection with this offering. The aggregate gross consideration received for these issuances was $30.3 million.

The table below sets forth the number of shares of Series B convertible preferred stock, the number of shares of Series B convertible preferred stock in exchange for conversion of notes payable, and the number of shares underlying the Series B Financing Warrants sold to our directors, executive officers or owners of more than 5% of a class of our capital stock, or an affiliate or immediate family member thereof:

Name	Number of Shares of Series B Convertible Preferred Stock	Number of Shares Underlying Series B Financing Warrants	Number of Shares of Series B Convertible Preferred Stock in exchange for conversion of notes payable from November 2010	Number of Shares of Series B Convertible Preferred Stock in exchange for conversion of notes payable from April 2011	Aggregate Purchase Price ($)
New Enterprise Associates 12, Limited Partnership(1)	2,906,334	290,633	761,141	737,412	$ 15,322,402
CMEA Ventures VII, L.P.(2)	1,758,833	175,882	460,621	446,261	9,272,695
CMEA Ventures VII (Parallel), L.P.(2)	45,098	4,509	11,810	11,442	237,762
Amgen Ventures, LLC	785,447	—	—	—	2,732,178
Peter G. Schultz, Ph.D.(3)	143,740	60,802	159,236	154,272	1,590,543
Jean Frechet, Ph.D.(4)	—	18,176	47,602	46,118	326,011

(1) David Mott, the Chairman of our board of directors, is a partner of New Enterprise Associates.
(2) David Collier, M.D., was a member of our board of directors until his resignation in March 2014, and is a managing director of CMEA Ventures.
(3) Dr. Schultz is a member of our board of directors.
(4) Dr. Frechet was a member of our board of directors until his resignation in March 2014.

Participation in this Offering

Certain of our existing investors have agreed to purchase an aggregate of 888,054 shares of our common stock (or approximately $12.4 million) in this offering at the initial public offering price.

Indemnification Agreements and Directors' and Officers' Liability Insurance

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us to indemnify each director and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, penalties fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Investor Rights Agreements

We entered into an amended and restated investor rights agreement with the purchasers of our outstanding convertible preferred stock and certain holders of common stock and warrants to purchase our convertible preferred stock, including entities with which certain of our directors are affiliated. As of March 31, 2014, the holders of approximately 12.4 million shares of our common stock, including the shares of common stock issuable upon the conversion of our convertible preferred stock and shares of common stock issued upon exercise of warrants, are entitled to rights with respect to the registration of their shares under the Securities Act. For a more detailed description of these registration rights, see "Description of Capital Stock—Registration Rights." The investor rights agreement also provides for a right of first refusal in favor of certain holders of convertible preferred stock with regard to certain issuances of our capital stock. The rights of first refusal will not apply to, and will terminate upon the closing of, this offering.

Voting Agreement

We entered into an amended and restated voting agreement with certain holders of our common stock and convertible preferred stock. Upon the consummation of this offering, the amended and restated voting agreement will terminate. For a description of the amended and restated voting agreement, see "Management—Board Composition—Voting Arrangements."

Right of First Refusal and Co-Sale Agreement

We entered into an amended and restated right of first refusal and co-sale agreement with certain holders of our common stock and convertible preferred stock. This agreement provides for rights of first refusal and co-sale relating to the shares of our common stock held by the parties thereto. Upon the closing of this offering, the amended and restated right of first refusal and co-sale agreement will terminate.

Other Transactions

In November 2012, we entered into a consulting agreement with Susan Rosenbaum, Ph.D. the wife of Dr. David Rosenbaum, our Vice President, Drug Development. Dr. Susan Rosenbaum provides clinical operation services to us, and she is compensated at a rate of $125 per hour for her services. For the year ended December 31, 2013 and for the three months ended March 31, 2014, Dr. Susan Rosenbaum was a paid a total of $242,500 and $57,750, respectively, for her services pursuant to the consulting agreement. The consulting agreement is in effect until December 31, 2014, although it can be terminated by us with 14 days' written notice.

Policies and Procedures for Related Party Transactions

Our board of directors has adopted a written related person transaction policy, to be effective upon the consummation of this offering, setting forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act of 1933, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related

person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction with an unrelated third party and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

Principal Stockholders

The following table sets forth information relating to the beneficial ownership of our common stock as of June 6, 2014, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our directors;
- each of our named executive officers; and
- all directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of June 6, 2014 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The underwriters have allocated an aggregate of 888,054 shares of our common stock to certain of our existing investors as set forth below on the same terms as the other shares that are being offered and sold in this offering to the public.

The percentage of shares beneficially owned is computed on the basis of 13,028,923 shares of our common stock outstanding as of June 6, 2014, which reflects the assumed conversion of all of our outstanding shares of convertible preferred stock into an aggregate of 11,517,222 shares of common stock. Shares of our common stock that a person has the right to acquire within 60 days of June 6, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Ardelyx, Inc., at 34175 Ardenwood Blvd., Fremont, CA 94555.

	Beneficial Ownership Prior to this Offering				Beneficial Ownership After this Offering	
Name and Address of Beneficial Owner	Number of Outstanding Shares Beneficially Owned	Number of Shares Exercisable Within 60 Days	Number of Shares Beneficially Owned	Percentage of Beneficial Ownership	Number of Shares Beneficially Owned	Percentage of Beneficial Ownership
5% and Greater Stockholders						
Entities Associated with New Enterprise Associates(1)	5,821,994	290,633	6,112,627	45.89%	6,623,069	37.62%
Entities Associated with CMEA(2)	3,613,651	180,391	3,794,042	28.72%	4,110,868	23.50%
Amgen Ventures(3)	785,447	—	785,447	6.03%	846,233	4.89%
Named Executive Officers and Directors						
Michael Raab(4)	83,658	304,015	387,673	2.91%	387,673	2.20%
David Rosenbaum, Ph.D.(5)	111,803	—	111,803	*	111,803	*
Dominique Charmot, Ph.D.(6)	574,933	—	574,933	4.41%	574,933	3.32%
David Mott	—	—	—	—	—	—
Gordon Ringold, Ph.D.	—	—	—	—	—	—
Richard Rodgers	—	—	—	—	—	—
Peter Schultz, Ph.D.(7)	854,188	60,802	914,990	6.99%	914,990	5.27%
All directors and executive officers as a group (11 persons)(8)	1,777,901	669,034	2,332,007	17.02%	2,332,007	12.97%

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

(1) Consists of (a) 5,821,994 shares and 290,633 shares that may be acquired pursuant to the exercise of warrants within 60 days of June 6, 2014 held by New Enterprise Associates 12, Limited Partnership ("NEA 12") and (b) 1,465 shares held by NEA Ventures 2008, L.P, or Ven 2008. Also includes 510,442 shares allocated in this offering. NEA 12 GP, LLC, or NEA 12 LLC, is the sole general partner of NEA Partners 12, Limited Partnership NEA Partners 12, which is the sole general partner of NEA 12. The individual managers of NEA 12 LLC are M. James Barrett, Peter J. Barris, Forest Baskett, Ryan D. Drant, Patrick J. Kerins, Krishna 'Kittu' Kolluri, and Scott D. Sandell. NEA Partners 12, NEA 12 LLC, and the individual managers of NEA 12 LLC share voting and dispositive power with regard to the shares directly held by NEA 12. The shares directly held by Ven 2008 are indirectly held by Karen P. Welsh, the general partner of Ven 2008. Karen P. Welsh shares voting and dispositive power with regard to the shares directly held by Ven 2008. Each individual identified in this footnote disclaims beneficial ownership of such shares except to the extent of any respective pecuniary interest therein. The address of NEA 12 and Ven 2008 is 1954 Greenspring Drive, Suite 600, Timonium, MD 21903.

(2) Consists of (a) 3,523,311 shares and 175,882 shares that may be acquired pursuant to the exercise of warrants within 60 days of June 6, 2014 held by CMEA Ventures VII, L.P. and (b) 90,340 shares and 4,509 shares that may be acquired pursuant to the exercise of warrants within 60 days of June 6, 2014 held by CMEA Ventures VII (Parallel), L.P. Also includes 316,826 shares allocated in this offering. David Collier is Managing Director of CMEA Ventures VII GP, L.P. and has voting and dispositive power with respect to the shares. The address of CMEA Ventures VII, L.P., and CMEA Ventures VII (Parallel) is 1 Letterman Drive, Building C, Suite CM500, San Francisco, CA 94129.

(3) Also includes 60,786 shares allocated in this offering. All of these shares are owned directly by Amgen Ventures LLC, a wholly-owned subsidiary of Amgen Inc., or Amgen, and Amgen has the power to vote, acquire, hold and dispose of all shares. Amgen disclaims beneficial ownership of the securities except to the extent of its pecuniary interest therein. The address of Amgen Ventures LLC is One Amgen Center Drive, Thousand Oaks, CA 91320.

(4) Consists of (i) 83,658 shares directly owned by Mr. Raab and (ii) 304,015 shares that may be acquired pursuant to the exercise of stock options within 60 days of June 6, 2014 by Mr. Raab.

(5) Consists of (i) 25,880 shares directly owned by Dr. Rosenbaum, (ii) 77,592 shares owned directly by the David Paul Rosenbaum Family Trust and (iii) 8,331 shares owned directly by Dr. Rosenbaum's children.

(6) Consists of (i) 524,933 shares directly owned by Dr. Charmot and (ii) 50,000 shares directly owned by Dominique Charmot and Sylvie Charmot, Trustees of the Charmot 2012 Irrevocable Trust.

(7) Consists of (i) 800,290 shares directly owned by Dr. Schultz (ii) 53,898 shares held by certain trusts for the benefit of members of Dr. Schultz's family and (iii) 60,802 shares that may be acquired pursuant to the exercise of warrants within 60 days of June 6, 2014 by Dr. Schultz.

(8) Consists of 1,777,901 shares, 608,232 shares that may be acquired pursuant to the exercise of stock options within 60 days of June 6, 2014 and 60,802 shares that may be acquired pursuant to the exercise of warrants within 60 days of June 6, 2014.

