ARDELYX, INC.
Form 10-Q
August 08, 2016
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 JUNE 30, 2016

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 x
Non-accelerated filer ¨ (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 August 3, 2016 was 47,250,496.

Table of Contents

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 and per share amounts)

	June 30, 2016 (Unaudited)	December 31, 2015 (1)
Assets		
Current assets:		
Cash and cash equivalents	$ 146,669	$ 107,004
Prepaid expenses and other current assets	3,735	5,027
Total current assets	150,404	112,031
Property and equipment, net	4,827	4,711
Other assets	148	104
Restricted cash		100
Total assets	$ 155,379	$ 116,946
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 4,746	$ 2,777
Accrued compensation and benefits	2,038	2,366
Accrued and other liabilities	7,277	2,580
Total current liabilities	14,061	7,723
Other long-term liabilities	713	322
Total liabilities	14,774	8,045
Commitments and contingencies		
Stockholders equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized as of June 30, 2016 and December 31, 2015, respectively; no shares issued and outstanding as of June 30, 2016 and December 31, 2015, respectively.		
Common stock, $0.0001 par value; 300,000,000 shares authorized as of June 30, 2016 and December 31, 2015, respectively; 34,650,266 and 25,964,886 shares issued and outstanding as of June 30 2016 and December 31, 2015, respectively.	4	3
Additional paid-in capital	294,171	210,386

Accumulated deficit	(153,570)	(101,488)
Total stockholders equity	140,605	108,901
Total liabilities and stockholders equity	$ 155,379	$ 116,946

(1) Derived from the audited financial statements included in the Company s Annual Report on Form 10-K for the year ended December 31, 2015.

See accompanying notes to Condensed Financial Statements.

Table of Contents

ARDELYX, INC.

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE (LOSS) INCOME

(in thousands, except share and per share amounts)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016 (Unaudited)	2015 (Unaudited)	2016 (Unaudited)	2015 (Unaudited)
Revenue:				
Licensing revenue	$	$ 17,727	$	$ 21,611
Collaborative development revenue		416		2,415
Total revenue		18,143		24,026
Operating expenses:				
Research and development	23,838	6,198	43,091	12,396
General and administrative	4,852	2,889	9,130	6,064
Total operating expenses	28,690	9,087	52,221	18,460
(Loss) income from operations	(28,690)	9,056	(52,221)	5,566
Other income (expense), net	77	(49)	139	(61)
(Loss) income before provision for income taxes	(28,613)	9,007	(52,082)	5,505
Provision for income taxes				
Net (loss) income and comprehensive (loss) income	$ (28,613)	$ 9,007	$ (52,082)	$ 5,505
Basic net (loss) income per common share	$ (0.83)	$ 0.43	$ (1.53)	$ 0.28
Diluted net (loss) income per common share	$ (0.83)	$ 0.42	$ (1.53)	$ 0.27
Shares used in computing basic net (loss) income per share	34,636,559	20,880,235	34,051,785	19,749,778
Shares used in computing diluted net (loss) income per share	34,636,559	21,636,487	34,051,785	20,506,916

See accompanying notes to Condensed Financial Statements.

Table of Contents

ARDELYX, INC.

CONDENSED STATEMENTS OF CASH FLOWS

(in thousands)

	Six Months Ended June 30,	
	2016 (Unaudited)	**2015 (Unaudited)**
Operating activities		
Net (loss) income	$ (52,082)	$ 5,505
Adjustments to reconcile net (loss) income to net cash used in operating activities:		
Depreciation expense	631	278
Amortization of deferred financing costs	174	
Amortization of deferred compensation for services	101	
Stock-based compensation	2,476	1,165
Loss from disposal of fixed assets		11
Changes in operating assets and liabilities:		
Accounts receivable		2,557
Prepaid expenses and other assets	1,073	(959)
Accounts payable	1,717	(631)
Accrued compensation and benefits	(328)	(192)
Accrued and other liabilities	5,089	886
Deferred revenue		(47,053)
Net cash used in operating activities	(41,149)	(38,433)
Investing activities		
Purchases of property and equipment	(495)	(2,320)
Net cash used in investing activities	(495)	(2,320)
Financing activities		
Proceeds from issuance of common stock, net of issuance costs	80,837	74,654
Proceeds from exercise of stock options	472	317
Other		30
Net cash provided by financing activities	81,309	75,001
Net increase in cash and cash equivalents	39,665	34,248
Cash and cash equivalents at beginning of period	107,004	107,286
Cash and cash equivalents at end of period	$ 146,669	$ 141,534

Supplemental cash flow disclosure:

Cash paid during the period for income taxes	$	$ 310
Supplemental noncash financing activities:		
Acquisition of property and equipment included in accounts payable and accrued liabilities	$ 252	$ 134
Common stock issuance costs included in accounts payable and accrued liabilities	$	$ 287

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., or the Company, is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-systemic therapeutic drugs that work exclusively in the gastrointestinal, or GI, tract to treat cardio-renal and GI diseases. The Company has developed a proprietary 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 its lead product candidate, tenapanor, which is currently being evaluated in two pivotal Phase 3 clinical studies in patients with constipation-predominant irritable bowel syndrome, or IBS-C. In a Phase 2b clinical study, tenapanor demonstrated the ability to lower elevated serum phosphorus levels in patients with end-stage renal disease, or ESRD. The Company has initiated the first of two registration studies to evaluate efficacy, safety and dosing regimens of tenapanor for the treatment of hyperphosphatemia, or elevated serum phosphorus in ESRD patients on dialysis. The Company is developing another drug candidate, RDX227675, the lead product candidate from its RDX022 program, for the treatment of hyperkalemia, or elevated serum potassium. The Company is pursuing a 505(b)(2) regulatory pathway for RDX227675. The Company has additional drug candidates in earlier research and development programs focused in GI and cardio-renal diseases, including RDX98940, the lead development compound from its RDX009 program focused on secretagogues of glucagon-like peptide-1, or GLP-1, and glucagon-like peptide-2, or GLP-2, and RDX013 program compounds focused on potassium secretagogues.

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, or 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 (U.S. GAAP) 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 and six months ended June 30, 2016 are not necessarily indicative of results to be expected for the entire year ending December 31, 2016 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, 2015, included in the Company s Annual Report on Form 10-K filed with the SEC (the 2015 Form 10-K). The balance sheet at December 31, 2015 has been derived from the audited financial statements at that date, as filed with the 2015 Form 10-K.

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP 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.

Clinical Trial Accruals

Clinical trial costs are a component of research and development expenses. The Company accrues and expenses clinical trial activities performed by third parties based upon actual work completed in accordance with agreements established with clinical research organizations and clinical sites. The Company determines estimated costs through discussions with internal personnel and external service providers as to the progress or stage of completion of trials or services and the agreed-upon fee to be paid for such services.

Nonrefundable advance payments for goods and services that will be used or rendered in future research and development activities, are deferred and recognized as expense in the period that the related goods are delivered or services are performed.

