ARDELYX, INC.
Form 10-Q
May 12, 2015
Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED MARCH 31, 2015

OR

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

FOR THE TRANSITION PERIOD FROM _____ TO _____

COMMISSION FILE NUMBER: 001-36485

ARDELYX, INC.

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE	26-1303944
(STATE OR OTHER JURISDICTION OF INCORPORATION OR ORGANIZATION)	(I.R.S. EMPLOYER IDENTIFICATION NUMBER)

34175 Ardenwood Boulevard, Suite 200

Fremont, California 94555

(ADDRESS OF PRINCIPAL EXECUTIVE OFFICES, INCLUDING ZIPCODE)

(510) 745-1700

(REGISTRANT S TELEPHONE NUMBER, INCLUDING AREA CODE)

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (do not check if a smaller reporting company)	Smaller reporting company ¨

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

The number of issued and outstanding shares of the registrant s Common Stock, $0.0001 par value per share, as of May 8, 2015 was 18,651,835.

Table of Contents

ARDELYX, INC.

Table of Contents

PART I. FINANCIAL INFORMATION

ITEM 1. CONDENSED FINANCIAL STATEMENTS

ARDELYX, INC.

CONDENSED BALANCE SHEETS

(in thousands, except share amounts)

	March 31, 2015 (Unaudited)	December 31, 2014 (1)
Assets		
Current assets:		
Cash and cash equivalents	$ 98,318	$ 107,286
Accounts receivable	2,043	2,584
Prepaid expenses and other current assets	1,545	1,209
Total current assets	101,906	111,079
Property and equipment, net	3,289	2,131
Other assets	104	104
Restricted cash	100	100
Total assets	$ 105,399	$ 113,414
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 2,544	$ 3,129
Accrued compensation and benefits	945	1,648
Accrued and other liabilities	470	780
Deferred revenue, current portion	15,953	15,979
Total current liabilities	19,912	21,536
Other long-term liabilities	297	122
Deferred revenue, non-current	27,190	31,074
Total liabilities	47,399	52,732
Commitments and contingencies		
Stockholders equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized as of March 31, 2015 and December 31, 2014, respectively; no shares issued and outstanding as of March 31, 2015 and December 31, 2014, respectively		
Common stock, $0.0001 par value 300,000,000 shares authorized as of March 31, 2015 and December 31, 2014, respectively; 18,635,071 and 18,589,245 shares	3	2

issued and outstanding as of March 31, 2015 and December 31, 2014, respectively.		
Additional paid-in capital	133,366	132,547
Accumulated deficit	(75,369)	(71,867)
Total stockholders equity	58,000	60,682
Total liabilities and stockholders equity	$ 105,399	$ 113,414

(1) Derived from the audited financial statements included in the Company s Annual Report on Form 10-K for the year ended December 31, 2014.

See accompanying notes to Condensed Financial Statements.

Table of Contents

ARDELYX, INC.

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share amounts)

	Three Months Ended March 31,	
	2015 (Unaudited)	**2014 (Unaudited)**
Revenue:		
Licensing revenue	$ 3,884	$ 3,236
Collaborative development revenue	1,999	5,314
Total revenue	5,883	8,550
Operating expenses:		
Research and development	6,198	7,637
General and administrative	3,175	1,377
Total operating expenses	9,373	9,014
Loss from operations	(3,490)	(464)
Other expense, net	(12)	(4)
Change in fair value of preferred stock warrant liability		(2,603)
Loss before provision for income taxes	(3,502)	(3,071)
Provision for income taxes		
Net loss and comprehensive loss	$ (3,502)	$ (3,071)
Basic net loss per share	$ (0.19)	$ (2.44)
Diluted net loss per share	$ (0.19)	$ (2.44)
Shares used in computing basic net loss per share	18,606,760	1,256,245
Shares used in computing diluted net loss per share	18,606,760	1,256,245

See accompanying notes to Condensed Financial Statements.

Table of Contents

ARDELYX, INC.

CONDENSED STATEMENTS OF CASH FLOWS

(in thousands)

	Three Months Ended March 31,	
	2015 (Unaudited)	**2014 (Unaudited)**
Operating activities		
Net loss	$ (3,502)	$ (3,071)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	119	73
Stock-based compensation	524	64
Change in fair value of preferred stock warrant liability		2,603
Loss from disposal of fixed assets	11	
Changes in operating assets and liabilities:		
Accounts receivable	541	1,459
Prepaid expenses and other assets	(336)	(296)
Accounts payable	(819)	246
Accrued compensation and benefits	(703)	(326)
Accrued and other liabilities	(134)	562
Deferred revenue	(3,910)	(2,434)
Net cash used in operating activities	(8,209)	(1,120)
Investing activities		
Purchases of property and equipment	(1,055)	(94)
Net cash used in investing activities	(1,055)	(94)
Financing activities		
Proceeds from exercise of stock options	296	
Net cash provided by financing activities	296	
Net decrease in cash and cash equivalents	(8,968)	(1,214)
Cash and cash equivalents at beginning of period	107,286	34,435
Cash and cash equivalents at end of period	$ 98,318	$ 33,221
Supplemental cash flow disclosure:		
Cash paid during the period for income taxes	$ 236	$
Supplemental noncash financing activities:		

Acquisition of property and equipment included in accounts payable and accrued liabilities	$ 234	$

See accompanying notes to Condensed Financial Statements.