Description of Capital Stock

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective immediately prior to the consummation of this offering, the investor rights agreement to which we and certain of our stockholders are parties and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated investor rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is part.

General

Immediately prior to the consummation of this offering, we will file our amended and restated certificate of incorporation that authorizes 300,000,000 shares of common stock, $0.0001 par value per share, and 5,000,000 shares of preferred stock, $0.0001 par value per share. As of March 31, 2014, there were outstanding:

- 13,028,923 shares of our common stock, on an as-converted basis, held by approximately 64 stockholders of record;
- 574,953 shares of our common stock issuable upon exercise of outstanding warrants; and
- 880,497 shares of our common stock issuable upon exercise of outstanding stock options.

In connection with this offering, we have consummated a 1-for-9 reverse stock split of our outstanding capital stock.

Common Stock

Voting Rights

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. In addition, the affirmative vote of holders of 66 2/3% of the voting power of all of the then outstanding voting stock will be required to take certain actions, including amending certain provisions of our amended and restated certificate of incorporation, such as the provisions relating to amending our amended and restated bylaws, the classified board and director liability.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. The terms of our credit facility currently prohibit us from paying cash dividends on our common stock.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable.

All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering will be, fully paid and nonassessable.

Preferred Stock

Immediately prior to the consummation of this offering, all outstanding shares of our convertible preferred stock will be converted into shares of our common stock. See Note 7 to our audited financial statements for a description of our currently outstanding convertible preferred stock. Immediately prior to the consummation of this offering, our amended and restated certificate of incorporation will be amended and restated to delete all references to such shares of convertible preferred stock. Upon the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Warrants

The following table sets forth information about outstanding warrants to purchase shares of our stock as of March 31, 2014. All of our warrants will expire upon completion of this offering if not exercised.

Class of stock underlying warrants	Number of shares exercisable prior to this offering	Number of shares of common stock exercisable following this offering	Exercise price per share ($)	Expiration Date
Series B convertible preferred stock, par value $0.0001	431,217	— (1)	0.09	11/16/2020
Series B convertible preferred stock, par value $0.0001	143,736	— (2)	0.09	4/14/2021
	574,953	—		

(1) Automatically net exercises into 428,439 shares of common stock at the consummation of this offering based on the initial public offering price per share.

(2) Automatically net exercises into 142,805 shares of common stock at the consummation of this offering based on the initial public offering price per share.

Registration Rights

Under our amended and restated investor rights agreement, following the closing of this offering, the holders of approximately 12.4 million shares of common stock, including shares issuable upon exercise of warrants, or their transferees, have the right to require us to register their shares under the Securities Act of 1933, or Securities Act, so that those shares may be publicly resold, or to include their shares in any registration statement we file, in each case as described below.

Demand Registration Rights

Based on the number of shares outstanding as of March 31, 2014, after the consummation of this offering, the holders of approximately 12.1 million shares of our common stock, including shares issuable upon exercise of warrants, or their transferees, will be entitled to certain demand registration rights. Beginning 180 days following the effectiveness of the registration statement of which this prospectus is a part, the holders of at least 25% of these shares can, on not more than two occasions, request that we register all or a portion of their shares. Additionally, we will not be required to effect a demand registration during the period beginning 60 days prior to the filing and ending 180 days following the effectiveness of a company-initiated registration statement relating to an initial public offering of our securities, provided that we have complied with certain notice requirements to the holders of these shares.

Piggyback Registration Rights

Based on the number of shares outstanding as of March 31, 2014, after the consummation of this offering, in the event that we determine to register any of our securities under the Securities Act (subject to certain exceptions), either for our own account or for the account of other security holders, the holders of approximately 12.4 million shares of our common stock, including shares issuable upon exercise of warrants, or their transferees, will be entitled to certain "piggyback" registration rights allowing the holders to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, other than with respect to a registration related to employee benefit plans, the offer and sale of debt securities, or corporate reorganizations or certain other transactions, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration. In an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include.

Form S-3 Registration Rights

Based on the number of shares outstanding as of March 31, 2014, after the consummation of this offering, the holders of approximately 12.1 million shares of our common stock, including shares issuable upon exercise of warrants, or their transferees, will be entitled to certain Form S-3 registration rights. The holders of at least 25% of these shares can make a written request that we register their shares on Form S-3 if we are eligible to file a registration statement on Form S-3 and if the aggregate price to the public of the shares offered is at least $1.0 million. These stockholders may make an unlimited number of requests for registration on Form S-3, but in no event shall we be required to file more than two registrations on Form S-3 in any six month period.

Expenses of Registration

We will pay the registration expenses of the holders of the shares registered pursuant to the demand, piggyback and Form S-3 registration rights described above, including the expenses of one counsel for the selling holders.

Expiration of Registration Rights

The demand, piggyback and Form S-3 registration rights described above will expire, with respect to any particular stockholder, upon the earlier of five years after the consummation of this offering or when that stockholder can sell all of its shares under Rule 144 of the Securities Act during any 90 day period.

Anti-Takeover Effects of Provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws and Delaware Law

Some provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws that will be in effect immediately prior to the consummation of this offering contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly-held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Special Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board of directors, Chief Executive Officer or President, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Classified Board; Election and Removal of Directors; Filling Vacancies

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of common stock outstanding will be able to elect all of our directors. Our amended and restated certificate of incorporation provides for the removal of any of our directors only for cause and requires at least a 66 2/3% stockholder vote. For more information on the classified board, see "Management—Board Composition." Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of the board, may only be filled by a resolution of the board of directors unless the board of directors determines that such vacancies shall be filled by the stockholders. This system of electing and removing directors and filling vacancies may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Choice of Forum

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. Although our amended and restated certificate of incorporation contains the choice of forum provision described above, it is possible that a court could find that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least 66 2/3% of the voting power of our then outstanding voting stock.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our Common Stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Limitations of Liability and Indemnification Matters

For a discussion of liability and indemnification, see "Management—Limitation on Liability and Indemnification Matters."

The NASDAQ Global Market Listing

Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "ARDX."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, New York 11219.

Shares Eligible for Future Sale

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after consummation of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

Based on the number of shares of our common stock outstanding as of March 31, 2014 and the initial public offering price, upon the closing of this offering and assuming (1) the conversion of our outstanding convertible preferred stock into 11,517,222 shares of common stock, (2) no exercise of the underwriters' option to purchase additional shares of common stock to cover over-allotments, (3) the net exercise of outstanding warrants that will expire or automatically exercise upon consummation of this offering into an aggregate of 571,244 shares of common stock and (4) no exercise of any of our other outstanding options, we will have outstanding an aggregate of approximately 17,886,167 shares of common stock. Of these shares, all of the shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares to cover over-allotments, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the consummation of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on the number of shares of our common stock outstanding as of March 31, 2014 and assumptions (1) – (4) described above, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Approximate Number of Shares	First Date Available for Sale into Public Market
13,600,167 shares	180 days after the date of this prospectus upon expiration of the lock-up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144

Lock-Up Agreements

In connection with this offering, we, our directors, our executive officers and substantially all of our other stockholders and option holders have agreed, subject to certain exceptions, with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of Citigroup and Leerink.

Prior to the completion of the offering, certain of our employees, including our executive officers, and/or directors may enter into written trading plans that are intended to comply with Rule 10b5-1 under the Exchange

Act. Sales under these trading plans would not be permitted until the expiration of the lock-up agreements relating to the offering described above.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the shares proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately 178,861 shares of common stock immediately after this offering (calculated as of March 31, 2014 on the basis of the assumptions (1) – (4) described above); or
- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our "affiliates," as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and

persons who are our "affiliates" may resell those shares without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to below, if applicable).

Registration Rights

Based on the number of shares outstanding as of March 31, 2014, after the consummation of this offering, the holders of approximately 12.4 million shares of our common stock, including shares issuable upon exercise of warrants, or their transferees, will, subject to any lock-up agreements they have entered into, be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. For a description of these registration rights, see "Description of Capital Stock—Registration Rights." If the offer and sale of these shares are registered, they will be freely tradable without restriction under the Securities Act.

Stock Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options reserved for issuance under our 2008 Stock Incentive Plan, as amended, and shares reserved for issuance under our 2014 Equity Incentive Award Plan and 2014 Employee Stock Purchase Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the consummation of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

Material U.S. Federal Income Tax Consequences to Non-U.S. Holders

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the Internal Revenue Code of 1986, as amended (the "Code"), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service ("IRS"), in each case in effect as of the date of this Registration Statement. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the tax on net investment income imposed by Section 1411 of the Code. In addition, it does not address consequences relevant to Non-U.S. Holders subject to particular rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies" and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT INTENDED AS TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND

DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "U.S. person" nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "—Sale or Other Taxable Disposition."

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the applicable withholding agent with the required certification, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest ("USRPI") by reason of our status as a U.S. real property holding corporation ("USRPHC") for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually or constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. Proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or "FATCA") on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends paid on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and IRS guidance, withholding under FATCA generally will apply to payments of dividends on our common stock made on or after July 1, 2014, and to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2017.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Underwriting

Citigroup Global Markets Inc. and Leerink Partners LLC are acting as joint book-running managers of the offering and as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter's name.

Underwriter	Number of Shares
Citigroup Global Markets Inc.	1,714,400
Leerink Partners LLC	1,285,800
JMP Securities LLC	642,900
Wedbush Securities Inc.	642,900
Total	4,286,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the option to purchase additional shares described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount from the public offering price not to exceed $0.5880 per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms. The representatives have advised us that the underwriters do not intend to make sales to discretionary accounts.

If the underwriters sell more shares than the total number set forth in the table above, we have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 642,900 additional shares at the public offering price less the underwriting discount solely to cover over-allotments, if any. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We, and our officers and directors have agreed that, for a period of 180 days from the date of this prospectus, we and they will not, without the prior written consent of Citigroup and Leerink, dispose of or hedge any shares or any securities convertible into or exchangeable for our common stock. Citigroup and Leerink in their sole discretion may release any of the securities subject to these lock-up agreements at any time, which, in the case of officers and directors, shall be with notice. Our common stock has been approved for listing on The NASDAQ Global Market under the symbol "ARDX."