Table of Contents

Recent Accounting Pronouncements

In May, 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2014-09, *Revenue from Contracts with Customers* (ASU 2014-09), which requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. ASU 2014-09 will replace most existing revenue recognition guidance in U.S. GAAP when it becomes effective. In July 2015, the FASB voted to approve a deferral of the effective date of this ASU by one year, and to permit entities to adopt up to one year earlier if they choose. Therefore, the new standard will become effective for the Company on January 1, 2018 and early application is permitted for periods beginning on or after January 1, 2017. The standard permits the use of either the retrospective or cumulative effect transition method. The Company is evaluating the effect that ASU 2014-09 will have on its condensed financial statements and related disclosures. The Company has not yet selected an implementation date or a transition method nor has it determined the effect of the standard on its ongoing financial reporting.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements Going Concern: Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern* (ASU 2014-15). ASU 2014-15 is intended to define management s responsibility to evaluate whether there is substantial doubt about an organization s ability to continue as a going concern and to provide related footnote disclosures, if required. ASU 2014-15 is effective for annual reporting periods ending after December 15, 2016, and applies to annual and interim periods thereafter. The Company is evaluating the impact that the adoption of ASU 2014-15 will have on its condensed financial statements and related disclosures.

In January 2016, the FASB issued ASU 2016-01*, Financial Instruments-Overall.* This ASU addresses certain aspects of recognition, measurement, presentation, and disclosure of financial instruments. This ASU will become effective for annual periods beginning after December 15, 2017. The Company is currently evaluating the impact of the adoption of this ASU on its condensed financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. Under the new guidance, lessees will be required to recognize a lease liability and a right-of-use asset for all leases (with the exception of short term leases) at the commencement date. Lessor accounting under ASU 2016-02 is largely unchanged. ASU 2016-02 is effective for annual and interim periods beginning on or after December 15, 2018 and early adoption is permitted. Under ASU 2016-02, lessees (for capital and operating leases) and lessors (for sales-type, direct financing, and operating leases) must apply a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. Lessees and lessors may not apply a full retrospective transition approach. The Company has not yet selected an implementation date nor has it determined the effect of the standard on its ongoing financial reporting.

In March 2016, the FASB issued Accounting Standards 2016-09, *Improvements to Employee Share-Based Payment Accounting*, which amends ASC Topic 718, Stock Compensation. The objective of this amendment is part of the FASB s Simplification Initiative as it applies to several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. This pronouncement is effective for the Company on July 1, 2017, and allows for prospective, retrospective or modified retrospective adoption, depending on the area covered in the update, with early adoption permitted. The Company is currently evaluating the impact on our condensed financial statements and the timing of adoption.

In April 2016, the FASB issued ASU 2016-10*, Identifying Performance Obligations and Licensing.* This ASU clarifies two aspects of ASU 2014-09, Revenue from Contracts with Customers (Topic 606): identifying performance

obligations and the licensing implementation guidance. This ASU will become effective for annual periods beginning after December 15, 2017. The Company is currently evaluating the impact of the adoption of this ASU on its condensed financial statements.

In May 2016, the FASB issued ASU 2016-12*, Narrow-Scope Improvements and Practical Expedients.* This ASU addresses certain issues in ASU 2014-09, Revenue from Contracts with Customers (Topic 606) regarding assessing collectability, presentation of sales taxes, noncash consideration, and completed contracts and contract modifications at transition. This ASU will become effective for annual periods beginning after December 15, 2017. The Company is currently evaluating the impact of the adoption of this ASU on its condensed financial statements.

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

Table of Contents

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

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):

	June 30, 2016			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 147,202	$ 147,202	$	$
Total	$ 147,202	$ 147,202	$	$

	December 31, 2015			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 105,819	$ 105,819	$	$
Certificates of deposit	100		100	
Total	$ 105,919	$ 105,819	$ 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.

The carrying amounts reflected in the condensed balance sheets for cash equivalents, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at June 30, 2016 and December 31, 2015, due to their short-term nature.

Table of Contents

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, or the AstraZeneca Agreement, the Company received $75.0 million in up-front license fees and milestone payments which was recorded as deferred revenue when received and were recognized as revenue on a straight-line basis over the remaining estimated period of performance under the AstraZeneca Agreement, which, prior to its termination in June 2015, we estimated to be December 2017.

In June 2015, the Company entered into a termination agreement with AstraZeneca (the Termination Agreement) pursuant to which all licenses granted to AstraZeneca to the Company s portfolio of NHE3 inhibitors, including the Company s lead product candidate, tenapanor, were terminated, except for the limited purpose of allowing AstraZeneca to satisfy its obligations under the Termination Agreement. AstraZeneca was obligated to supply the Company with clinical trial materials, drug substance and drug product. The Company was obligated to pay for clinical trial materials, drug substance and drug product with a maximum amount initially set at $10 million in the Termination Agreement, which maximum amount was subsequently reduced to $8.0 million pursuant to an amendment to the Termination Agreement (Amendment Number One) of which $6.0 million was paid during 2015 and $2.0 million was paid during the second quarter of 2016.

As the AstraZeneca Agreement was terminated in June 2015, the Company recognized the remaining deferred revenue balance of $43.1 million during the three months ended June 30, 2015. Also in the three months ended June 30, 2015, the Company recorded a $15.0 million upfront payment for the return of the licenses as well as the $10.0 million payment for reimbursement of research and development expenses and the acceleration of the transfer of information and materials as a reduction in licensing revenue in the condensed statements of operations and comprehensive (loss) income.

NOTE 5. STOCK-BASED COMPENSATION

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Research and development	$ 681	$ 346	$ 1,306	$ 632
General and administrative	605	295	1,170	533
Total	$ 1,286	$ 641	$ 2,476	$ 1,165

At June 30, 2016, the Company had $11.8 million, $0.9 million and $0.1 million of total unrecognized compensation expense, net of estimated forfeitures, related to stock option grants, restricted stock unit grants and ESPP, respectively, that will be recognized over an average vesting period of 3.1 years, 3.4 years and 0.2 years, respectively.

NOTE 6. NET (LOSS) INCOME PER SHARE

Basic net (loss) income per share is calculated by dividing the net (loss) income by the weighted-average number of shares of common stock outstanding during the period. Diluted net (loss) income 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. The Company uses the treasury-stock method to compute diluted earnings per share with respect to its stock options and common stock equivalents. For purposes of this calculation, options to purchase stock are considered to be potential common shares

Table of Contents

and are only included in the calculation of diluted net (loss) income per share when their effect is dilutive. Basic and diluted earnings per common share are calculated as follows (in thousands, except share and per share data):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Numerator:				
Net (loss) income	$ (28,613)	$ 9,007	$ (52,082)	$ 5,505
Denominator:				
Basic shares:				
Weighted average common shares outstanding	34,636,559	20,880,235	34,051,785	19,749,778
Diluted shares:				
Weighted average effect of dilutive stock options		692,110		724,890
Weighted average private placement warrants outstanding		64,142		32,248
	34,636,559	21,636,487	34,051,785	20,506,916
Net (loss) income per share - basic	$ (0.83)	$ 0.43	$ (1.53)	$ 0.28
Net (loss) income per share - diluted	$ (0.83)	$ 0.42	$ (1.53)	$ 0.27

For the three and six months ended June 30, 2016, the total number of anti-dilutive outstanding common stock equivalents excluded from the net loss per common share computation was 4.7 million and 4.6 million, respectively. For the three and six months ended June 30, 2015 the total number of anti-dilutive outstanding common stock equivalents excluded from the net loss per common share computation was 0.5 million and 0.4 million, respectively.