Table of Contents

ARDELYX, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

(Unaudited)

NOTE 1. ORGANIZATION AND BASIS OF PRESENTATION

Ardelyx, Inc. (the Company) is a clinical stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-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. Utilizing its platform, the Company discovered and designed our lead product candidate, tenapanor, which in clinical studies has demonstrated the ability to improve the symptoms of constipation-predominant irritable bowel syndrome, or IBS-C, and to reduce the absorption of dietary sodium as well as phosphorus, a key component in the management of hyperphosphatemia in dialysis patients.

Basis of Presentation

These unaudited condensed financial statements and the related footnote information of the Company have been prepared pursuant to the requirements of the Securities and Exchange Commission (the SEC) for interim reporting. As permitted under those rules and regulations, certain footnotes or other financial information that are normally required by U.S. generally accepted accounting principles have been condensed or omitted pursuant to such rules and regulations. In the opinion of the Company s management, the accompanying interim unaudited condensed financial statements include all adjustments (consisting only of normal recurring adjustments) necessary for a fair presentation of the information for the periods presented. The results for the quarter ended March 31, 2015 are not necessarily indicative of results to be expected for the entire year ending December 31, 2015 or future operating periods.

The accompanying condensed financial statements and related financial information should be read in conjunction with the audited financial statements and the related notes thereto for the year ended December 31, 2014, included in the Company s Annual Report on Form 10-K filed with the SEC (the 2014 Form 10-K). The balance sheet at December 31, 2014 has been derived from the audited financial statements at that date, as filed with the 2014 Form 10-K.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Although management believes these estimates are based upon reasonable assumptions within the bounds of its knowledge of the Company s business and operations, actual results could differ materially from those 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 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 deliverable based on the relative selling price of each deliverable. 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 deliverable.

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.

Table of Contents

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.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board (the FASB) issued Accounting Standards Update 2014-09, *Revenue from Contracts with Customers* (ASU 2014-09), which converges the FASB and the International Accounting Standards Board standards on revenue recognition. Areas of revenue recognition that will be affected include, but are not limited to, transfer of control, variable consideration, allocation of transfer pricing, licenses, time value of money, contract costs and disclosures. This guidance is effective for the fiscal years and interim reporting periods beginning after December 15, 2016, at which time the Company may adopt the new standard under the full retrospective method or the modified retrospective method. Early adoption is not permitted.

On April 1, 2015, the FASB voted to propose a delay in the effective date of ASU No. 2014-09. The proposed new effective date will be annual reporting periods beginning after December 15, 2017, and the interim periods within that year and will allow early adoption for all entities as of the original effective date for public business entities, which was annual reporting periods beginning after December 15, 2016. The Company has not yet selected a transition method nor has the Company determined the impact of the new standard on its condensed financial statements and related disclosures.

NOTE 3. FAIR VALUE MEASUREMENTS

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

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

Level 1	Valuations are based on quoted prices in active markets for identical assets or liabilities and readily accessible by us at the reporting date. Examples of assets and liabilities utilizing Level 1 inputs are certain money market funds, U.S. Treasuries and trading securities with quoted prices on active markets.
Level 2	Valuations based on inputs other than the quoted prices in active markets that are observable either directly or indirectly in active markets. Examples of assets and liabilities utilizing Level 2 inputs are U.S. government agency bonds, corporate bonds, commercial paper, certificates of deposit and over-the-counter derivatives.
Level 3	Valuations based on unobservable inputs in which there is little or no market data, which require us to develop our own assumptions.

Table of Contents

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

	March 31, 2015			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 97,737	$ 97,737	$	$
Certificates of deposit	100		100	
Total	$ 97,837	$ 97,737	$ 100	$

	December 31, 2014			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 105,410	$ 105,410	$	$
Certificates of deposit	100		100	
Total	$ 105,510	$ 105,410	$ 100	$

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.

NOTE 4. COLLABORATION AND LICENSING AGREEMENTS

AstraZeneca AB (AstraZeneca)

In October 2012, the Company entered into a collaboration partnership with AstraZeneca for the worldwide development and commercialization of tenapanor. Under the terms of the AstraZeneca collaboration partnership agreement (the AstraZeneca 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. The estimated period of performance during the three months ended March 31, 2015 was estimated to be December 2017, which represented the estimated completion date of the Phase 2b clinical trials in chronic kidney disease, or CKD, to be conducted with tenapanor. The expected period of performance is reviewed quarterly and adjusted, as needed, to reflect our current assumptions regarding the timing of clinical studies. 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.

In May 2014, the Company received from AstraZeneca a $25.0 million payment as a result of the dosing of the first patient in the Phase 2b clinical trial in hyperphosphatemia. As the $25.0 million did not meet the criteria to be considered the achievement of a substantive milestone for accounting purposes, the amount was recorded as deferred revenue when received and is being recognized as revenue on a straight-line basis over the remaining estimated period of performance under the AstraZeneca Agreement, which during the three months ended March 31, 2015 was estimated to be December 2017.

For the three months ended March 31, 2015 and 2014, the Company recognized revenue of $3.9 million and $3.2 million, respectively, related to amortization of the up-front and other license fees, and $2.0 million and $5.3 million, respectively, for collaborative development services. As of March 31, 2015 and December 31, 2014, the Company had total deferred revenue of $43.1 million and $47.1 million related to the AstraZeneca Agreement, respectively.