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Paid by Ardelyx	
	No Exercise	Full Exercise
Per share	$ 0.98	$ 0.98
Total	$ 4,200,280	$ 4,830,322

We estimate that our portion of the total expenses of this offering will be approximately $3.4 million.

We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $32,500 as set forth in the underwriting agreement.

In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the underwriters' option to purchase additional shares, and stabilizing purchases.

- Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.
    - "Covered" short sales are sales of shares in an amount up to the number of shares represented by the underwriters' option to purchase additional shares.
    - "Naked" short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters' option to purchase additional shares.
- Covering transactions involve purchases of shares either pursuant to the underwriters' option to purchase additional shares or in the open market in order to cover short positions.
    - To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
    - To close a covered short position, the underwriters must purchase shares in the open market or must exercise the option to purchase additional shares. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.
- Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates for which they received, or may in the future receive, customary fees and commissions for these transactions.

Conflicts of Interest

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and/or credit default swaps) for their own account and for the

accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of shares described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a "relevant person"). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in France

Neither this prospectus nor any other offering material relating to the shares described in this prospectus has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be:

- released, issued, distributed or caused to be released, issued or distributed to the public in France; or
- used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

- to qualified investors (*investisseurs qualifiés*) and/or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code *monétaire et financier*;
- to investment services providers authorized to engage in portfolio management on behalf of third parties; or
- in a transaction that, in accordance with article L.411-2-II-1°-or-2°-or 3° of the French Code *monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia ("Corporations Act")) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission ("ASIC"). This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

a) you confirm and warrant that you are either:

i) a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

ii) a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

iii) a person associated with the company under section 708(12) of the Corporations Act; or

iv) a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

b) you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance

(Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than $0.2 million (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;
- where no consideration is or will be given for the transfer; or
- where the transfer is by operation of law.

The form of Underwriting Agreement attached as Exhibit 1.1 hereto provides for indemnification by the underwriters of us and our officers who sign this Registration Statement and directors for specified liabilities, including matters arising under the Securities Act.

Legal Matters

The validity of the issuance of our common stock offered in this prospectus will be passed upon for us by Latham & Watkins LLP, Menlo Park, California. Ropes & Gray LLP is acting as counsel for the underwriters in connection with this offering.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements at December 31, 2012 and 2013, and for each of the two years in the period ended December 31, 2013, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

Where You Can Find More Information

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to Ardelyx, Inc. and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits and schedules filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street N.E., Room 1580, Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from such offices upon the payment of the fees prescribed by the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon consummation of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at www.ardelyx.com. Upon consummation of this offering, you may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

ARDELYX, INC.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Ardelyx, Inc.

We have audited the accompanying balance sheets of Ardelyx, Inc. (the Company) as of December 31, 2012 and 2013, and the related statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for each of the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ardelyx, Inc. at December 31, 2012 and 2013, and the results of its operations and its cash flows for each of the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Redwood City, California
April 11, 2014, except for the last paragraph of Note 1,
as to which the date is June 18, 2014

Ardelyx, Inc.

Balance Sheets
(In thousands, except share and per share amounts)

	December 31,	
	2012	2013
Assets		
Current assets:		
Cash and cash equivalents	$ 32,903	$ 34,435
Accounts receivable	3,072	6,436
Prepaid expenses and other current assets	885	965
Total current assets	36,860	41,836
Property and equipment, net	844	530
Other assets	—	358
Restricted cash	180	180
Total assets	$ 37,884	$ 42,904
Liabilities, convertible preferred stock, and stockholders' deficit		
Current liabilities:		
Accounts payable	$ 1,146	$ 2,284
Accrued compensation and benefits	965	927
Other accrued liabilities	745	95
Deferred rent	364	5
Deferred revenue, current portion	13,571	13,828
Total current liabilities	16,791	17,139
Deferred revenue, non-current	19,091	26,470
Convertible preferred stock warrant liability	2,950	6,456
Liabilities related to early exercise of options	289	163
Total liabilities	39,121	50,228
Commitments and contingencies (Note 6)		
Convertible preferred stock, $0.0001 par value per share—108,829,748 shares authorized; 11,517,222 shares issued and outstanding as of December 31, 2012 and 2013; aggregate liquidation preferences of $59,074 as of December 31, 2012 and 2013	56,155	56,155
Stockholders' deficit:		
Common stock, $0.0001 par value per share—129,360,120 and 130,360,121 shares authorized as of December 31, 2012 and 2013; 1,001,616 and 1,225,481 shares issued and outstanding as of December 31, 2012 and 2013	—	—
Additional paid-in capital	4,697	5,174
Accumulated deficit	(62,089)	(68,653)
Total stockholders' deficit	(57,392)	(63,479)
Total liabilities, convertible preferred stock, and stockholders' deficit	$ 37,884	$ 42,904

See accompanying notes.

Ardelyx, Inc.

Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31,	
	2012	2013
Revenue:		
Licensing revenue	$ 3,182	$ 8,063
Collaborative development revenue	2,228	20,865
Total revenue	5,410	28,928
Operating expenses:		
Research and development	10,184	28,093
General and administrative	4,031	3,700
Total operating expenses	14,215	31,793
Loss from operations	(8,805)	(2,865)
Other expense, net	(30)	(52)
Change in fair value of preferred stock warrant liability	(950)	(3,506)
Loss before provision for income taxes	(9,785)	(6,423)
Provision for income taxes	—	(141)
Net loss and comprehensive loss	$ (9,785)	$ (6,564)
Net loss per common share, basic and diluted	$ (11.32)	$ (5.82)
Shares used to compute net loss per common share, basic and diluted	864,020	1,127,948
Pro forma net loss per common share, basic and diluted (unaudited)		$ (0.23)
Shares used to compute pro forma net loss per common share, basic and diluted (unaudited)		13,216,414

See accompanying notes.

Ardelyx, Inc.

Statements of Convertible Preferred Stock and Stockholders' Deficit
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balance as of January 1, 2012	11,517,222	$56,155	659,485	—	$ 4,049	$ (52,304)	$ (48,255)
Exercise of stock options and lapse of repurchase rights related to common shares issued pursuant to early exercises	—	—	342,131	—	175	—	175
Stock-based compensation	—	—	—	—	473	—	473
Net loss	—	—	—	—	—	(9,785)	(9,785)
Balance as of December 31, 2012	11,517,222	56,155	1,001,616	—	4,697	(62,089)	(57,392)
Exercise of stock options and lapse of repurchase rights related to common shares issued pursuant to early exercises	—	—	223,865	—	125	—	125
Stock-based compensation	—	—	—	—	352	—	352
Net loss	—	—	—	—	—	(6,564)	(6,564)
Balance as of December 31, 2013	11,517,222	$56,155	1,225,481	—	$ 5,174	$ (68,653)	$ (63,479)

See accompanying notes.

Ardelyx, Inc.

Statements of Cash Flows
(In thousands)

	Year Ended December 31,	
	2012	2013
Operating activities		
Net loss	$ (9,785)	$ (6,564)
Adjustments to reconcile net loss to net cash provided by operating activities:		
Depreciation and amortization expense	675	592
Stock-based compensation	473	352
Change in fair value of preferred stock warrant liability	950	3,506
Changes in operating assets and liabilities:		
Accounts receivable	(3,072)	(3,364)
Prepaid and other current assets	(790)	(80)
Other assets	—	(358)
Accounts payable	(105)	1,138
Accrued compensation and benefits	760	(38)
Other accrued liabilities	715	(650)
Deferred revenue	32,662	7,636
Deferred rent	(503)	(359)
Net cash provided by operating activities	21,980	1,811
Investing activities		
Purchases of property and equipment	(128)	(278)
Net cash used in investing activities	(128)	(278)
Financing activities		
Proceeds from issuance of common stock, including early exercise of stock options	290	1
Repurchase of unvested common stock	(20)	(2)
Net cash provided by (used in) financing activities	270	(1)
Net increase in cash and cash equivalents	22,122	1,532
Cash and cash equivalents at beginning of period	10,781	32,903
Cash and cash equivalents at end of period	$ 32,903	$ 34,435
Supplementary disclosure of cash flow information		
Income taxes paid	$ —	$ 160

See accompanying notes.

Ardelyx, Inc.

Notes to Financial Statements

1. Organization and Basis of Presentation

Ardelyx, Inc. (the "Company") a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the gastrointestinal tract to treat cardio-renal, gastrointestinal and metabolic diseases. The Company has developed a drug discovery and design platform enabling it, in a rapid and cost-efficient manner, to discover and design novel drug candidates. The Company was incorporated in Delaware on October 17, 2007, under the name Nteryx and changed its name to Ardelyx, Inc. in June 2008.

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

Reverse Stock Split

In June 2014, the Company's board of directors approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of the Company's common stock and convertible preferred stock at a 1-for-9 ratio (the "Reverse Stock Split"). The par value and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the Reverse Stock Split. All issued and outstanding common stock, convertible preferred stock, warrants for preferred stock, options for common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented. The Reverse Stock Split was effected on June 18, 2014.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to revenue recognition, clinical trial accruals, fair value of convertible preferred stock and related warrants, fair value of common stock, 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 may differ from those estimates.

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. The Company invests its cash in bank deposits and money market accounts.

Restricted Cash

The Company is required to guarantee the credit limit on its corporate credit card with a certificate of deposit of $100,000. The collateral will be released upon the cancellation of the corporate credit card.

The Company is required under its facility lease agreement to maintain a line of credit with a bank in the amount of $80,000 for the benefit of the lessor. The line of credit is secured by a cash deposit with the bank. The cash deposit will be released upon expiration of the line of credit.

Ardelyx, Inc.

Notes to Financial Statements

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist principally of cash, cash equivalents, and certificates of deposit. Cash and cash equivalents, as well as certificates of deposit held with financial institutions, may exceed the Federal Deposit Insurance Corporation insurance limits. The Company is exposed to credit risk in the event of default by the financial institutions holding its cash and cash equivalents to the extent of the amounts on its balance sheets. The Company has not experienced any losses on its cash, cash equivalents and certificates of deposit during the years ended December 31, 2012 and 2013.