NOTE 7. ACCRUED AND OTHER LIABILITIES

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

	June 30, 2016	December 31, 2015
Accrued clinical trial expenses	$ 4,202	$ 311
Accrued contract manufacturing	1,694	289
Accrued professional and consulting services	610	272
AZ clinical trial material accrual		1,328
Other	771	380

	$ 7,277	$ 2,580

NOTE 8. STOCKHOLDERS EQUITY

Option Exercises

For the three and six months ended June 30, 2016, employees exercised options to purchase zero and 6,250 shares, respectively, of the Company s common stock with insignificant net proceeds to the Company. For the three and six months ended June 30, 2015, employees and consultants exercised options to purchase 20,189 and 46,401 shares of the Company s common stock, respectively, with net proceeds to the Company of insignificant and approximately $0.1 million, respectively.

Employee Stock Purchase Plan

In February 2016, the Company sold 34,012 shares under the ESPP. The shares were purchased at a purchase price of $8.21 per share with proceeds to the Company of approximately $0.3 million.

Offerings of Common Stock and Warrants

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

Table of Contents

Other than with respect to warrants issued to holders affiliated with New Enterprise Associates, the warrants contain limitations that prevent each holder of warrants from acquiring shares upon exercise of the warrants that would cause the number of shares beneficially owned by it and its affiliates to exceed 9.99% of the total number of shares of the Company s common stock then issued and outstanding. In addition, upon certain changes in control of the Company, each holder of a warrant can elect to receive, subject to certain limitations and assumptions, securities in a successor entity. None of the warrants issued in June 2015 have been exercised as of June 30, 2016.

In January 2016, the Company completed an underwritten public offering of 8,625,000 shares of common stock at an offering price of $10.00 per share for gross proceeds of $86.3 million. The Company received net proceeds from the offering of approximately $80.8 million, after deducting the underwriters discounts and commissions and offering expenses.

NOTE 9. SUBSEQUENT EVENTS

In July 2016, the Company sold and issued an aggregate of 12,600,230 shares of common stock in a private placement transaction for net proceeds of approximately $110.0 million. The price paid for the common stock was $8.73 per share which was equal to the consolidated closing bid price on the Nasdaq Global Market on the day of pricing, July 14, 2016.

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, 2015. 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 therapeutic drugs that work exclusively in the gastrointestinal, or GI, tract to treat cardio-renal and GI 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 is currently being evaluated in two pivotal Phase 3 clinical trials (T3MPO-1 and T3MPO-2) in patients with constipation predominant irritable bowel syndrome, or IBS-C. We, currently expect to receive results from T3MPO-1 in mid-2017, and results from T3MPO-2 are currently expected to be received at the end of 2017. In a Phase 2b clinical study, tenapanor demonstrated the ability to improve the symptoms of IBS-C. In a separate Phase 2b clinical trial, tenapanor demonstrated the ability to lower elevated serum phosphorus levels in patients with end-stage renal disease, or ESRD on dialysis. We have initiated the first of two registration studies to evaluate efficacy, safety and dosing regimens of tenapanor for the treatment of hyperphosphatemia, or elevated serum phosphorus, in ESRD patients on dialysis, and we expect to receive results from this trial in the first quarter of 2017. We are developing another drug candidate RDX227675, the lead product candidate from our RDX022 program, for the treatment of hyperkalemia, or elevated serum potassium. In June 2016, we announced the results of the final dosing arm of an open label clinical trial evaluating the pharmacodynamic activity of RDX227675 in healthy adult volunteers. Results from the last cohort evaluating once a day dosing (QD) of RDX227675 were consistent with the results of the twice daily (BID) and three times daily (TID) dosing cohorts which we announced in January 2016 which demonstrated that RDX227675 was generally well-tolerated at all doses evaluated and effectively binds to potassium in the GI tract. Results from the QD dosing cohort, demonstrated that a 13.8 g dose exhibited similar stool and urine potassium results to the previously reported BID and TID dosing with the same total daily dose of 13.8 g. These results support our plans to proceed with a Phase 3 clinical trial for RDX227675, which we currently expect to initiate in the fourth quarter of 2016. In the fourth quarter of 2016, we also plan to initiate an onset-of-action clinical trial in hyperkalemia patients with chronic kidney disease (CKD) on inhibitors of the renin angiotensin aldosterone system (RAASi) with results currently expected in the first half of 2017. We are pursuing a 505(b) (2) regulatory pathway for RDX227675. We have additional drug candidates in earlier research and development programs focused in GI and cardio-renal diseases including RDX98940, the lead development candidate from our RDX009 program focused on secretagogues of glucagon-like peptide-1, or GLP-1, and glucagon-like peptide-2, or GLP-2, and RDX013 program compounds, focused on potassium secretagogues. We currently expect to file an investigational new drug application, or IND, for RDX98940 in the fourth quarter of 2016.

AstraZeneca AB (AstraZeneca)

In October 2012, we entered into a collaboration partnership with AstraZeneca for the worldwide development and commercialization of tenapanor. Under the terms of the AstraZeneca collaboration partnership agreement, or the AstraZeneca Agreement, we received $75 million of up-front license and milestone fees. The amounts were recorded as deferred revenue when received and were recognized as revenue on a straight-line basis over the remaining estimated period of performance under the AstraZeneca Agreement, which, prior to its termination in June 2015, we estimated to be December 2017.

In June 2015, we entered into a termination agreement with AstraZeneca (the Termination Agreement) pursuant to which all licenses granted to AstraZeneca to our portfolio of NHE3 inhibitors, including our lead product candidate, tenapanor, were terminated, except for the limited purpose of allowing AstraZeneca to satisfy its obligations under the Termination Agreement. We also paid AstraZeneca $10.0 million as reimbursement for certain research and development expenses incurred by AstraZeneca under the collaboration agreement during 2015, and the acceleration of the transfer of the information and materials to us. We also were obligated to pay for clinical trial materials, drug substance and drug product with a maximum amount initially set at $10 million in the Termination Agreement, which maximum amount was subsequently reduced to $8.0 million pursuant to an amendment to the Termination Agreement (Amendment Number One) of which $6.0 million was paid during 2015 and $2.0 million was paid during the three months ended June 30, 2016.

Table of Contents

As the AstraZeneca Agreement was terminated in June 2015, we recognized the remaining deferred revenue balance of $43.1 million during the three months ended June 30, 2015. Also in the three months ended June 30, 2015, we recorded a $15.0 million upfront payment for the return of the licenses as well as the $10.0 million payment for reimbursement of research and development expenses and the acceleration of the transfer of information and materials as a reduction in licensing revenue in the condensed statements of operations and comprehensive (loss) income.

Financial Operations Overview

Revenue

We have not generated any revenue from product sales. Our revenue in 2015 was generated from non-refundable license payments and reimbursements for research and development expenses under our past license agreements. We consider upfront payments to be licensing revenue, and we recognize licensing revenue ratably over the term of our estimated period of performance under the agreement. In addition to receiving upfront payments, under our past license agreements, we also received 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 the AstraZeneca Agreement were classified as collaborative development revenue. There was no recognition of licensing and collaborative development revenue after the six-month period ended June 30, 2015.