Sanofi SA (Sanofi)

In February 2014, the Company entered into a license option and license agreement with Sanofi (the Sanofi Agreement) for its phosphate transport NaP2b inhibitor program. Under the terms of the Sanofi 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 potential products under the agreement. Under the License 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.

Table of Contents

Under the Sanofi Agreement, the Company received a payment of $1.25 million in March 2014, which was fully recognized as licensing revenue in May 2014 after the Company completed its obligation to provide to Sanofi the background know-how, listed patents, and materials described in the Sanofi Agreement.

NOTE 5. STOCK-BASED COMPENSATION

The following table presents stock-based compensation expense recognized for stock options and the Company s employee stock purchase program (the ESPP) in the Company s statements of operations (in thousands):

	Three Months Ended March 31,	
	2015	2014
Research and development	$ 286	$ 37
General and administrative	238	27
Total	$ 524	$ 64

At March 31, 2015, the Company had $5.9 million and $0.2 million of total unrecognized compensation expense, net of estimated forfeitures, related to stock option grants and purchase rights, respectively, that will be recognized over an average vesting period of 2.9 years and 0.4 years, respectively.

NOTE 6. NET LOSS PER COMMON SHARE

Basic net loss per common share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period. 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 three months ended March 31, 2015 and 2014, all potential common shares were determined to be anti-dilutive. Basic and diluted earnings per common share are calculated as follows (in thousands, except share and per share data):

	Three Months Ended March 31,	
	2015	2014
Numerator:		
Net loss	$ (3,502)	$ (3,071)
Denominator:		
Weighted average number of shares outstanding - basic and diluted	18,606,760	1,256,245
Net loss per share - basic and diluted	$ (0.19)	$ (2.44)

For the three months ended March 31, 2015 and 2014, the total number of anti-dilutive outstanding common stock options excluded from the net income per common share computation was 1.2 million and 1.1 million, respectively.

NOTE 7. STOCKHOLDERS EQUITY

Option Exercises

For the three months ended March 31, 2015 employees exercised options to purchase 26,212 shares of the Company s common stock with net proceeds to the Company of approximately $0.1 million. For the three months ended March 31, 2014, employees exercised options to purchase 46,797 shares of the Company s common stock with insignificant net proceeds to the Company.

Employee Stock Purchase Plan

In February 2015, the Company sold 19,614 shares under the ESPP. The shares were purchased at a purchase price of $12.43 per share with proceeds to the Company of approximately $0.2 million.

Table of Contents

NOTE 8. SUBSEQUENT EVENTS

On May 5, 2015, the Company announced that a 154-patient Phase 2a clinical trial evaluating tenapanor in Stage 3 chronic kidney disease patients with type 2 diabetes mellitus and albuminuria did not meet the primary endpoint of decreasing the urinary albumin-creatinine ratio in tenapanor-treated patients compared to patients receiving placebo. With the completion of this Phase 2a clinical trial, the Company and AstraZeneca are assessing the data from all the trials. Under the terms of the AstraZeneca Agreement, AstraZeneca is obligated to communicate to the Company, on or before June 29, 2015, whether it will continue the development of tenapanor.

Table of Contents

ITEM 2.

MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the condensed financial statements and notes thereto included elsewhere in this report and with the audited consolidated financial statements and related notes thereto included as part of our Annual Report on Form 10-K for the year ended December 31, 2014. This discussion and analysis and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this report entitled Risk Factors. These forward-looking statements speak only as of the date hereof. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason. Unless the context requires otherwise, the terms Ardelyx, Company, we, us, and our refer to Ardelyx, Inc.

ABOUT ARDELYX

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-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 clinical studies has demonstrated the ability to improve the symptoms of constipation-predominant irritable bowel syndrome, or IBS-C, and to reduce the absorption of dietary sodium as well as phosphorus, a key component in the management of hyperphosphatemia in dialysis patients.

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.

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 were directly responsible for the conduct of certain specified clinical trials being conducted with tenapanor. AstraZeneca reimbursed us for our internal and external costs related to those development efforts, and AstraZeneca will reimburse us on other development efforts that may be assigned to us by the development collaboration committee.

Under the terms of the collaboration partnership agreement with AstraZeneca, or the AstraZeneca 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 as of March 31, 2015.

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, 2015, we received $36.7 million in reimbursement for our development efforts provided under the AstraZeneca 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 three deliverables within the arrangement: 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. These three items are accounted for as a single unit of accounting since 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 included the initial supply of the compound of the licensed product. 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 the Phase 2b clinical trials in CKD to be conducted with tenapanor, which during the three months ended March 31, 2015, we estimated to be December 2017. The expected period of performance is reviewed quarterly and adjusted, as needed, to reflect our current assumptions regarding the timing of clinical studies. In addition, we recognize revenue from the $40.0 in development milestone payments on a straight-line basis over the same estimated completion date.

In February 2014, we entered into an option and license agreement with Sanofi, or the Sanofi Agreement, under which we granted Sanofi an exclusive worldwide license to conduct research utilizing our program evaluating small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in CKD patients on dialysis. In addition, Sanofi has the option to obtain an exclusive license to

Table of Contents

develop, manufacture and commercialize our NaP2b inhibitors. Under our Sanofi 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 Sanofi Agreement, we received an upfront payment of $1.25 million in March 2014, which was fully recognized as licensing revenue in May 2014 after we completed our obligation to provide Sanofi the background know-how, listed patents, and materials described in the Sanofi Agreement. 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.