Accounts receivable are unsecured and are concentrated with one collaboration partner in the pharmaceutical industry, AstraZeneca AB ("AstraZeneca"). Accordingly, the Company may be exposed to credit risk generally associated with pharmaceutical companies or specific to the license and collaboration agreement with AstraZeneca. To date the Company has not experienced any losses related to its receivables.

Fair Value of Financial Instruments

Fair value accounting is applied for all financial assets and liabilities and non-financial assets and liabilities that are recognized or disclosed at fair value in the financial statements on a recurring basis (at least annually).

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 Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If indicators of impairment exist, an impairment loss would be recognized when estimated, undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. The impairment charge is determined based upon the excess of the carrying value of the asset over its fair value, with fair value determined based upon an estimate of discounted future cash flows or another appropriate measure of fair value. The Company has not recorded any impairment of long-lived assets during the years ended December 31, 2012 and 2013.

Revenue Recognition

Revenue from research activities made under collaboration partnership agreements are recognized as the services are provided and when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue generated from research and licensing agreements typically includes up-front signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments, and royalties on future licensees' product sales.

For revenue agreements with multiple-element arrangements, such as license and development agreements, the Company allocates revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each

deliverable using vendor-specific objective evidence or third-party evidence. If neither exists, the Company uses its best estimate of selling price for that deliverable. Revenue allocated is then recognized when the four basic revenue recognition criteria are met for each element.

The Company recognizes revenue from upfront payments ratably over the term of its estimated period of performance under the agreement which is recorded as licensing revenue. Reimbursements for development costs incurred under the Company's license agreement with AstraZeneca are classified as collaborative development revenue. The Company recognizes cost reimbursement revenue under collaboration partnership agreements as the related research and development costs for services are rendered. Deferred revenue represents the portion of research or license payments received which has not been earned.

Revenue from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. To the extent that non-substantive milestones are achieved and the Company has remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance. The Company will recognize revenue associated with the non-substantive milestones upon achievement of the milestone if there are no undelivered elements and it has no remaining performance obligations. The Company will account for sales-based milestones as royalties that will be recognized as revenue upon achievement of the milestone.

Stock-Based Compensation

The Company measures its stock-based payment awards made to employees and directors based on the estimated fair values of the awards and recognizes the compensation expense over the requisite service period. The Company has selected the Black-Scholes option-pricing model to estimate the fair value of its stock-based awards. Stock-based compensation expense is recognized using the straight-line method. Stock-based compensation expense is based on the value of the portion of stock-based payment awards that is ultimately expected to vest. As such, 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 compensation expense related to stock options granted to non-employees based on the fair values estimated using the Black-Scholes model. Stock options granted to non-employees are remeasured at each reporting date until the award is vested.

Research and Development Costs

Research and development expenditures are expensed as incurred. Major components of research and development expenses consist of personnel costs, materials and supplies, and allocations of facilities-related costs, as well as fees paid to consultants and third parties that conduct certain research and development activities on the Company's behalf. Payments made to other entities are under agreements that are generally cancelable by the Company. Nonrefundable advance payments for goods or services to be rendered in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Convertible Preferred Stock Warrant Liability

The Company accounts for freestanding warrants to purchase shares of convertible preferred stock that are contingently redeemable as liabilities in the balance sheets at their estimated fair value. Convertible preferred stock warrants are subject to remeasurement at each balance sheet date, and any change in fair value is recognized as a component of other expense, net in the statements of operations and comprehensive loss.

Ardelyx, Inc.

Notes to Financial Statements

The Company will continue to adjust the liability for changes in fair value until the earlier of: (1) the exercise or expiration of the warrants or (2) the completion of a liquidation event, including the completion of an IPO, at which time all convertible preferred stock warrants will be net exercised and the liability will be reclassified to additional paid-in capital in stockholders' deficit.

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.

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 GAAP are recorded as an element of stockholders' deficit, but are excluded from net loss. The Company did not record any transactions within other comprehensive income (loss) in the periods presented and, therefore, the net loss and comprehensive loss were the same for all periods presented.

Net Loss per Common 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 common stock equivalents. Diluted net loss per common share is the same as basic net loss per common share, since the effects of potentially dilutive securities are antidilutive.

Unaudited Pro Forma Net Loss per Common Share

Pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of all outstanding shares of the convertible preferred stock and the net exercise of the preferred stock warrants upon the closing of the IPO. Also, the numerator in the pro forma basic and diluted net loss per share attributable to common stockholders calculation has been adjusted to remove gains or losses resulting from the remeasurement of the convertible preferred stock warrant liability related to warrants to purchase shares of convertible preferred stock, as it will be reclassified to additional paid-in capital upon a IPO of the Company's common stock.

Recent Accounting Pronouncement

In July 2013, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update (ASU) 2013-11, *Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists*. The ASU concludes an unrecognized tax benefit should be presented as a reduction of a deferred tax asset when settlement in this manner is available under the law. The Company will adopt this amendment as of January 1, 2014. The result of adoption may be to reclassify certain long term tax liabilities to long term deferred tax assets, and the adoption will not result in a change to the tax provision. Management does not believe that the impact on the balance sheet will be significant.

Ardelyx, Inc.

Notes to Financial Statements

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amounts of certain of the Company's financial instruments, including cash equivalents, accounts receivable and accounts payable, are valued at cost, which approximates fair value due to their short maturities. The accounting guidance for fair value provides a framework for measuring fair value, and requires certain new disclosures about how fair value is determined. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance also establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity.

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

Level 1—Observable inputs such as quoted prices (unadjusted) for *identical* instruments in active markets.

Level 2—Observable inputs such as quoted prices for *similar* instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, or model-derived valuations whose significant inputs are observable.

Level 3—Unobservable inputs that reflect the reporting entity's own assumptions.

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

	December 31, 2012			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Assets:				
Money market funds	$30,844	$30,844	$ —	$ —
Certificates of deposit	180	—	180	—
Total	$31,024	$30,844	$ 180	$ —
Liabilities:				
Preferred stock warrant liability	$ 2,950	$ —	$ —	$2,950
Total	$ 2,950	$ —	$ —	$2,950

	December 31, 2013			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Assets:				
Money market funds	$32,472	$32,472	$ —	$ —
Certificates of deposit	180	—	180	—
Total	$32,652	$32,472	$ 180	$ —
Liabilities:				
Preferred stock warrant liability	$ 6,456	$ —	$ —	$6,456
Total	$ 6,456	$ —	$ —	$6,456

Ardelyx, Inc.

Notes to Financial Statements

Where quoted prices are available in an active market, securities are classified as Level 1. The Company classifies money market funds as Level 1. When quoted market prices are not available for the specific security, then the Company estimates fair value by using benchmark yields, reported trades, broker/dealer quotes, and issuer spreads. The Company classifies certificates of deposit as Level 2. In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. Level 3 liabilities that are measured at fair value on a recurring basis consist of the preferred stock warrant liability, which was measured in 2012 using its intrinsic value given the low exercise price of the warrants. In 2013, the Company estimated the fair value of the warrant liability using the probability weighted expected return method that calculated the probability of the Company going public or being acquired, and the option-pricing method for remaining private in the near to mid-term. The determination of the fair value of the preferred stock warrants is discussed in Note 8. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability. There were no transfers between Level 1 and Level 2 during the periods presented.

The following table presents changes in liabilities measured at fair value on a recurring basis using Level 3 inputs:

	Preferred Stock Warrant Liability (in thousands)
Balance at January 1, 2012	$ 2,000
Net increase in fair value of warrant liabilities upon revaluation	950
Balance at December 31, 2012	2,950
Net increase in fair value of warrant liabilities upon revaluation	3,506
Balance at December 31, 2013	$ 6,456

4. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2012	2013
	(In thousands)	
Laboratory equipment	$ 2,037	$ 2,315
Office equipment and furniture	91	91
Leasehold improvements	1,456	1,456
Property and equipment, gross	3,584	3,862
Less: accumulated depreciation and amortization	(2,740)	(3,332)
Total property and equipment, net	$ 844	$ 530

Depreciation and amortization expense totaled $675,000 and $592,000 for the years ended December 31, 2012 and 2013.

5. License Agreement with AstraZeneca

In October 2012, the Company entered into a license agreement (the “License Agreement”) pursuant to which the Company and AstraZeneca collaborate to research, develop, and commercialize the Company’s small

Ardelyx, Inc.

Notes to Financial Statements

molecule NHE3 inhibitors program, which includes the Company's lead product candidate, tenapanor, as well as back-up compounds. Pursuant to the agreement, the Company granted a worldwide exclusive right and license to exploit such licensed compounds solely for development and commercialization purposes.

The Company is responsible for certain development activities from the effective date of the agreement through completion of the Chronic Kidney Disease ("CKD") Phase 2a clinical trial. AstraZeneca reimburses the Company for its internal and external development-related costs. The Company is also obligated to participate on a Development Collaboration Committee through the completion of all Phase 2 clinical trials for tenapanor. The Company will initially be responsible for supplying the compound of the licensed product for use in the development. The License Agreement also provides for the Company to transfer the technology and other necessary information such that AstraZeneca will be able to assume the responsibility for the supply of the drug product for use in later-stage clinical trials. As part of the transaction, the Company has an option to co-promote the product in the United States, subject to agreed limitations.

Under the License Agreement, AstraZeneca paid the Company an up-front license fee of $35.0 million in October 2012. In December 2013, AstraZeneca and the Company entered into an amendment to the License Agreement to acknowledge the intention of AstraZeneca to commence development of tenapanor for the treatment of hyperphosphatemia in End-Stage Renal Disease ("ESRD") patients, and to provide additional clarification for the payment of certain development milestones (the "License Amendment"). The License Amendment was not deemed to be a material modification to the arrangement since there were no changes in the total arrangement consideration or key provisions. AstraZeneca made a payment of $15.0 million in December 2013 pursuant to the amendment. The payment was combined with the unamortized upfront payment and is being recognized as revenue on a straight-line basis over the estimated period of performance.