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, and prior to the termination of the AstraZeneca Agreement, research and development expenses also included costs we incurred in connection with the development of tenapanor under the AstraZeneca Agreement. 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 and investigative sites where a substantial portion of our clinical studies are conducted, and with contract manufacturing organizations where our clinical supplies are produced;
- expenses associated with supplies and materials consumed in connection with our research operations; employee-related expenses, which include salaries, 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.

We expect our research and development expenses for the remainder of 2016 to increase substantially from the levels incurred in the six months ended June 30, 2016, as we progress the development of tenapanor, RDX227675 and our other our internal product candidates, advance our discovery research projects into the preclinical stage and continue our early stage research including further development of our proprietary drug discovery and design platform. The

process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for any of our product candidates. 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.

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 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, including tenapanor and RDX227675.

Table of Contents

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 expect general and administrative expense for the remainder of 2016 to increase from the levels incurred in the six months ended June 30, 2016.

Provision for Income Taxes

We did not record a provision for income taxes for the three and six months ended June 30, 2016 because we expect to generate a net operating loss for the year ending December 31, 2016. 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 2015 Annual Report on Form 10-K, or 2015 Form 10-K, with the SEC on March 5, 2016. For a description of our critical accounting policies, please refer to our 2015 Form 10-K.

Results of Operations

Three and Six Months Ended June 30, 2016 and 2015

Revenue

Licensing revenues for the three and six months ended June 30, 2016 as compared to the same period in the prior year was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Licensing revenue	$	$ 17,727	$	$ 21,611
Dollar change from prior year	(17,727)		(21,611)	
Percent change from prior year	-100%		-100%	

Licensing revenue for the three months ended June 30, 2016 was zero, a decrease of $17.7 million, or 100%, compared to licensing revenue of $17.7 million for the three months ended June 30, 2015. Licensing revenue for the six months ended June 30, 2016 was zero, a decrease of $21.6 million, or 100%, compared to licensing revenue of

$21.6 million for the six months ended June 30, 2015. Licensing revenue for the three and six months ended June 30, 2015 was related to the recognition of revenue from upfront and milestone payments. As our collaboration agreement with AstraZeneca was terminated in June 2015, there was no further recognition of revenue related to the upfront and milestone payments after the six-month period ended June 30, 2015.

Table of Contents

Collaborative development revenue for the three and six months ended June 30, 2016 as compared to the same period in the prior year was as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Collaborative development revenue	$	$ 416	$	$ 2,415
Dollar change from prior year	(416)		(2,415)	
Percent change from prior year	-100%		-100%	

Collaborative development revenue consists of our development expenses that were reimbursable to us by AstraZeneca as part of our license agreement. Collaborative development revenue for the three months ended June 30, 2016 was zero, a decrease of $0.4 million, or 100%, compared to $0.4 million for the three months ended June 30, 2015. Collaborative development revenue for the six months ended June 30, 2016 was zero, a decrease of $2.4 million, or 100%, compared to $2.4 million for the six months ended June 30, 2015. The decrease in both periods was due the termination of our collaboration with AstraZeneca and related cessation of reimbursement of research and development expenses.

Research and Development

Research and development expenses for the three and six months ended June 30, 2016 as compared to same period in the prior year were as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
Research and development	$ 23,838	$ 6,198	$ 43,091	$ 12,396
Dollar change from prior year	17,640		30,695	
Percent change from prior year	285%		248%	

Research and development expenses were $23.8 million for the three months ended June 30, 2016, an increase of $17.6 million, or 285%, compared to $6.2 million for the three months ended June 30, 2015. Research and development expenses were $43.1 million for the six months ended June 30, 2016, an increase of $30.7 million, or 248%, compared to $12.4 million for the six months ended June 30, 2015. The change in both periods was primarily due to expenses incurred for clinical development activities associated with tenapanor as well as clinical manufacturing and process development activities associated with tenapanor, RDX227675 and RDX98940.

General and Administrative

General and administrative expenses for the three and six months ended June 30, 2016 as compared to the same period in the prior year were as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2016	2015	2016	2015
General and administrative	$ 4,852	$ 2,889	$ 9,130	$ 6,064
Dollar change from prior year	1,963		3,066	

Percent change from prior year	68%	51%

General and administrative expenses were $4.9 million for the three months ended June 30, 2016, an increase of $2.0 million, or 68%, compared to $2.9 million for the three months ended June 30, 2015. General and administrative expenses were $9.1 million for the six months ended June 30, 2016, an increase of $3.1 million, or 51%, compared to $6.1 million for the six months ended June 30, 2015. The increase in both periods was primarily due to an increase in professional services fees including fees for market research and commercialization activities, systems implementation and intellectual property management, as well as increases in personnel-related expenses and facility costs.

Table of Contents

Liquidity and Capital Resources

The following table displays a summary of our cash and cash equivalents as of June 30, 2016 and December 31, 2015 (in thousands):

	June 30, 2016	December 31, 2015
Cash and cash equivalents	$ 146,669	$ 107,004

In June 2015, we closed a private placement financing in which we raised approximately $77.8 million in gross proceeds or $74.3 million in net proceeds, after deducting issuance costs.

On July 13, 2015, we filed a shelf registration statement on Form S-3 (File No. 333-205631) with the SEC, under which we may sell an aggregate of up to $200.0 million of common stock, preferred stock, debt securities, warrants, purchase contract and/or units. The S-3 shelf registration statement included a prospectus covering the offering, issuance and sale of up to $50.0 million of shares of common stock from time to time in at the market offerings pursuant to a Controlled Equity Offering Sales Agreement entered into with Cantor Fitzgerald on July 13, 2015.

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

Subsequent to June 30, 2016, we sold and issued an aggregate of 12,600,230 million shares of common stock in a private placement transaction in July 2016 for net proceeds of approximately $110.0 million.

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 June 30, 2016 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. We anticipate that we will require significant additional financing in the future to fund our operations, including to support the development, pre-commercialization and commercialization efforts for tenapanor and RDX227675. We may obtain such additional financing through debt financings, credit facilities, additional equity offerings and/or strategic collaborations. We currently have no credit facility or committed sources of capital, and there can be no assurances that such sources of capital or additional financing will be available to us when needed or on acceptable terms. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we may 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 progress, timing, scope, results and costs of our clinical trial programs evaluating tenapanor in IBS-C and for the treatment of hyperphosphatemia in patients with ESRD on dialysis, as well as our decision whether or not to pursue other indications for tenapanor;

the progress, timing, scope, results and costs of our clinical program for RDX227675, our lead product candidate from our RDX022 program;

the progress, timing, scope, results and costs of our IND enabling studies and early clinical development of RDX98940, our lead compound in the RDX009 program;

the time and cost necessary to obtain regulatory approvals for our product candidates and the costs of post-marketing studies that could be required by regulatory authorities;

our ability to successfully commercialize our product candidates, either alone or with one or more collaboration partners;

the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;

the selling and marketing costs associated with our product candidates, including the cost and timing of building our sales and marketing capabilities;

our ability to establish and maintain collaboration partnerships to in-license or out-license our current programs 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;

Table of Contents

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, and any clinical trials we decide to pursue for other product candidates;

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.