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, 2015 we had accumulated deficit of $75.4 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. In addition, should AstraZeneca elect to terminate the license agreement and return the tenapanor program to us, we will continue to incur substantial losses as we advance the clinical development of tenapanor.

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. We also expect revenue we generate from AstraZeneca to fluctuate based on changes to clinical timelines or strategy that determine the recognition period of upfront and milestone payments.

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 expenses 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, 2015, we incurred $37.4 million in research and development expenses related to tenapanor, all of which are reimbursable by AstraZeneca under the license agreement. The reimbursements are recognized in collaborative development revenue in the Statement of Operations and Comprehensive Loss.

Table of Contents

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 including further development of our APECCS cell-culture system. 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

General and administrative expenses include personnel costs, travel expenses and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs includes salaries, bonus, benefits and stock-based compensation. We have incurred, and expect to continue to incur, additional expenses as a result of being a public company following the completion of our initial public offering, or IPO, in June 2014, including expenses to comply with the rules and regulations applicable to companies listed on a national securities exchange and costs related to compliance and reporting obligations pursuant to the rules and regulations of the SEC, as well as increases in expenses for additional insurance, investor relations activities and other administration and professional services.

Provision for Income Taxes

We did not record a provision for income taxes for the three months ended March 31, 2015 because we expect to generate a net operating loss for the year ending December 31, 2015. Our deferred tax assets continue to be fully offset by a valuation allowance.

Critical Accounting Polices and Estimates

Our management s discussion and analysis of our financial condition and results of operations is based upon our unaudited condensed 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 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 values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We consider certain accounting policies related to revenue recognition, research

and development expense and accruals and stock-based compensation to be critical policies. There have been no changes to our critical accounting policies since we filed our 2014 Annual Report on Form 10-K, or 2014 Form 10-K, with the SEC on March 5, 2015. For a description of our critical accounting policies, please refer to our 2014 Form 10-K.

Table of Contents

Results of Operations

Three Months Ended March 31, 2015 and 2014

Revenue

Licensing revenues for the three months ended March 31, 2015 as compared to the prior year was as follows (in thousands):

	For the Three Months Ended March 31,	
	2015	2014
Licensing revenue	$ 3,884	$ 3,236
Dollar change from prior year	648	
Percent change from prior year	20%	

Licensing revenue for the three months ended March 31, 2015 was $3.9 million, an increase of $0.6 million, or 20%, compared to licensing revenue of $3.2 million for the three months ended March 31, 2014. The increase was primarily due to the amortization of deferred revenue from the $25.0 million development milestone payment we received in May 2014, which is being recognized ratably over our expected period of performance under the agreement. The estimated period of performance is based on the completion of all of the Phase 2b clinical trials in CKD for tenapanor, which during the three months ended March 31, 2015 we estimated will be December 2017. The expected period of performance is reviewed quarterly and adjusted, as needed, to reflect our current assumptions regarding the timing of clinical studies.

Collaborative development revenues for the three months ended March 31, 2015 as compared to the prior year was as follows (in thousands):

	For the Three Months Ended March 31,	
	2015	2014
Collaborative development revenue	$ 1,999	$ 5,314
Dollar change from prior year	(3,315)	
Percent change from prior year	-62%	

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, 2015 was $2.0 million, a decrease of $3.3 million, or 62%, compared to $5.3 million for the three months ended March 31, 2014. The decrease was due to a decrease in development activities conducted by us related to the clinical trials that are a part of the AstraZeneca agreement.

Research and Development

Research and development expenses for the three months ended March 31, 2015 as compared to the prior year was as follows (in thousands):

	For the Three Months Ended March 31,	
	2015	2014
Research and development	$ 6,198	$ 7,637
Dollar change from prior year	(1,439)	
Percent change from prior year	-19%	

Table of Contents

The following table summarizes our research and development expenses during the three months ended March 31, 2015 and 2014 (in thousands):

	Three Months Ended March 31,	
	2015	2014
Discovery research expense	$ 4,179	$ 2,360
AstraZeneca collaboration development expense	2,019	5,277
Total research and development expenses	$ 6,198	$ 7,637

Research and development expenses were $6.2 million for the three months ended March 31, 2015, a decrease of $1.4 million, or 19%, compared to $7.6 million for the three months ended March 31, 2014. The change was due to a decrease in AstraZeneca collaboration development expense of $3.3 million which was primarily driven by the decrease in development activities related to tenapanor conducted by us under the license agreement with AstraZeneca. The decrease was offset by a $1.8 million increase in discovery research expenses primarily due to an increase in our personnel costs, consultant service fees, process development costs and lab supply expenses from increased research activities for unpartnered programs.

General and Administrative

General and administrative expenses for the three months ended March 31, 2015 as compared to the prior year was as follows (in thousands):

	For the Three Months Ended March 31,	
	2015	2014
General and administrative	$ 3,175	$ 1,377
Dollar change from prior year	1,798	
Percent change from prior year	131%	

General and administrative expenses were $3.2 million for the three months ended March 31, 2015, an increase of $1.8 million, or 131%, compared to $1.4 million for the three months ended March 31, 2014. The increase was primarily due to an increase in professional services fees, personnel and operational costs as a result of our being a public company.