The Company may also receive future contingent payments up to a total of $820.0 million, which is comprised of development milestones up to an additional $222.5 million and launch, commercialization, and sales milestones up to an additional $597.5 million. The contingent payments are triggered upon the activities expected to be undertaken by AstraZeneca. Revenue from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. The Company will recognize revenue associated with the non-substantive milestones upon achievement of the milestones if there are no undelivered elements and it has no remaining performance obligations. To the extent that non-substantive milestones are achieved and the Company has remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance.

Upon product sales, the Company is eligible to receive royalties that adjust depending on sales volume with royalty percentage ranges starting in the high single digits and moving into tiered double digits in mid-teens as net sales increase, subject to reductions in certain specified circumstances.

The Company has identified the deliverables within the arrangement as a license to the technology, the initial supply of the compound of the licensed product for use in development, and ongoing development activities through completion of all Phase 2 clinical trials for tenapanor, which are accounted for as a single unit of accounting. The Company has concluded that the license is not a separate unit of accounting. It does not have stand-alone value to AstraZeneca, separable from the development services to be performed pursuant to the agreement, as AstraZeneca is unable to use the license for its intended purpose without the Company's performance of the development services, which includes the initial supply of the compound. As a result, the Company will recognize revenue from the up-front payment on a straight-line basis over the period from the effective date of the agreement through the completion of all Phase 2 clinical trials for tenapanor (the estimated period of performance). The Company initially estimated the period of performance to be through June 2015. In connection with its process for re-evaluating the progress of clinical activities, the Company subsequently

revised its estimate for the period of performance for the completion of all Phase 2 clinical trials to be through December 2016. The $15.0 million payment received under the amendment was combined with the unamortized up-front payment and is being recognized as revenue on a straight-line basis over the estimated period of performance.

For the years ended December 31, 2012 and 2013, the Company recognized revenue amounting $3.2 million and $8.1 million, respectively, related to amortization of the up-front and other license fees, and $2.2 million and $20.9 million for collaborative development services. As of December 31, 2013, the Company has total deferred revenue of $40.3 million related to the AstraZeneca license agreement.

6. Commitments and Contingencies

The Company entered into a lease agreement beginning in September 2008 for a facility in Fremont, California. The lease term was 60 months and ended in September 2013. The master lease agreement included scheduled rent increases over the term of the lease. Rent increases, including the impact of a rent holiday and a leasehold improvement allowance from the landlord, were recognized as deferred rent and amortized on a straight-line basis over the term of the original lease.

On December 20, 2012, the Company extended the lease agreement for 36 months. The extension period commenced in September 2013, and will end in September 2016. The extended lease agreement included scheduled rent increases, which are amortized on a straight-line basis over the term of the extension. The Company has the option to renew the lease for an additional three years. The future minimum payments under the noncancelable operating lease at December 31, 2013, are as follows:

Year ending December 31,	Amount (in thousands)
2014	$ 569
2015	585
2016	414
Total future minimum lease payments	$ 1,568

Rent expense under operating leases was $436,000 and $480,000 for the years ended December 31, 2012 and 2013, respectively.

Guarantees and Indemnifications

As permitted under Delaware law and in accordance with the Company's bylaws, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is or was serving 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 the risk associated with the Company's exposure and may enable it to recover a portion of any future amounts paid. The Company may terminate the indemnification agreements with its officers and directors upon a 90-day written notification, but termination will not affect claims for indemnification related to events occurring prior to the effective date of termination. The Company believes the fair value of these indemnification agreements is minimal. Accordingly, the Company has not recorded any liabilities associated with these indemnification agreements as of December 31, 2012 or 2013.

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7. Convertible Preferred Stock

Convertible preferred stock as of December 31, 2012 and 2013 consisted of the following:

Convertible Preferred Stock:	Shares Authorized	Shares Issued and Outstanding	Net Carrying Value	Aggregate Liquidation Preference
		(In thousands, except share data)		
Series A	25,231,213	2,803,462	$25,957	$ 28,764
Series B	83,598,535	8,713,760	30,198	30,311
Total convertible preferred stock	108,829,748	11,517,222	$56,155	$ 59,074

The Company recorded the Series A and Series B convertible preferred stock at fair value on the dates of issuance, net of issuance costs. Shares of the convertible preferred stock are not currently redeemable. A redemption event will only occur upon liquidation or winding up of the Company, a greater than 50% change of control, or sale of substantially all of its assets. The Company classified the convertible preferred stock outside of stockholders' deficit because, in the event of certain liquidation events that are not solely within its control, the shares would become redeemable at the option of the holders. The Company did not adjust the carrying values of the convertible preferred stock to the deemed liquidation values of such shares since a liquidation event was not probable at any of the balance sheet dates. Subsequent adjustments to increase or decrease the carrying values to the ultimate liquidation values will be made only if and when it becomes probable that such a liquidation event will occur. The redemption amount of outstanding Series A is equal to its liquidation value, or $10.26 per share. The redemption amount of outstanding Series B is equal to its liquidation value, or $3.4785 per share.

The rights, privileges, and preferences of convertible preferred stock are as follows:

Conversion: Each share of convertible preferred stock is convertible, at the option of the holder, into one fully paid non-assessable share of common stock. The conversion formula is adjusted for such events as dilutive issuances, stock splits, or reclassification. Each and every series of preferred stock shall convert automatically into common stock at the earlier of (i) a firmly underwritten public offering meeting certain criteria, including an offering price per share of not less than $30.78, at least $30.0 million in gross proceeds, and pursuant to which the common stock shall be listed on the New York Stock Exchange or NASDAQ or (ii) the date specified by written request or agreement of holders of at least two-third of the then outstanding shares of convertible preferred stock (voting together as a separate class on an as-if converted to common stock basis).

Dividends: Holders of Series A and Series B are each entitled to non-cumulative dividends of $8.181 per share and $0.2781 per share, respectively, per annum, if and when declared by the Board of Directors. Dividends to Series A and Series B stockholders are to be paid in advance of any distributions to common stockholders. No dividends have been declared as of December 31, 2013.

Voting: Each holder of shares of convertible preferred stock is entitled to voting rights equivalent to the number of shares of common stock into which their respective shares are convertible. Certain financing, acquisition, disposition, and recapitalization transactions require the vote of a majority of the shares of outstanding preferred stock, provided at least 25% of the aggregate number of shares of convertible preferred stock that have been issued and remain outstanding.

Liquidation Preference: In the event of a liquidation or winding up of the Company, whether voluntary or involuntary, before payment is made to the holders of any other series of preferred stock or to the holders of common stock, holders of the Series A are entitled to be paid a liquidation preference of $10.26 per share and

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Series B a liquidation preference of $3.4785 per share, together with any declared but unpaid dividends on the stockholders' preferred shares. If assets are insufficient to make payments in full to all holders of Series A and Series B, then the assets or consideration will be distributed ratably among the holders of convertible preferred stockholders. Remaining assets shall be distributed among the holders of the common stock on a pro rata basis based on the number of shares of common stock held.

Election of Board of Directors: The holders of convertible preferred stock are entitled to elect two members of the Board of Directors, and holders of common stock are entitled to elect two members. Convertible preferred stockholders, together with common stockholders voting together as a single class, are entitled to elect all remaining members of the Board of Directors.

8. Preferred Stock Warrants

In connection with the closing of the Series B financing in August 2011, the Company issued warrants for the purchase of 574,953 shares of Series B convertible preferred stock. The exercise price of the warrants is $0.09 per share. The warrants will be exercisable through the earliest to occur of an IPO, a change in control, or their expiration date. Warrants exercisable for 431,217 of the shares have an expiration date of November 16, 2020 and warrants exercisable for 143,736 of the shares have an expiration date of April 14, 2021. The preferred stock warrant liability is measured at fair value on a recurring basis. Changes in fair value are recorded in change in fair value of preferred stock warrant liability in the Statements of Operations and Comprehensive Loss. As a result of the low exercise price for the warrants, the Company used the intrinsic value of the warrants as a proxy for the fair value for financial reporting purposes. The Company revalued the warrants as of December 31, 2012 using their intrinsic value given their low exercise price. As of December 31, 2013, the Company revalued the warrants using a hybrid of the option pricing method and the probability-weighted expected return method. The hybrid methodology was applied to reflect two exit scenarios, IPO and merger using a market approach and the income approach was used in the stay private scenario. The scenarios were weighted based on the Company's estimate of the probability of each scenario: 20% for IPO; 10% for merger and 70% for stay private. As of December 31, 2012 and 2013, the fair value of this convertible preferred stock warrant liability amounted to $2.9 million and $6.5 million, respectively.

9. Stockholders' Deficit

2008 Stock Incentive Plan

In 2008, the Board of Directors approved the 2008 Stock Incentive Plan (the Plan), which provides for the granting of incentive and non-statutory stock options and stock purchase rights to employees, directors, and consultants at the discretion of management and the Board of Directors. In May 2008, the Board of Directors authorized the number of shares available for grant under the Plan to be 787,777. In August 2011, the Board of Directors authorized an additional 1,213,483 shares available for grant under the Plan. In November 2012, the Board of Directors authorized an additional 114,428 shares available for grant under the Plan.

Incentive stock options are granted with exercise prices not less than the estimated fair value of common stock, and non-statutory stock options may be granted with an exercise price of not less than 100% of the estimated fair value of the common stock on the date of grant. Options granted under the Plan expire no later than 10 years from the date of grant. Incentive stock options granted under the Plan vest over periods determined by the Board of Directors, generally over four years. Non-statutory stock options vest based on the terms of the individual agreement, generally from six months to four years.

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A summary of activities under the Plan is as follows:

	Shares Available for Grant	Options Issued and Outstanding		
		Number of Shares	Weighted-Average Exercise Price per Share	Aggregate Intrinsic Value (in thousands)
Balances at December 31, 2011	19,798	1,598,513	$ 0.57	
Options authorized	114,428	—		
Options granted	(81,233)	81,233	3.46	
Options exercised	—	(342,131)	0.52	
Options canceled	43,848	(43,848)	0.52	
Balance at December 31, 2012	96,841	1,293,767	$ 0.77	
Options granted	(99,552)	99,552	3.42	
Options exercised	—	(223,865)	0.56	
Options canceled	6,625	(6,625)	2.23	
Balance at December 31, 2013	3,914	1,162,829	$ 1.03	$ 9,899
Vested and expected to vest at December 31, 2013		1,162,829	$ 1.03	$ 9,899
Vested at December 31, 2013		948,887	$ 0.46	$ 8,619

The intrinsic value of options exercised was $3.1 million and $2.0 million for the years ended December 31, 2012 and 2013, respectively. The intrinsic value was calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock of $9.54 per share as of December 31, 2013.