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

	Six Months Ended June 30,	
	2016	2015
Cash used in operating activities	$ (41,149)	$ (38,433)
Cash used in investing activities	(495)	(2,320)
Cash provided by financing activities	81,309	75,001
Net decrease in cash and cash equivalents	$ 39,665	$ 34,248

Cash Flows from Operating Activities

Net cash used in operating activities during the six months ended June 30, 2016 was approximately $41.1 million. The net loss of $52.1 million was offset by non-cash charges of $0.6 million for depreciation and amortization and $2.5 million for stock-based compensation. Cash was used to make advance payments of $1.1 million to vendors for clinical manufacturing activities. Accounts payable and accrued liabilities increased by $6.5 million due to expenses incurred for the clinical manufacturing, process development, and clinical development activities for tenapanor, RDX227675 and RDX98940. Additionally, cash was also used to fund general and administrative expenses incurred for market research and commercialization activities, systems implementation and intellectual property management

Net cash used in operating activities during the six months ended June 30, 2015 was approximately $38.4 million. The net income of $5.5 million was adjusted for non-cash charges of $0.3 million for depreciation and amortization $1.2 million for stock-based compensation. Deferred revenues of $47.1 million related to upfront payments from AstraZeneca were recognized in the six months ended June 30, 2015, and $1.7 million (net) cash was provided by payments from AstraZeneca offset by advance payments made to vendors for clinical manufacturing activities as well as an increase in accounts payable and other accrued liabilities at June 30, 2015.

Cash Flows from Investing Activities

Net cash used by investing activities was $0.5 million for the six months ended June 30, 2016 and was primarily due to the acquisition of property and equipment for our laboratory and office space.

Net cash used by investing activities was $2.3 million for the six months ended June 30, 2015 and was primarily due to the acquisition of property and equipment related to the expansion of our laboratory and related equipment.

Cash Flows from Financing Activities

Net cash provided by financing activities for the six months ended June 30, 2016 was $81.3 million and was primarily due to net proceeds of $80.8 million from a public offering of common stock and the exercise of stock options and purchase rights.

Net cash provided by financing activities for the six months ended June 30, 2015 was $75.0 million and was primarily due to net proceeds of $74.7 million from issuance of common stock and 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 June 30, 2016 (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**
Operating leases [1]	1,358	4,926	2,464		8,748
Total contractual obligations	$ 1,358	$ 4,926	$ 2,464		$ 8,748

[1] Operating leases include total future minimum rent payments under non-cancelable operating lease agreements. In May 2016, we signed an amendment to our facility lease agreement in Fremont, California to add space and to extend the lease term through September 2021 (the Third Amendment). The Third Amendment provides for a tenant improvement allowance of up to $0.4 million and the extended lease has rent escalation clauses through the lease term. Rent increases, including the impact of a rent holiday and leasehold improvement allowance from the landlord, will be recognized as deferred rent and amortized on a straight-line basis over the term of the lease.

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 2015 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 accounting and 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 June 30, 2016. Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance

of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on such evaluation, our principal executive officer and principal accounting and financial officer have concluded that, as of June 30, 2016, 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 June 30, 2016 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Internal control over financial reporting has inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements will not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Table of Contents

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

From time to time, we may be involved in legal proceedings arising in the ordinary course of business. As of June 30, 2016, there is no litigation pending that would reasonably be expected to have a material adverse effect on our results of operations and financial condition

ITEM 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.

Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

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

We are a clinical-stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused substantially all of our efforts on our research and development activities, including developing our clinical product candidates, tenapanor and RDX227675, our lead product candidate from our RDX022 program, and developing our proprietary drug discovery and design platform. To date, we have not commercialized any products or generated any revenue from the sale of products.

We are not profitable and have incurred losses in each year since our inception in October 2007, and we do not know whether or when we will become profitable. We have only a limited operating history upon which to evaluate our business and prospects. We continue to incur significant research, development and other expenses related to our ongoing operations. As of June 30, 2016, we had an accumulated deficit of $153.6 million.

We expect that our operating losses will substantially increase for the foreseeable future as we continue the development of tenapanor and RDX227675. In the fourth quarter of 2015, we initiated two Phase 3 clinical trials to evaluate tenapanor for the treatment of IBS-C. In December 2015, we initiated a clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in end stage renal disease patients, and following an End-of-Phase 2 meeting with the FDA, we incorporated suggested changes to the statistical analysis plan allowing it to serve as the first of two registration trials to support the filing of an NDA. In addition, we expect our operating losses to substantially increase as we incur manufacturing costs for tenapanor and RDX227675, commence an onset-of-action and a Phase 3 clinical trial for RDX227675, complete IND enabling studies and commence a Phase 1 clinical trial for RDX98940, our lead development compound in our RDX009 program, and as we continue our discovery, research, development, manufacturing and commercialization activities.

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

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

We have no products approved for sale and have never generated any revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully complete the development of and obtain the regulatory and marketing approvals necessary to commercialize 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 nonclinical and clinical development of our product candidates;
- obtaining regulatory approvals for our product candidates, either on our own, or with one or more collaboration partners;
- our ability to successfully commercialize our product candidates, either on our own, or with one or more collaboration partners;

Table of Contents

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 an adequate (in amount and quality) supply of product 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 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 are commercializing the product or the product is being commercialized by a collaboration partner, and in such case, whether we have royalty and/or co-promotion rights for that territory. 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 will 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 planned clinical programs for tenapanor and RDX227675, or our other product development and platform development activities.

Since our inception, most of our resources have been dedicated to our research and development activities, including developing our clinical product candidates, tenapanor and RDX227675, 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 conducting the Phase 3 clinical programs for tenapanor and RDX227675, research and development, conducting preclinical studies and clinical trials for our other programs, obtaining regulatory approvals, developing and maintaining scalable manufacturing processes for our product candidates and

sales and marketing. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization or co-promotion of any of our product candidates. Our future funding requirements will depend on many factors, including, but not limited to:

- the progress, timing, scope, results and costs of our clinical trial programs evaluating tenapanor in IBS-C and for the treatment of hyperphosphatemia in ESRD patients on dialysis as well as our decision whether or not to pursue other indications for tenapanor;

- the progress, timing, scope, results and costs of our clinical program for RDX227675;

- the progress, timing, scope, results and costs of IND enabling studies for RDX98940;

- the time and cost necessary to obtain regulatory approvals for our product candidates and the costs of post-marketing studies that could be required by regulatory authorities;

- our ability to successfully commercialize our product candidates, either alone or with one or more collaboration partners;

- the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;

- the selling and marketing costs associated with 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;

Table of Contents

- 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, and any clinical trials we decide to pursue for other product candidates;
- 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 the clinical development of tenapanor and/or RDX227675, delay, limit, reduce or terminate our research activities, preclinical and clinical trials for our other product candidates and our establishment and maintenance of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates, either alone or with a collaboration partner.