Change in Fair Value of Preferred Stock Warrant Liability

Change in fair value of preferred stock warrant liability for the three months ended March 31, 2015 as compared to the prior year was as follows (in thousands):

	For the Three Months Ended March 31,

	2015	2014
Change in fair value of preferred stock warranty	$	$ (2,603)
Dollar change from prior year	2,603	
Percent change from prior year	100%	

Change in fair value of preferred stock warrant liability was zero for the three months ended March 31, 2015 compared to $2.6 million for the three months ended March 31, 2014. The preferred stock warrants were net exercised upon the completion of the IPO.

Liquidity and Capital Resources

The following table displays a summary of our cash and cash equivalents as of March 31, 2015 and December 31, 2014:

	March 31, 2015	December 31, 2014
Cash and cash equivalents	$ 98,318	$ 107,286

Table of Contents

In connection with our IPO, we received cash proceeds of $61.2 million, net of underwriters discounts and commissions and expenses paid by us. Prior to the IPO, we funded our operations primarily with cash flows from the sales of our convertible preferred stock in private placements and from the upfront payments and other collaboration related payments received from our collaboration partners AstraZeneca and Sanofi.

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 as of March 31, 2015 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 partnerships. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, the potential for one or more of our existing collaboration partners to terminate the agreement with us and return the program to us, 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:

- the decision of AstraZeneca whether to continue the development of tenapanor or exercise its right of termination under the agreement to return the program to us;
- if AstraZeneca exercises its right of termination under the agreement and returns the program to us, our decision as to the future development plan for tenapanor and the timing thereof;
- 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;
- if AstraZeneca continues the development of tenapanor, our decision whether 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 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.

Table of Contents

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

	Three Months Ended March 31,	
	2015	2014
Cash used in operating activities	$ (8,209)	$ (1,120)
Cash used in investing activities	(1,055)	(94)
Cash provided by financing activities	296	
Net decrease in cash and cash equivalents	$ (8,968)	$ (1,214)

Cash Flows from Operating Activities

Net cash used in operating activities during the three months ended March 31, 2015 and 2014 was approximately $8.2 million, and $1.1 million, respectively, and was primarily due to net loss for each respective period adjusted for stock-based compensation, depreciation expense and movements in working capital.

Cash Flows from Investing Activities

Cash used in investing activities for the three months ended March 31, 2015 and 2014 was approximately $1.1 million, and $0.1 million, respectively, and was related to our acquisition of property and equipment related to the expansion of our laboratory and related equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the three months ended March 31, 2015 and 2014 was approximately $0.3 million, and zero, respectively, and was due to proceeds from issuance of common stock upon the exercise of stock options and purchase rights.

Table of Contents

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of March 31, 2015 (in thousands):

	Payments Due by Period				
Contractual Obligation:	**Less than 1 year**	**1 to 3 Years**	**4 to 5 Years**	**More Than 5 Years**	**Total**
Purchase commitments	$ 758				$ 758
Operating leases [1]	849	1,776	1,346		3,971
Capital expenditures	827				827
Total contractual obligations	$ 2,434	$ 1,776	$ 1,346		$ 5,556

[1] Operating leases include total future minimum rent payments under non-cancelable operating lease agreements.

Off-Balance Sheet Arrangements

None.

Recent Accounting Pronouncements

Refer to Note 2 in the accompanying notes to our unaudited interim condensed financial statements for a discussion of recent accounting pronouncements.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

There have been no material changes in the sources and effects of our market risk compared to the disclosures in Item 7A of our 2014 Form 10-K.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended (the Exchange Act), our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of March 31, 2015. Based on such evaluation, our principal executive officer and principal financial officer have concluded that, as of March 31, 2015, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Controls

There were no changes in our internal controls over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the quarter ended March 31, 2015 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

We are not currently a party to any material litigation or other material legal proceedings.

ITEM 1A. RISK FACTORS

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

Table of Contents

Risk Related to Our Collaboration Partnership with AstraZeneca

Our Phase 2a clinical trial evaluating tenapanor in Stage 3 chronic kidney disease patients with type 2 diabetes mellitus and albuminuria did not meet the primary endpoint, and under our agreement, AstraZeneca is obligated to communicate to us on or before June 29, 2015, whether it will continue the development of tenapanor.