The total estimated grant date fair value of options vested during the years ended December 31, 2012 and 2013 was $271,000 and $289,000, respectively.

The following table summarizes information concerning outstanding and exercisable options under the Plan as of December 31, 2013:

	Options Outstanding and Exercisable		Options Vested	
Exercise Price	Number of Shares	Remaining Contractual Life (in Years)	Number of Shares	Remaining Contractual Life (in Years)
$0.27	13,031	5.03	475,626	5.22
$0.54	859,332	7.60	382,793	7.58
$0.99	1,666	4.03	3,333	4.02
$1.08	112,026	6.78	86,801	6.69
$3.42	176,774	9.08	334	8.83
	1,162,829		948,887	

Ardelyx, Inc.

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Early Exercise of Stock Options

The Plan allows for the granting of options that may be exercised before the options have vested. Shares issued as a result of early exercise that have not vested are subject to repurchase by the Company upon termination of the purchaser's employment or services, at the price paid by the purchaser, and are not deemed to be issued for accounting purposes until those related shares vest. The amounts received in exchange for these shares have been recorded as a liability on the accompanying balance sheets and will be reclassified into common stock and additional paid-in-capital as the shares vest. The Company's right to repurchase these shares generally lapses 1/48 of the original grant date per month over four years.

At December 31, 2012 and 2013, there were 512,693 and 286,217 shares of common stock outstanding, respectively, subject to the Company's right of repurchase at prices ranging from $0.27 to $1.08 per share. At December 31, 2012 and 2013, the Company recorded $289,000 and $163,000, respectively, as liabilities associated with shares issued with repurchase rights.

Stock-based Compensation

Total stock-based compensation recognized was as follows:

	Year Ended December 31,	
	2012	2013
	(in thousands)	
Research and development	$221	$200
General and administrative	252	152
Total stock-based compensation	$473	$352

At December 31, 2013, there was $549,000 of unrecognized stock-based compensation expense, net of estimated forfeitures, related to unvested share options with a weighted-average remaining recognition period of 1.8 years.

In determining the fair value of the stock-based awards, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term—The Company's expected term represents the period that the Company's stock-based awards are expected to be outstanding. The Company used the simplified method to determine the expected term, which is calculated as the average of the time-to-vesting and the contractual life of the options.

Expected Volatility—Since the Company is privately held and does not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. When selecting comparable publicly traded biopharmaceutical companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry, and with historical share price information sufficient to meet the expected life of the stock-based awards. The historical volatility data was computed using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available.

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Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

The fair value of stock option awards to employees was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31	
	2012	2013
Expected term (years)	5.73	6.07
Volatility	97%	98%
Risk-free interest rate	0.79%	1.35%
Dividend yield	— %	— %

The weighted-average, estimated grant-date fair value of employee stock options granted during the years ended December 31, 2012 and 2013 was $2.56 and $2.68 per share, respectively.

10. 401(k) Plan

The Company sponsors a 401(k) Plan that stipulates that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations, on a pretax basis. Pursuant to the 401(k) Plan, the Company does not match any employee contributions.

11. Income Taxes

For the year ended December 31, 2013, the Company recorded an income tax provision of $141,000 due primarily to the recognition of the upfront payment received for the license agreement with AstraZeneca for alternative minimum tax purposes that could not be fully offset by tax attributes. For the year ended December 31, 2012, the Company did not record an income tax provision on pre-tax income because the Company incurred taxable losses for both state and federal income tax purposes.

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

	Year Ended December 31,	
	2012	2013
Expected income tax provision at the federal statutory rate	(35.0)%	(35.0)%
State taxes, net of federal benefit	0.0	1.4
Change in valuation allowance	38.6	22.6
Nondeductible expenses	5.2	20.8
Tax credits	(4.4)	(7.3)
Other	(4.4)	(0.3)
Income tax provision	— %	2.2%

Ardelyx, Inc.

Notes to Financial Statements

Significant components of the Company's deferred tax assets are as follows:

	December 31,	
	2012	2013
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 21,891	$ 13,069
Deferred revenue	—	9,723
Research credits	1,306	1,734
Other	323	475
Total deferred tax assets	23,520	25,001
Valuation allowance	(23,520)	(25,001)
Net deferred tax assets	$ —	$ —

Realization of deferred tax assets is dependent on future earnings, if any, the timing and amount of which are uncertain. Accordingly, the deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $3.8 million and $1.5 million for the years ended December 31, 2012 and 2013, respectively. At December 31, 2013, deferred tax assets do not include any benefits associated with stock option activities. If future events occur that result in stock option deductions in excess of previously recognized expense for book purposes, such difference will be recorded directly to additional paid-in capital as part of stockholders' deficit.

At December 31, 2013, the Company had net operating loss carryforwards for federal income tax purposes of approximately $32.1 million that expire beginning in 2024 if not utilized, and federal research and development tax credit carryforwards of approximately $1.7 million that expire beginning in 2024 if not utilized. In addition, the Company had net operating loss carryforwards for state income tax purposes of approximately $31.5 million that expire beginning in 2014 if not utilized, and state research and development tax credit carryforwards of approximately $1.8 million, which do not expire. Utilization of the net operating loss and tax credit carryforwards may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the net operating loss and tax credits before their utilization.

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

	December 31,	
	2012	2013
	(in thousands)	
Balance at beginning of year	$ 807	$1,064
Additions based on tax positions related to current year	257	347
Balance at end of year	$1,064	$1,411

The unrecognized tax benefits, if recognized and in absence of full valuation allowance, would impact the income tax provision by $1.1 million and $1.4 million as of December 31, 2012 and 2013, respectively.

The Company has elected to include interest and penalties as a component of tax expense. During the years ended December 31, 2012 and 2013, the Company did not recognize accrued interest and penalties related to unrecognized tax benefits. The Company does not anticipate that the amount of existing unrecognized tax benefits will significantly change during the next 12 months.

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The Company files income tax returns in the U.S. federal jurisdiction and California tax jurisdictions. The federal and state income tax returns all remain open to U.S. federal and California state tax examinations.

12. Net Loss per Common Share and Unaudited Pro Forma Net Loss per Common 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 share-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, 2012 and 2013, all potential common shares were determined to be anti-dilutive.

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

	December 31,	
	2012	2013
Numerator:		
Net loss	$ (9,785)	$ (6,564)
Denominator:		
Weighted average number of shares outstanding—basic and diluted	864,020	1,127,948
Net loss per share—basic and diluted	$ (11.32)	$ (5.82)

Potentially dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	December 31,	
	2012	2013
Convertible preferred stock	11,517,222	11,517,222
Options to purchase common stock	1,293,767	1,162,829
Warrants to purchase convertible preferred stock	574,953	574,953
Total	13,385,942	13,255,004

Ardelyx, Inc.

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The Company has presented unaudited pro forma basic and diluted net loss per common share, which has been computed to give effect to the conversion of all shares of convertible preferred stock into shares of common stock as if such conversion had occurred as of the beginning of the period presented, and the automatic net exercise of preferred stock warrants into shares of common stock upon an initial public offering. The following table sets forth the computation of the Company's pro forma basic and diluted net loss per common share (in thousands, except per share amounts):

	Year Ended December 31, 2013 (Unaudited)
Net loss used in computing net loss per common share, basic and diluted	$ (6,564)
Change in fair value of convertible preferred stock warrants liability	3,506
Net loss used in computing pro forma net loss per common share, basic and diluted	$ (3,058)
Weighted-average shares used in computing net loss per common share, basic and diluted	1,127,948
Pro forma adjustment to reflect assumed conversion of convertible preferred stock	11,517,222
Pro forma adjustment to reflect assumed net exercise of preferred stock warrants	571,244
Weighted-average shares of common stock used in computing pro forma net loss per common share, basic and diluted	13,216,414
Pro forma net loss per common share, basic and diluted	$ (0.23)

13. Related Party Transactions

The Company entered into a consulting agreement with the spouse of an executive of the Company to provide research and development services related to clinical operations. The Company incurred expenses of $138,000 and $245,000 for services rendered during the years ended December 31, 2012 and 2013, respectively. As of December 31, 2012 and 2013, the Company owed $16,000 and $18,000, respectively, to the individual, which is recorded in accounts payable. The consulting agreement is in effect until December 31, 2014, unless terminated earlier by the Company with at least 14 days' advance notice.

14. Subsequent Events

In February 2014, the Company entered into a license agreement with Sanofi S.A. ("Sanofi") for the development rights to its NaP2b inhibitor program. Under the terms of the agreement, Sanofi provided the Company with an upfront and nonrefundable fee of $1.25 million, and may pay up to $196.75 million in future milestones if the program delivers an appropriate therapy that can be used to treat hyperphosphatemia.