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 one of only two product candidates in clinical trials. The clinical and commercial success of tenapanor will depend on a number of factors, including the following:

- our ability to, in a timely manner and under terms that are acceptable to us, to establish one or more collaborative relationships for the commercialization of tenapanor;
- the ability of the third-party manufacturers we contract with, to successfully execute and scale up the manufacturing processes for tenapanor, which has not yet been demonstrated, and to manufacture supplies of tenapanor and to develop, validate and maintain a commercially viable manufacturing processes that are compliant with current good manufacturing practice, or cGMP, requirements;

whether the long-term rat carcinogenicity study required for regulatory approval of tenapanor, which is currently ongoing, will provide data acceptable to the FDA, or whether we will be required to start a new long-term rat carcinogenicity study, which if required, could delay the development of tenapanor;

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 and/or clinical studies, which could delay the commercialization of tenapanor;

whether FDA or foreign regulatory authorities require additional clinical trials than those anticipated prior to approval to market tenapanor;

whether we will be required to conduct clinical trials in addition to those anticipated to obtain adequate commercial pricing;

the prevalence and severity of adverse side effects of tenapanor;

whether tenapanor s safety and efficacy profile is satisfactory to the FDA and foreign regulatory authorities to gain marketing approval;

the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;

our ability, either alone, or with a collaboration partner, to successfully commercialize tenapanor, if approved for marketing and sale by the FDA or foreign regulatory authorities, including educating physicians and patients about the benefits, administration and use of tenapanor;

achieving and maintaining compliance with all regulatory requirements applicable to tenapanor;

Table of Contents

acceptance of tenapanor as safe, effective and well-tolerated by patients and the medical community;

our ability to manage the complex pricing and reimbursement negotiations associated with marketing the same product at different doses for separate indications, if tenapanor is approved for marketing and sale by the FDA or foreign regulatory authorities for both IBS-C and hyperphosphatemia in dialysis patients;

the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;

obtaining and sustaining an adequate level of coverage and reimbursement for tenapanor by third-party payors;

enforcing intellectual property rights in and to tenapanor;

avoiding third-party interference, opposition, derivation or similar proceedings with respect to our patent rights, and avoiding other challenges to our patent rights and patent infringement claims; and

a continued acceptable safety and tolerability profile of tenapanor following approval.

As tenapanor is a first-in-class drug, there is a higher likelihood that approval may not be attained as compared to a class of drugs with approved products. We cannot be certain that tenapanor will be successful in non-clinical safety studies or clinical trials, or that it will 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 ESRD 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 are not successful in completing the development of, obtaining approval for, and commercializing tenapanor, or are significantly delayed in doing so, our business will be materially harmed.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we may encounter substantial delays in 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 must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical and clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. For example, the positive results generated to date in preclinical and clinical studies for tenapanor do not ensure that the ongoing Phase 3 clinical trials for tenapanor, or future clinical trials, will demonstrate similar results. An unexpected adverse event profile, or the results of drug-drug interaction studies, may present challenges for the future development and commercialization of a product candidate

for a particular condition despite receipt of positive efficacy data in a clinical study. For example, in a Phase 2b study evaluating tenapanor for the treatment of hyperphosphatemia in ESRD 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, or if such regulatory approval is obtained, the content of the label approved by regulatory authorities may materially and adversely impact our ability to commercialize the product.

We do not know whether future clinical trials will begin on time, or whether our ongoing or future clinical trials will 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:

manufacture sufficient quantities of product candidate meeting specified quality standards for use in clinical trials;

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;

Table of Contents

recruit suitable patients in a timely manner to participate in our trials;

have patients complete a trial or return for post-treatment follow-up;

ensure that clinical sites observe trial protocol, comply with good clinical practices, or GCPs, or continue to participate in a trial;

address any patient safety concerns that arise during the course of a trial;

address any conflicts with new or existing laws or regulations; or

initiate or add a sufficient number of clinical trial sites.

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

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by an independent data safety monitoring board 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, 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.

We intend to devote significant resources to the development of RDX227675, our lead product candidate in our RDX022 program, which may not be successful in nonclinical studies or clinical trials, receive regulatory approval or be successfully commercialized.

With the advancement of RDX227675 into human studies in June 2015, and the expected initiation of both an onset-of-action clinical trial and a Phase 3 clinical trial for RDX227675 in the fourth quarter of 2016, we expect to invest a significant amount of our efforts and financial resources in the development of RDX227675. We are pursuing

a 505(b)(2) regulatory path for approval of RDX227675, which, among other things allows us to rely on the FDA s previous findings of safety and efficacy and may eliminate the need to conduct certain nonclinical and clinical studies of our product candidate. This regulatory pathway, which can accelerate development, may not be available to us if a pharmaceutically equivalent product to RDX227675 were approved prior to the approval of our 505(b)(2) application. If we are unable to rely upon a 505(b)(2) regulatory pathway for the approval of RDX227675, the development of RDX227675 may be substantially delayed or we may be required to abandon such development.

The clinical and commercial success of RDX227675will depend on a number of factors, including the following:

- the ability of the third-party manufacturers we contract with, to successfully develop and scale up the manufacturing processes for RDX227675, which has not yet been demonstrated, to manufacture supplies of RDX227675 and to develop, validate and maintain a commercially viable manufacturing process that is compliant with current good manufacturing practice, or cGMP, requirements;

- the significant expansion of the market for the treatment of hyperkalemia beyond its currently limited size, including the success of commercial launches of new hyperkalemia products and the use of any such products by nephrologists and cardiologists in the chronic setting;

- our ability to successfully obtain labeling claims necessary or desirable for the commercial success of RDX227675;

- the availability of, and the perceived advantages regarding the relative palatability, relative cost, relative safety, relative tolerance and relative efficacy of alternative and competing treatments;

Table of Contents

the strength and breadth of any intellectual property protection that we may be granted for RDX227675, and our enforcement of any intellectual property rights in RDX227675;

the timely receipt of necessary marketing approvals and exclusivity periods, if any, from the FDA and foreign regulatory authorities;

our ability to successfully commercialize RDX227675, 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 RDX227675;

obtaining and sustaining an adequate level of coverage and reimbursement for RDX227675 by third-party payors; and

the effectiveness of our marketing, sales and distribution strategy and operations.

As a result of pursuing a 505(b)(2) path for RDX227675, we will not evaluate the efficacy of RDX227675 in patients with hyperkalemia prior to the initiation of the Phase 3 clinical program. We cannot be certain that clinical trials evaluating RDX227675 will establish a safety and efficacy profile sufficient to enable RDX227675 to gain approval by the FDA, or if approved, compete effectively with alternative and competing treatments. 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 RDX227675 may possess. Accordingly, there can be no assurance that RDX227675 will ever be successfully commercialized or that we will ever generate revenue from sales of RDX227675. If we are not successful in completing the development of, obtaining approval for, and commercializing RDX227675, or are significantly delayed in doing so, our business will be materially harmed.

We may not be successful in our efforts to develop our product candidates that are at an early stage of development, including RDX98940, the development candidate selected from our RDX009 program, or expand our pipeline of product candidates.

A key element of our strategy is to expand our pipeline of product candidates utilizing our proprietary drug discovery and design platform and to advance such product candidates through clinical development. In December 2015, we selected RDX98940 as our development candidate for our RDX009 program and we intend to file an IND in the fourth quarter of 2016 to commence clinical trials in the U.S. This product candidate, and those product candidates that are in the discovery and lead identification stages of preclinical development will require substantial preclinical and clinical development, testing and regulatory approval prior to commercialization. In particular, tenapanor and RDX227675 are our only product candidates in clinical trials and all of our other product candidates are in the preclinical stage with significant research and development required before we could 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 research programs, there can be no assurance that any product candidates will reach the clinic or be successfully developed or commercialized.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Although our research and development efforts to date have resulted in several development programs, we may not be able to develop product candidates that are safe,

effective and well-tolerated. Our research programs may initially show promise in identifying potential product candidates, and we may select candidates for development, yet we may fail to 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 or commercial criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe, effective and well-tolerated by patients, the medical community or third-party payors, if applicable.