In October 2012, we entered into a license agreement with AstraZeneca AB, or AstraZeneca granting it an exclusive worldwide license to our small molecule NHE3 inhibitor program, which includes our lead product candidate, tenapanor, for all indications. We and AstraZeneca have evaluated tenapanor in patients with IBS-C, CKD stage 5 on dialysis with hyperphosphatemia and CKD stage 3 with type 2 diabetes mellitus and albuminuria. AstraZeneca is assessing the data from all of the studies, including the recent results of the Phase 2a clinical trial evaluating tenapanor in Stage 3 CKD patients with type 2 diabetes mellitus and albuminuria, which did not meet the primary endpoint. Provided that AstraZeneca is pursuing development of at least one indication, under the agreement, either by itself or through a sublicensee, AstraZeneca has the right to elect which indication or indications it will develop, and is not obligated to develop any specific indication. Additionally, as long as AstraZeneca is using commercially reasonable efforts to develop tenapanor or one of the other small molecule NHE3 inhibitors licensed under the agreement, AstraZeneca has the right to determine the development plan, which may include conducting additional research or performing early stage clinical trials for tenapanor or other NHE3 inhibitors. AstraZeneca has the obligation to communicate to us by June 29, 2015 whether it will continue the development of tenapanor. If AstraZeneca elects to continue the development of tenapanor, AstraZeneca may choose to pursue an indication that is not in our strategic best interest or to delay the pursuit of, or forego, an indication, even if clinical data is supportive of further development for such indication. There can be no assurances as to which indication or indications AstraZeneca will pursue, what the timing will be of the initiation of additional clinical development for tenapanor, or what AstraZeneca s future development plan for tenapanor will be. Additionally, we do not have a right to regain rights to those indications that AstraZeneca elects not to pursue. Should AstraZeneca elect to forego development of the IBS-C indication and/or the hyperphosphatemia indication, our business could be materially and adversely harmed.

If AstraZeneca exercises its right to terminate its collaboration partnership with us, we would not receive any additional milestone payments or revenue from this collaboration partnership, and our results of operations and financial condition could be materially and adversely affected.

Under our agreement with AstraZeneca, AstraZeneca has responsibility for completing all nonclinical and clinical development and obtaining and maintaining regulatory approval for tenapanor from the Food and Drug Administration, or 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. AstraZeneca has the right to terminate this collaborative partnership at any time for any reason upon written notice to us. If AstraZeneca elects to terminate the collaborative partnership with us, our business could be materially and adversely harmed and depending on the timing of such event:

- we would not be eligible to receive any of the remaining development or regulatory milestone payments or royalties on product sales of tenapanor;

the development of tenapanor may be significantly delayed as a result of the need to transition the program back to us;

we would bear all of the risks and costs related to the further development and commercialization of tenapanor;

we may not be able to obtain a sufficient supply of raw materials, work in progress or clinical trial material from AstraZeneca to support the continued development of tenapanor, and as a result the development of tenapanor may be significantly delayed;

we may encounter difficulty and delay associated with the transfer of the manufacturing process from AstraZeneca to a third party contract manufacturer, and such third party contract manufacturer may not be able to manufacture clinical or commercial supplies of tenapanor in the time frame, at the scale or to the specifications required;

we may encounter difficulty and delay in obtaining all clinical trial reports, all nonclinical reports, all drug manufacturing reports, appropriate transfer of INDs to us, appropriate transfer of ongoing animal and human studies to us and other clinical and regulatory materials that may be necessary for us to support the development of tenapanor, and as a result, our continued development of tenapanor may be significantly delayed;

Table of Contents

in order to fund further development and commercialization of tenapanor, we would need to raise substantial additional capital in order to internally pursue the development of the program, and even if we raise additional capital, 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 program or delay the program, in either case, in a manner that would adversely impact our ability to realize value from the program; and

our cash expenditures would increase significantly if it is necessary for us to hire a significant number of additional employees and allocate limited resources to the development and commercialization of tenapanor.

Any of these events would have a material adverse effect on our results of operations and financial condition. For a discussion of the other risks associated with our collaboration partnership with AstraZeneca, see below under Risks Related to Our Business.

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 to evaluate our business and prospects. We continue to incur significant research, development and other expenses related to our ongoing operations. Our net loss for the three months ended March 31, 2015 and 2014 was $3.5 million and $3.1 million, respectively. As of March 31, 2015, we had an accumulated deficit of $75.4 million.

If we do not receive anticipated milestone payments from our collaboration partners, 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. There can be no assurance 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 above under Risks Related to Our Collaboration with AstraZeneca and 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.

Table of Contents

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;
- obtaining regulatory approvals for our product candidates, either on our own, or with a collaboration partner;
- 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 our stockholders to lose all or part of their 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. 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.

Table of Contents

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:

- the decision of AstraZeneca whether to continue the development of tenapanor or exercise its right of termination under the agreement to return the program to us;
- if AstraZeneca exercise its right of termination under the agreement and return the program to us, our decision as to the future development plan for tenapanor and the timing thereof;
- if AstraZeneca does not exercise its right of termination under the agreement, its right to determine the development plan it will follow, which may include conducting earlier stage clinical trials than we currently anticipate or conducting trials with an NHE3 inhibitor other than tenapanor, which in either case would result in a significant delay in our receipt of additional milestone payments.
- 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;
- if AstraZeneca continues the development of tenapanor, 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 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.

Table of Contents

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. 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 AstraZeneca s decision whether or not to continue the development of tenapanor, and should it determine to continue development, 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:

- whether tenapanor s safety and efficacy profile is satisfactory to the FDA and foreign regulatory authorities to warrant marketing approval;
- whether FDA or foreign regulatory authorities require additional clinical trials than anticipated prior to approval to market tenapanor;
- the prevalence and severity of adverse side effects of tenapanor;
- the results of a long-term rat carcinogenicity study required for approval of tenapanor, which will not be known for at least one 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, as a result of the observation of the absorption of inactive metabolites of tenapanor seen in our radiolabeled human ADME study, the FDA or foreign regulatory authorities require additional nonclinical studies prior to the commencement of Phase 3 activities, which, if required, could delay the development 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, effective and well-tolerated 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 and tolerability 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.