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Ardelyx, Inc.
Condensed Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2013 (Note 1)	March 31, 2014 (unaudited)	Pro Forma Stockholders' Deficit March 31, 2014 (unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 34,435	$ 33,221	
Accounts receivable	6,436	4,977	
Prepaid expenses and other current assets	965	917	
Total current assets	41,836	39,115	
Property and equipment, net	530	551	
Other assets	358	702	
Restricted cash	180	180	
Total assets	$ 42,904	$ 40,548	
Liabilities, convertible preferred stock, and stockholders' deficit			
Current liabilities:			
Accounts payable	$ 2,284	$ 2,530	
Accrued compensation and benefits	927	601	
Other accrued liabilities	95	652	
Deferred rent	5	10	
Deferred revenue, current portion	13,828	14,975	
Total current liabilities	17,139	18,768	
Deferred revenue, non-current	26,470	22,889	
Convertible preferred stock warrant liability	6,456	9,059	$ —
Liabilities related to early exercise of options	163	135	
Total liabilities	50,228	50,851	
Commitments and contingencies			
Convertible preferred stock, $0.0001 par value per share—108,829,748 shares authorized as of December 31, 2013 and March 31, 2014 (unaudited); 11,517,222 shares issued and outstanding as of December 31, 2013 and March 31, 2014 (unaudited), actual; aggregate liquidation preferences of $59,074 as of December 31, 2013 and March 31, 2014 (unaudited), actual; no shares issued and outstanding as of March 31, 2014, pro forma (unaudited)	56,155	56,155	—
Stockholders' deficit:			
Common stock, $0.0001 par value per share—130,360,121 shares authorized as of December 31, 2013 and March 31, 2014 (unaudited); 1,225,481 and 1,272,278 shares issued and outstanding as of December 31, 2013 and March 31, 2014 (unaudited), actual; 13,360,744 shares issued and outstanding as of March 31, 2014, pro forma (unaudited)	—	—	1
Additional paid-in capital	5,174	5,266	70,479
Accumulated deficit	(68,653)	(71,724)	(71,724)
Total stockholders' deficit	(63,479)	(66,458)	$ (1,244)
Total liabilities, convertible preferred stock, and stockholders' deficit	$ 42,904	$ 40,548	

See accompanying notes.

Ardelyx, Inc.
Condensed Statements of Operations and Comprehensive Loss
(unaudited)
(In thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2013	2014
Revenue:		
Licensing revenue	$ 1,989	$ 3,236
Collaborative development revenue	4,567	5,314
Total revenue	6,556	8,550
Operating expenses:		
Research and development	5,939	7,637
General and administrative	1,027	1,377
Total operating expenses	6,966	9,014
Loss from operations	(410)	(464)
Other expense, net	(25)	(4)
Change in fair value of preferred stock warrant liability	—	(2,603)
Loss before provision for income taxes	(435)	(3,071)
Provision for income taxes	(35)	—
Net loss and comprehensive loss	$ (470)	$ (3,071)
Net loss per common share, basic and diluted	$ (0.45)	$ (2.44)
Shares used to compute net loss per common share, basic and diluted	1,042,675	1,256,245
Pro forma net loss per common share, basic and diluted		$ (0.04)
Shares used to compute pro forma net loss per common share, basic and diluted		13,344,711

See accompanying notes.

Ardelyx, Inc.
Condensed Statements of Cash Flows
(unaudited)
(In thousands)

	Three Months Ended March 31,	
	2013	2014
Operating activities		
Net loss	$ (470)	$ (3,071)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	176	73
Stock-based compensation	107	64
Change in fair value of preferred stock warrant liability	—	2,603
Changes in operating assets and liabilities:		
Accounts receivable	(1,294)	1,459
Prepaid and other current assets	367	48
Other assets	(32)	(344)
Accounts payable	685	246
Accrued compensation and benefits	(557)	(326)
Other accrued liabilities	(620)	557
Deferred revenue	(2,356)	(2,434)
Deferred rent	(131)	5
Net cash used in operating activities	(4,125)	(1,120)
Investing activities		
Purchases of property and equipment	(70)	(94)
Net cash used in investing activities	(70)	(94)
Net decrease in cash and cash equivalents	(4,195)	(1,214)
Cash and cash equivalents at beginning of period	32,903	34,435
Cash and cash equivalents at end of period	$28,708	$33,221

See accompanying notes.

ARDELYX, INC.

Notes to Unaudited Interim Condensed Financial Statements

1. Summary of Significant Accounting Policies

Unaudited Interim Financial Statements

The unaudited interim balance sheet as of March 31, 2014, and the statements of operations and comprehensive loss, and cash flows for the three months ended March 31, 2013 and 2014 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly the Company's financial position as of March 31, 2014 and its results of operations and cash flows for the three months ended March 31, 2013 and 2014. The financial data and the other financial information disclosed in these notes to the financial statements related to the three month periods are also unaudited. The results of operations for the three months ended March 31, 2014 are not necessarily indicative of the results to be expected for the year ending December 31, 2014 or for any other future annual or interim period. The condensed balance sheet as of December 31, 2013 included herein was derived from the audited financial statements as of that date. These financial statements should be read in conjunction with the Company's audited financial statements included elsewhere in this prospectus.

Unaudited Pro Forma Stockholders' Deficit

The pro forma stockholders' deficit as of March 31, 2014 presents the Company's stockholders' deficit as though all of the Company's outstanding convertible preferred stock had automatically converted into shares of common stock upon the completion of an initial public offering (an "IPO") of the Company's common stock. In addition, the pro forma stockholders' deficit assumes the reclassification of the convertible preferred stock warrant liability in stockholders' equity upon completion of an IPO of the Company's common stock, as the warrants are net exercised for common stock upon an IPO.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and judgments that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to revenue recognition, clinical trial accruals, fair value of convertible preferred stock and related warrants, fair value of common stock, 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 may differ from those estimates.

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. The Company invests its cash in bank deposits and money market accounts.

Restricted Cash

The Company is required to guarantee the credit limit on its corporate credit card with a certificate of deposit of $100,000. The collateral will be released upon the cancellation of the corporate credit card.

The Company is required under its facility lease agreement to maintain a line of credit with a bank in the amount of $80,000 for the benefit of the lessor. The line of credit is secured by a cash deposit with the bank. The cash deposit will be released upon expiration of the line of credit.

ARDELYX, INC.

Notes to Unaudited Interim Condensed Financial Statements

Deferred Offering Costs

Deferred offering costs, which primarily consist of direct incremental legal and accounting fees relating to the IPO, are capitalized. The deferred offering costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. As of March 31, 2014, the Company capitalized $517,000 of deferred offering costs in noncurrent other assets on the balance sheet.

Convertible Preferred Stock Warrant Liability

The Company accounts for freestanding warrants to purchase shares of convertible preferred stock that are contingently redeemable as liabilities in the balance sheets at their estimated fair value. Convertible preferred stock warrants are subject to remeasurement at each balance sheet date, and any change in fair value is recognized as a component of other expense, net in the statements of operations and comprehensive loss.

The Company will continue to adjust the liability for changes in fair value until the earlier of: (1) the exercise or expiration of the warrants or (2) the completion of a liquidation event, including the completion of an IPO, at which time all convertible preferred stock warrants will be net exercised and the liability will be reclassified to additional paid-in capital in stockholders' deficit.

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 GAAP are recorded as an element of stockholders' deficit, but are excluded from net loss. The Company did not record any transactions within other comprehensive income (loss) in the periods presented and, therefore, the net loss and comprehensive loss were the same for all periods presented.

Revenue Recognition

Revenue from research activities made under collaboration partnership agreements are recognized as the services are provided and when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue generated from research and licensing agreements typically includes up-front signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments, and royalties on future licensees' product sales.

For revenue agreements with multiple-element arrangements, such as license and development agreements, the Company allocates revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each deliverable using vendor-specific objective evidence or third-party evidence. If neither exists, the Company uses its best estimate of selling price for that deliverable. Revenue allocated is then recognized when the four basic revenue recognition criteria are met for each element.

The Company recognizes revenue from upfront payments ratably over the term of its estimated period of performance under the agreement which is recorded as licensing revenue. Reimbursements for development costs incurred under the Company's license agreement with AstraZeneca are classified as collaborative development revenue. The Company recognizes cost reimbursement revenue under collaboration partnership agreements as the related research and development costs for services are rendered. Deferred revenue represents the portion of research or license payments received which has not been earned.

ARDELYX, INC.

Notes to Unaudited Interim Condensed Financial Statements

Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. To the extent that non-substantive milestones are achieved and the Company has remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance. The Company will recognize revenue associated with the non-substantive milestones upon achievement of the milestone if there are no undelivered elements and it has no remaining performance obligations. The Company will account for sales-based milestones as royalties that will be recognized as revenue upon achievement of the milestone.

Net Loss per Common 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 common stock equivalents. Diluted net loss per common share is the same as basic net loss per common share, since the effects of potentially dilutive securities are antidilutive.

Unaudited Pro Forma Net Loss per Common Share

Pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of all outstanding shares of the convertible preferred stock and the net exercise of the preferred stock warrants upon the closing of the IPO. Also, the numerator in the pro forma basic and diluted net loss per share attributable to common stockholders calculation has been adjusted to remove gains or losses resulting from the remeasurement of the convertible preferred stock warrant liability related to warrants to purchase shares of convertible preferred stock, as it will be reclassified to additional paid-in capital upon a IPO of the Company's common stock.

Recent Accounting Pronouncement

In July 2013, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update (ASU) 2013-11, *Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists*. The ASU concludes an unrecognized tax benefit should be presented as a reduction of a deferred tax asset when settlement in this manner is available under the law. The Company adopted this amendment as of January 1, 2014, which did not have a significant impact on the balance sheet.

Reverse Stock Split

In June 2014, the Company's board of directors approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of the Company's common stock and convertible preferred stock at a 1-for-9 ratio (the "Reverse Stock Split"). The par value and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the Reverse Stock Split. All issued and outstanding common stock, convertible preferred stock, warrants for preferred stock, options for common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented. The Reverse Stock Split was effected on June 18, 2014.

2. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amounts of certain of the Company's financial instruments, including cash equivalents, accounts receivable and accounts payable, are valued at cost,

which approximates fair value due to their short maturities. The accounting guidance for fair value provides a framework for measuring fair value, and requires certain new disclosures about how fair value is determined. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance also establishes a three-level valuation hierarchy that prioritizes the inputs to valuation techniques used to measure fair value based upon whether such inputs are observable or unobservable. Observable inputs reflect market data obtained from independent sources, while unobservable inputs reflect market assumptions made by the reporting entity.

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

Level 1—Observable inputs such as quoted prices (unadjusted) for *identical* instruments in active markets.

Level 2—Observable inputs such as quoted prices for *similar* instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, or model-derived valuations whose significant inputs are observable.

Level 3—Unobservable inputs that reflect the reporting entity's own assumptions.