Even if we are successful in continuing to expand our pipeline, through our own research and development efforts 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.

Table of Contents

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 have developed APECCS as a component of this of this platform. We utilize APECCS in the design of our small molecules and to identify new and potentially novel targets in the GI tract. However, there can be no assurance that APECCS will be able to identify new targets in the GI tract or that any of these potential targets or other aspects of our proprietary drug discovery and design platform will yield product candidates that could enter clinical development and, ultimately, be commercially valuable.

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. In addition, we may not be able to enter into agreements on suitable terms to utilize technologies required to exploit certain capabilities of APECCS, and in such case, we may be forced to limit our use or further development of APECCS, or to modify APECCS for continued use. It may not be possible to modify APECCS in manner that avoids the utilization of certain technologies, without materially and adversely affecting the performance of APECCS or without incurring substantial cost and delay in advancement of the system. 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, or if we are forced to limit our use or further development of APECCS due to the inability to enter into agreements on suitable terms to permit the utilization of technologies required to exploit APECCS, 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 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, and other third parties, such as CROs, to conduct clinical trials on our product candidates. The third parties with whom we contract for execution of the clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely, and will continue to rely, on these third parties to conduct some of our 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 new or traditional or existing therapies, including recently approved therapies or therapies that the physician community anticipate will be approved;

acceptance by physicians, major operators of clinics and patients of 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 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 a Phase 2b clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, 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 with tenapanor or trials we conduct with our other product candidates, reveal an unacceptable severity and prevalence of these or other side effects, such trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of tenapanor, or any such other product candidate, for any or all targeted indications. Additionally, despite a positive efficacy profile, the prevalence and/or severity of these or other side effects could cause us to cease further development of a product candidate for a particular indication, or entirely. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

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

- regulatory authorities may withdraw their approval of the product or seize the product;
- we 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 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;

Table of Contents

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 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 and RDX227675, as well as 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 ESRD patients on dialysis, 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. 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. Additionally, RDX227675, if approved, will compete directly with Kayexalate and its generic equivalents, known as sodium polystyrene sulfonate, on the market in the United States. In addition, Relypsa recently launched patiromer (Veltassa) in the United States for the treatment of hyperkalemia and announced its acquisition by Galenica in July 2016. Finally, a new drug application, or NDA, was submitted in June 2015, for a sodium zirconium cyclosilicate-based oral potassium binder being developed for the treatment of hyperkalemia by AstraZeneca after its acquisition of ZS Pharma in December 2015.

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 is approved 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. Additionally, Synergy filed an NDA for Plecanatide for the treatment of CIC in January 2016, and is currently conducting two Phase 3 clinical trials of Plecanatide for the treatment of IBS-C.

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

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

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

Table of Contents

We currently do not have a sales organization. In order to commercialize or co-promote tenapanor and any of our other product candidates, either alone, or with a collaboration partner, 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. In order to commercialize tenapanor or RDX227675 outside of the United States, we expect to enter into collaborative relationships with one or more third parties. Additionally, in order to commercialize tenapanor for IBS-C, we expect to enter into a collaborative relationship with one or more third parties in the United States to address the primary care market. There can be no assurances that we will be successful in establishing such relationships in a timely manner or on terms that are acceptable to us. 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 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 we are completely dependent on our contract manufacturing partners for compliance with the regulatory requirements, known as cGMPs, for manufacture of both active drug substances and finished drug products.

If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would 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

Table of Contents

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 and RDX227675, if approved. We may be unable to sell tenapanor and/or RDX227675, if approved, to dialysis providers on a profitable basis if third-party payors reduce their current levels of payment, or if our costs of production increase faster than increases in reimbursement levels.

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

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for 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;

Table of Contents

costs to defend the related litigation;

a diversion of management s time and our resources;

substantial monetary awards to trial participants or patients;

regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;

loss of revenue; and

the inability to commercialize or co-promote our product candidates.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of any products we develop. We currently carry product liability insurance covering use in our clinical trials in the amount of $10.0 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

We are highly dependent on the services of our President and Chief Executive Officer, Michael Raab, our 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 clinical, 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. 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.

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Table of Contents

Our business is increasingly dependent on critical, complex and interdependent information technology systems to support business processes as well as internal and external communications. The size and complexity of our computer systems make them vulnerable to breakdown, malicious intrusion and computer viruses. We have developed systems and processes that are designed to protect our information and prevent data loss and other security breaches, including systems and processes designed to reduce the impact of a security breach; however, such measures cannot provide absolute security, and we have taken, and will take, additional security measures to protect against any future intrusion. Any failure to protect against breakdowns, malicious intrusions and computer viruses may result in the impairment of production and key business processes. In addition, our systems are potentially vulnerable to data security breaches, whether by employees or others, which may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personal information of our employees, clinical trial patients, customers, and others. Such disruptions and breaches of security could expose us to liability and have a material adverse effect on the operating results and financial condition of our business.

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.

In addition, we are in the process of implementing an enterprise resource planning, or ERP, system for our company. An ERP system is intended to combine and streamline the management of our financial, accounting, human resources, sales and marketing and other functions, enabling us to manage operations and track performance more effectively. However, an ERP system 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. 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.

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

Table of Contents

We may form collaboration partnerships in the future, 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 that we believe will complement or augment our existing business. In particular, we expect to form one or more collaboration partnerships in connection with the commercialization of tenapanor outside of the United States, and in the United States for IBS-C to address the primary care market, if approved. We face significant competition in seeking appropriate collaboration partners, and the negotiation process to secure appropriate terms is time-consuming and complex. Any delays in identifying suitable collaboration partners and entering into agreements to develop our product candidates could also delay the commercialization of our product candidates, which may reduce their competitiveness even if they reach the market. Moreover, we may not be successful in our efforts to establish such a collaboration partnership for any future product candidates and programs on terms that are acceptable to us, or at all. This may be because our product candidates and programs may be deemed to be at too early of a stage of development for collaborative effort, our research and development pipeline may be viewed as insufficient, and/or third parties may not view our product candidates and programs as having sufficient potential for commercialization, including the likelihood of an adequate safety and efficacy profile. Even if we are successful in entering into a collaboration partnership or license arrangement, there is no guarantee that the collaboration partnership will be successful, or that any future collaboration partner will commit sufficient resources to the development, regulatory approval, and commercialization effort for such products, or that such alliances will result in us achieving revenues that justify such transactions.

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

We intend to consider strategic transactions, such as acquisitions of companies, asset purchases, and or in-licensing of products, product candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, collaboration partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

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

write-downs of assets or goodwill or impairment charges;

increased amortization expenses;

difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;

impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and

inability to retain key employees of any acquired businesses.