Table of Contents

As tenapanor is a first-in-class drug, there is a higher likelihood that approval may not be attained as compared to a class of drugs with approved products. We cannot be certain that tenapanor will be successful in non-clinical safety studies, clinical trials or receive regulatory approval. 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. For example, the reduction of serum phosphorus is currently an approvable endpoint in CKD patients on dialysis, but not for 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 sufficient revenue from sales of tenapanor, if approved. Accordingly, there can be no assurance that tenapanor will ever be successfully commercialized or that we will ever generate income from sales of tenapanor. If we 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 exercises its right to terminate the agreement, does not elect to continue development of one or more indications for tenapanor, 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.

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:

- AstraZeneca may terminate the license agreement at any time and for any reason;
- 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;
- AstraZeneca may sublicense its rights with respect to tenapanor to one or more third parties without our consent;
- AstraZeneca has the unilateral ability to choose not to develop tenapanor for one or more indications for which it has been evaluated, including the IBS-C indication and the hyperphosphatemia indication, provided it pursues at least one indication;
- AstraZeneca may choose to pursue an indication that is not in our strategic best interest or to delay the pursuit of, or forego an indication, even if clinical data is supportive of further development for such indication;

AstraZeneca s 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 though the Phase 2b clinical data in IBS-C patients announced in October 2014 indicated that at the 50 mg twice daily dose, the study met its primary efficacy endpoint; 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 may elect to pursue the development and commercialization of tenapanor in combination with other active ingredients and, as a result our potential royalty revenue may be significantly reduced as a result of the manner in which tenapanor net sales would be calculated under the agreement;

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 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;

Table of Contents

- 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 not dedicate the resources that would be necessary to carry tenapanor through clinical development or may not obtain the necessary regulatory approvals; and

- 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.

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 following AstraZeneca s determination to proceed to the first Phase 3 clinical development program 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 well as on an analysis of the capital requirements to advance our other programs. 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 rights.

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.

Table of Contents

Exercising our co-promotion rights 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 CKD-5D 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.

Table of Contents

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, we recently announced that a Phase 2a study evaluating tenapanor in Stage 3 CKD patients with type 2 diabetes mellitus and albuminuria failed to meet the primary endpoint. 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 clinical trial, or future clinical trials, will demonstrate similar results. An unacceptable adverse event profile may present challenges for the future development and commercialization of a product candidate for a particular condition despite receipt of positive efficacy data in a clinical study. For example, in a Phase 2b study evaluating tenapanor for the treatment of hyperphosphatemia in CKD patients on dialysis, we observed that the study met its primary endpoint by demonstrating a statistically significant dose-related decrease in serum phosphate levels for tenapanor-treated patients compared to patients receiving placebo, while also observing that the rate of diarrhea and the discontinuation rate due to diarrhea at the highest doses were higher than expected based upon previous clinical trials. 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 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 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

Table of Contents

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.

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.

Most of 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. Most of our current unlicensed product candidates 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 most of 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, there can be no assurance that any product candidates will reach the clinic or be successfully developed or commercialized.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Although our research and development efforts to date have resulted in several development programs, we may not be able to develop product candidates that are safe, effective and well-tolerated. Our research programs may initially show promise in identifying potential product candidates, 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, well-tolerated 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, effective and well-tolerated by patients, the medical community or third-party payors, if applicable.

Even if we are successful in continuing to expand our pipeline, through our own research and development efforts 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 enhanced this platform with the addition of APECCS. We plan to utilize APECCS to identify new and potentially novel targets in the GI tract. However, there can be no assurance that APECCS will be able to identify new targets in the GI tract or that any of these potential targets or other aspects of our proprietary drug discovery and design platform will yield product candidates that could enter clinical development and, ultimately, be commercially valuable.

Table of Contents

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 minimally-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. There can be no assurance

that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices or 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;

Table of Contents

the prevalence and severity of any side effects and overall safety and tolerability 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, effective and well-tolerated 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, abdominal distention and changes in electrolytes, and in the Phase 2b evaluating

tenapanor for the treatment of hyperphosphatemia in CKD-5D patients, we observed that the rate of diarrhea and the discontinuation rate due to diarrhea at the highest doses was higher than expected based upon the results of previous clinical trials. 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. Additionally, despite a positive efficacy profile, the prevalence and/or severity of these or other side effects could cause us or AstraZeneca to cease further development of a product candidate for a particular indication, or entirely. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Table of Contents

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 hyperphosphatemia in patients with CKD-5D, including sevelamer hydrochloride (Renagel) and sevelamer carbonate (Renvela), which were launched by Genzyme. Synthon announced the successful completion of a Phase 3 multicenter,

randomized, double-blind, multiple-dose, crossover trial in Europe to compare safety and demonstrate equivalence of serum phosphate control of Synthon sevelamer carbonate tablets to Renvela tablets in chronic kidney disease patients on hemodialysis in April 2014. Currently, several pharmaceutical companies are distributing Synthon manufactured sevelamer carbonate tablets in multiple European countries including, but not limited to, the United Kingdom, Spain, Sweden and Denmark. In addition to the currently marketed phosphate binders, Keryx has received FDA approval for ferric citrate (Auryxia), an iron-based binder, that is also approved in Japan and we are aware of fermagate (Alpharen), an iron-based binder in Phase 2 being developed by Opko Health.

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.