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

	December 31, 2013			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Assets:				
Money market funds	$32,472	$32,472	$ —	$ —
Certificates of deposit	180	—	180	—
Total	$32,652	$32,472	$ 180	$ —
Liabilities:				
Convertible preferred stock warrant liability	$ 6,456	$ —	$ —	$6,456
Total	$ 6,456	$ —	$ —	$6,456

	March 31, 2014			
	Total	Level 1	Level 2	Level 3
	(in thousands)			
Assets:				
Money market funds	$30,976	$30,976	$ —	$ —
Certificates of deposit	180	—	180	—
Total	$31,156	$30,976	$ 180	$ —
Liabilities:				
Convertible preferred stock warrant liability	$ 9,059	$ —	$ —	$9,059
Total	$ 9,059	$ —	$ —	$9,059

Where quoted prices are available in an active market, securities are classified as Level 1. The Company classifies money market funds as Level 1. When quoted market prices are not available for the specific security, then the Company estimates fair value by using benchmark yields, reported trades, broker/dealer quotes, and issuer spreads. The Company classifies certificates of deposit 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.

Level 3 liabilities that are measured at fair value on a recurring basis consist of the preferred stock warrant liability, which was measured using the probability weighted expected return method that calculated the probability of the Company going public or being acquired, and the option-pricing method for remaining private in the near to mid-term. The scenarios were weighted based on the Company's estimate of the probability of each scenario: 20% for IPO; 10% for merger and 70% for stay private as of December 31, 2013, and 50% for IPO; 20% for merger and 30% for stay private as of March 31, 2014. At the end of each reporting period, the change in estimated fair value during the period is recorded in change in fair value of convertible preferred stock warrant liability in the statements of operations and comprehensive loss. Generally, increases or decreases in the fair value of the underlying convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

The following table sets forth a summary of the changes in the estimated fair value of our preferred stock warrant liability, which was measured at fair value on a recurring basis (in thousands):

Balance at December 31, 2013	$6,456
Net increase in fair value of warrant liabilities upon revaluation	2,603
Balance at March 31, 2014	$9,059

3. Collaboration and Licensing agreements

AstraZeneca AB ("AstraZeneca")

Under the terms of the AstraZeneca collaboration partnership agreement, the Company received an up-front license fee of $35.0 million in October 2012 and a $15.0 million payment in December 2013, which are both being recognized as revenue on a straight-line basis over the estimated period of performance, which is currently estimated to be December 2016. AstraZeneca reimburses the Company for its internal and external development-related costs. These reimbursements are recognized as collaborative development revenue when the development-related costs are incurred.

As of March 31, 2014, the Company was eligible to receive future contingent payments up to a total of $820.0 million, which is comprised of future development milestones up to an additional $222.5 million and launch, commercialization, and sales milestones up to an additional $597.5 million. The contingent payments are triggered upon the activities expected to be undertaken by AstraZeneca. Revenue from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestone. The Company will recognize revenue associated with the non-substantive milestones upon achievement of the milestones if there are no undelivered elements and it has no remaining performance obligation. To the extent that non-substantive milestones are achieved and the Company has remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance.

For the three months ended March 31, 2013 and 2014, the Company recognized revenue of $2.0 million and $3.2 million, respectively, related to amortization of the up-front and other license fees, and $4.6 million and $5.3 million, respectively, for collaborative development services. As of March 31, 2014, the Company has total deferred revenue of $36.6 million related to the AstraZeneca license agreement.

ARDELYX, INC.

Notes to Unaudited Interim Condensed Financial Statements

Sanofi SA ("Sanofi")

In February 2014, the Company entered into a License Option and License Agreement with Sanofi ("Option and License Agreement") for its phosphate transport NaP2b inhibitor program. NaP2b is an intestinal phosphate transporter whose activity accounts for a significant portion of dietary phosphate absorption in humans. The inhibition of NaP2b is believed to have utility for the treatment of hyperphosphatemia (elevated serum phosphate) in patients with end stage renal disease (ESRD) and other forms of chronic kidney disease (CKD). Under the Option and License Agreement, the Company granted Sanofi an exclusive worldwide license to conduct research utilizing the Company's small molecule NaP2b inhibitors. In addition, Sanofi has the option to obtain an exclusive license to develop, manufacture and commercialize the Company's NaP2b inhibitors. Sanofi is advancing this program towards first-in-human clinical trials. Under the Option and License Agreement, Sanofi is responsible for all of the costs and expenses for research and preclinical activities and, should it exercise its option, for the development and commercialization efforts under the program. Under the Option and License Agreement, the Company received a payment of $1.25 million and is responsible for up to $175,000 of patent costs after which any additional patent costs will be fully reimbursed to the Company by Sanofi. The Company will recognize the $1.25 million as revenue after the Company has provided to Sanofi the background know-how, listed patents, and materials (together, the "Technology Transfer Deliverables") pursuant to the Option and License Agreement.

The Company has the potential to earn future development, regulatory and commercial milestone payments of up to $196.75 million if Sanofi continues to advance the program into development and through commercialization. If a NaP2b inhibitor is commercialized by Sanofi as a result of this program, the Company will receive tiered royalties ranging from mid-single digits into the low double digits. As part of the arrangement with Sanofi, the Company retains an option to participate in co-promotional activities in the United States. Future potential milestone payments do not meet the criteria to be considered substantive milestones, and therefore will be treated as other contingent consideration and recognized as revenue as they are achieved as the Company has no performance obligations under of the Option and License Agreement.

No milestones have been received since the inception of the agreement. As of March 31, 2014, the Company had not completed the transfer for the Technology Transfer Deliverables and has deferred revenue of $1.25 million related to the Sanofi Option and License Agreement.

4. Stock Incentive Plan

As of March 31, 2014, a total of 2,115,688 shares of common stock have been authorized for issuance under the 2008 Stock Incentive Plan (the Stock Plan).

The following table summarizes activity under the Stock Plan, including grants to nonemployees and restricted stock issued:

	Shares Available for Grant	Options Outstanding	Weighted Average Exercise Price per Share	Aggregate Intrinsic Value (in thousands)
Balances at December 31, 2013	3,914	1,162,829	$ 1.03	
Options granted	(3,888)	3,888	13.23	
Options exercised	—	(46,797)	0.60	
Balances at March 31, 2014	26	1,119,920	$ 1.09	$ 15,715
Vested – March 31, 2014		995,689	$ 0.46	$ 14,594
Expected to vest – March 31, 2014		1,119,920	$ 1.09	$ 15,715

ARDELYX, INC.

Notes to Unaudited Interim Condensed Financial Statements

The weighted-average grant-date estimated fair value of options granted during the three months ended March 31, 2013 and 2014 was $2.65 and $10.53 per share, respectively. The intrinsic value was calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock of $15.12 per share as of March 31, 2014.

Liability for Early Exercise of Stock Options

At December 31, 2013 and March 31, 2014, there were 286,217 and 239,423 shares of common stock outstanding, respectively, subject to the Company's right of repurchase at prices ranging from $0.27 to $1.08 per share. At December 31, 2013 and March 31, 2014, the Company recorded $163,000 and $135,000, respectively, as liabilities associated with shares issued with repurchase rights.

Stock-based Compensation

Total stock-based compensation recognized was as follows:

	Three Months Ended March 31,	
	2013	2014
	(in thousands)	
Research and development	$ 48	$ 37
General and administrative	59	27
Total stock-based compensation	$ 107	$ 64

At March 31, 2014, there was $525,000 of unrecognized stock-based compensation expense, net of estimated forfeitures, related to unvested share options with a weighted-average remaining recognition period of 1.7 years.

The fair value of stock option awards to employees was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted-average assumptions:

	Three Months Ended March 31,	
	2013	2014
Expected term (years)	6.08	6.08
Volatility	97%	100%
Risk-free interest rate	1.05%	1.99%
Dividend yield	— %	— %

ARDELYX, INC.

Notes to Unaudited Interim Condensed Financial Statements

5. Net Loss per Common Share and Unaudited Pro Forma Net Loss per Common Share

The following outstanding shares of common stock equivalents were excluded from the computation of diluted net loss per common share for the periods presented because including them would have been antidilutive:

	March 31,	
	2013	2014
Convertible preferred stock	11,517,222	11,517,222
Options to purchase common stock	1,273,184	1,119,920
Warrants to purchase convertible preferred stock	574,953	574,953
Total	13,365,359	13,212,095

The following table sets forth the computation of the Company's unaudited pro forma basic and diluted net loss per common share during the three months ended March 31, 2014 (in thousands, except for share and per share amounts):

	Three Months Ended March 31, 2014
Net loss	$ (3,071)
Change in fair value of convertible preferred stock warrant liability	2,603
Net loss used in computing pro forma net loss per common share, basic and diluted	$ (468)
Shares used in computing net loss per common share, basic and diluted	1,256,245
Pro forma adjustment to reflect assumed conversion of convertible preferred stock	11,517,222
Pro forma adjustment to reflect assumed net exercise of preferred stock warrants	571,244
Shares used in computing pro forma net loss per common share, basic and diluted	13,344,711
Pro forma net loss per common share, basic and diluted	$ (0.04)

6. Related Party Transactions

As part of the consulting arrangement with the spouse of an executive of the Company to provide research and development services related to clinical operations, the Company incurred expenses of $62,000 and $61,000 for services rendered during the three months ended March 31, 2013 and 2014, respectively. As of December 31, 2013 and March 31, 2014, the Company owed $18,000 and $21,000, respectively, to the individual, which is recorded in accounts payable.

7. Subsequent Events

In May 2014, the Company received a $25.0 million development milestone payment from AstraZeneca as a result of the dosing of the first patient in the Phase 2b clinical trial in hyperphosphatemia. As the $25.0 million does not meet the criteria to be considered the achievement of a substantive milestone for accounting purposes, the amount was recorded as deferred revenue when it was received and will be recognized as revenue on a straight-line basis over the remaining estimated period of performance under the AstraZeneca collaboration partnership agreement, which is currently estimated to be December 2016.

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4,286,000 Shares

Common Stock

Prospectus

Citigroup | **Leerink Partners**

JMP Securities | **Wedbush PacGrow Life Sciences**

June 18, 2014