Table of Contents

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

We 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 promote tenapanor, either through the exercise of our co-promote rights under the agreement or on our own should AstraZeneca elect to terminate the agreement and return the program to us, and in order to 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, and

should AstraZeneca terminate the agreement, we would be completely dependent upon contract manufacturing partners, for all aspects of the manufacturing and validation process, as well as providing all commercial supply of tenapanor. In addition, if AstraZeneca elects to terminate the agreement, we would be completely dependent upon AstraZeneca s cooperation to achieve a smooth transition of the manufacturing process to our contract manufacturers and should AstraZeneca fail to provide such cooperation, our development plans for tenapanor could be significantly delayed, and the costs we incur in connection with the transfer could be substantially increased. 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.

Table of Contents

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, Japan, China and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medicinal products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Table of Contents

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.

Table of Contents

We are highly dependent on the services of our President and Chief Executive Officer, Michael Raab, our Executive Vice President and Chief Scientific Officer, Jeremy Caldwell, Ph.D., and our Senior Vice President of Drug Development, David Rosenbaum, Ph.D. If we are not able to retain these members of our management team, 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, Jeremy Caldwell, Ph.D., our Chief Scientific Officer and David Rosenbaum, Ph.D., our Senior Vice President of Drug Development. The loss of services of any of these individuals could delay or impair the successful development of our product pipeline, completion of our planned clinical trials or the commercialization of our product candidates. Although we have entered into employment agreements with our senior management team, including Mr. Raab and Drs. Caldwell 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 continue to increase the size of our organization, and we may experience difficulties in managing growth.

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

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

Table of Contents

In addition, we are in the process of implementing 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 will 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.

We are subject to Section 404 of The Sarbanes-Oxley Act of 2002, or Section 404, and the related rules of the Securities and Exchange Commission, or SEC, which generally require our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. 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 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 our IPO (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 not conducted any other review of our internal control for the purpose of providing the reports required by Section 404 and the related SEC 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 are required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

We may 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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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;

Table of Contents

- 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.

Table of Contents

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.

Table of Contents

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, abdominal distention and changes in electrolytes and in the Phase 2b evaluating tenapanor for the treatment of hyperphosphatemia in CKD-5D patients, we observed that the rate of diarrhea and the discontinuation rate due to diarrhea at the highest doses was higher than expected based upon the results of previous clinical trials. 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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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. There can be no assurances that we will not be subject to claims alleging that the manufacture, use or sale of tenapanor or any other product candidates 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

Table of Contents

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

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

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

Risks Related to Our Common Stock

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

The trading price of our common stock is highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. These factors include those discussed in this Risk Factors section of this Quarterly Report on Form 10-Q and others such as:

- announcements regarding decisions by AstraZeneca to terminate or delay development of tenapanor for one or more indications, or to terminate the collaboration partnership;
- results from, or any delays in, clinical trial programs relating to our product candidates, including the ongoing and planned clinical trials for tenapanor;
- announcements relating to our collaboration partnership with Sanofi regarding its option to develop and commercialize NaP2b inhibitors;
- 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;
- 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;

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.

Table of Contents

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. If some investors find our common stock less attractive as a result of our reliance on the JOBS Act exemption, 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 our IPO (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.

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, the trading price of our common stock could decline. As of March 31, 2015, we had 18,635,071 shares of common stock outstanding. Of those shares, 10,066,357 were held by current directors, executive officers and other affiliates, or may otherwise be subject to Rule 144 under the Securities Act of 1933, or the Securities Act.

In addition, as of March 31, 2015, 573,567 shares of common stock that are subject to outstanding options, were eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, 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.

The holders of approximately 9.7 million shares of our outstanding common stock as of March 31, 2015, are entitled to rights with respect to the registration of their shares under the Securities Act, subject to vesting schedules. 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, 2015, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately two-thirds of our outstanding voting stock. Therefore, 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 certain stockholders may feel are in their best interest as one of our stockholders.

Table of Contents

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

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

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 ⅔% 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 ⅔% 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.

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.

Table of Contents

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

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person s conduct was unlawful.

- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.

- We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.

- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

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

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

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

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

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Unregistered Sale of Equity Securities

None.

Use of Proceeds

On June 18, 2014, the U.S. Securities and Exchange Commission declared effective our registration statement on Form S-1 (File No. 333-196090), as amended in connection with our IPO.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

Table of Contents

ITEM 6. Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation.	8-K	6/24/2014	3.1	
3.2	Amended and Restated Bylaws.	8-K	6/24/2014	3.2	
4.1	Reference is made to exhibits 3.1 and 3.2.				
4.2	Form of Common Stock Certificate.	S-1/A	6/18/2014	4.2	
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.				X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.				X
32.1	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C §1350.				X
101	The following financial statements, formatted in XBRL: (i) Condensed Balance Sheets as of March 31, 2015 and December 31, 2014, (ii) Condensed Statements of Operations and Comprehensive Loss for the three months ended March 31, 2015 and 2014; (iii) Condensed Statements of Cash Flows for the three months ended March 31, 2015 and 2014; and (v) Notes to Unaudited Condensed Financial Statements.				X

Table of Contents

SIGNATURES

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

Ardelyx, Inc.

Date: May 12, 2015

By: /s/ Mark Kaufmann
Mark Kaufmann

Chief Financial Officer

(Principal Financial Officer)