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

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

Table of Contents

We may decide to seek marketing approval for certain of our product candidates outside the United States or otherwise engage in business outside the United States, including entering into contractual agreements with third-parties. We expect that we will be subject to additional risks related to entering into these international business markets and relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing United States and foreign drug import and export rules;
- reduced protection for intellectual property rights in foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems, and different competitive drugs;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from development work conducted by these distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

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

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

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

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

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

Our ability to attract and retain collaboration partners or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the

Table of Contents

prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, presidential elections, other political influences and inflationary pressures. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. We cannot anticipate all the ways in which the current global economic climate and global financial market conditions could adversely impact our business.

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

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

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

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

Risks Related to Government Regulation

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

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of drug products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country. Neither we nor any of our collaboration partners is permitted to market any drug product in the United States until we receive marketing approval from the FDA. We have not submitted an application or obtained marketing approval for any of our product candidates anywhere in the world. Obtaining regulatory approval of a 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

Table of Contents

refusal to approve pending NDAs or supplements to approved NDAs.

Prior to obtaining approval to commercialize a drug candidate in the United States or abroad, we or our collaboration partners must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory agencies, that such drug candidates are safe and effective for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the drug candidate, the disease or condition that the drug candidate is designed to address, and the regulations applicable to any particular drug candidate. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our drug candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering drug candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a drug candidate for any or all targeted indications.

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

the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our, or our collaboration partners , clinical studies;

the population studied in the clinical program may not be sufficiently broad or representative to assure safety in the full population for which approval is sought;

the FDA or comparable foreign regulatory authorities may disagree with the interpretation of data from preclinical studies or clinical studies;

the data collected from clinical studies of our product candidates may not be sufficient to support the submission of a NDA or other submission or to obtain regulatory approval in the United States or elsewhere;

we or our collaboration partners may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate s risk-benefit ratio for its proposed indication is acceptable;

- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers responsible for clinical and commercial supplies; and

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

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

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

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

Table of Contents

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

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

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

warning letters, fines or holds on clinical trials;

restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;

injunctions or the imposition of civil or criminal penalties;

suspension or revocation of existing regulatory approvals;

suspension of any of our ongoing clinical trials;

refusal to approve pending applications or supplements to approved applications submitted by us;

restrictions on our or our contract manufacturers operations; or

product seizure or detention, or refusal to permit the import or export of products.

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

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

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements or may not be able to meet supply demands.

All entities involved in the preparation of product candidates for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA or comparable regulatory filing on a timely basis and must adhere to cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with

Table of Contents

the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

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

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

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

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

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

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA and other government agencies. If tenapanor, RDX227675 or our other product candidates receive marketing approval, we and our collaborating partners, if any, will be restricted from marketing the product outside of its approved labeling, also referred to as off-label promotion. However, physicians may nevertheless prescribe an approved product to their patients in a manner that is inconsistent with the approved label, which is an off-label use. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations regarding off-label promotion. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of our product candidates for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

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

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

Table of Contents

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, RDX227675 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 ESRD patients on dialysis, 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.

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

Although we do not currently have any products on the market, once we begin commercializing our products, we and our collaboration partners, if any, 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.

Table of Contents

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

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

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

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the United States, the Affordable Care Act was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer s outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation s automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, the ATRA was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or

reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

Risks Related to Intellectual Property

We may become subject to claims alleging infringement of third parties patents or proprietary rights and/or claims seeking to invalidate our patents, which would be costly, time consuming and, if successfully asserted against us, delay or prevent the development and commercialization of tenapanor, RDX227675 or our other product candidates, or prevent or delay the continued use of our drug discovery and development platform, including APECCS.

There have been many lawsuits and other proceedings asserting infringement or misappropriation of patents and other intellectual property rights in the pharmaceutical and biotechnology industries. There can be no assurances that we will not be subject to claims alleging that the manufacture, use or sale of tenapanor, RDX227675 or any other product candidates, or that the use of our drug discovery and development platform, including APECCS, infringes existing or future third-party patents, or that such claims, if any, will not be successful. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of tenapanor, RDX227675 or other product candidates or by the use of APECCS. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant product revenue and against whom our own patent portfolio may thus have no deterrent effect. We may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of tenapanor, RDX227675 or our other product candidates, or by the use of APECCS.

Table of Contents

We may be subject to third-party patent infringement claims in the future against us or our that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney s fees if we are found to be willfully infringing a third party s patents. We may be required to indemnify future collaboration partners against such claims. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us we could be forced to stop or delay research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. In addition, if a patent infringement suit were brought against us regarding the use of APECCS, we could be forced to stop our use of APECCS or modify our processes to avoid infringement, which may not be possible at a reasonable cost, if at all, and which could result in substantial delay in our use of APECCS for the discovery of new product candidates or potential targets. As a result of patent infringement claims, or in order to avoid potential claims, we may choose to seek, or be required to seek, a license from the third party and would most likely be required to pay license fees or royalties or both. These licenses may not be available on acceptable terms, or at all. Even if we were able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to cease our use of APECCS or some other aspect of our business operations if, as a result of actual or threatened patent infringement claims, we 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

Table of Contents

requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability against our intellectual property related to a product candidate, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business. Moreover, our competitors could counterclaim that we infringe their intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

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

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

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

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, if any, one of the U.S. patents covering each of such approved product(s) or the use thereof may be eligible for up to five years of patent term restoration under the Hatch-Waxman Act. The Hatch-Waxman Act allows a maximum of one patent to be extended per FDA approved product. Patent term extension also may be available in certain foreign countries upon regulatory approval of our product candidates. Nevertheless, we may not be granted patent term extension either in the United States or in any foreign country because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

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

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.

Table of Contents

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

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

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

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

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

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

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

Many of our employees, consultants and contractors were previously employed at or engaged by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees, consultants and contractors, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees, consultants and contractors do not use the intellectual property and other proprietary information or know-how or trade secrets of others in their work for us, and do not perform work for us that is in conflict with their obligations to another employer or any other entity, we may be subject to claims that we or these employees, consultants and contractors have used or disclosed such intellectual property, including know-how, trade secrets or other proprietary information.

In addition, an employee, advisor or consultant who performs work for us may have obligations to a third party that are in conflict with their obligations to us, and as a result such third party may claim an ownership interest in the intellectual property arising out of work performed for us. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, or access to consultants and contractors. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

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 and others such as:

- results from, or any delays in, clinical trial programs relating to our product candidates, including the ongoing and planned clinical trials for tenapanor and RDX227675, our lead product candidate from our RDX022 program;
- 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 RDX227675, or specific label restrictions or patient populations for its use, or changes or delays in the regulatory review process;
- announcements relating to future collaboration partnerships;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to our product candidates;
- the success of our testing and clinical trials;
- Failure to meet any of our projected timelines or goals with regard to the clinical development of any of our product candidates
- the success of our efforts to acquire or license or discover additional product candidates;
- any intellectual property infringement actions in which we may become involved;

the success of our efforts to obtain adequate intellectual property protection for our product candidates;

announcements concerning our competitors or the pharmaceutical industry in general;

achievement of expected product sales and profitability;

manufacture, supply or distribution shortages;

actual or anticipated fluctuations in our operating results;

FDA or other U.S. or foreign regulatory actions affecting us or our industry or other healthcare reform measures in the 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

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

As of June 30, 2016, entities affiliated with New Enterprise Associates or NEA, a venture capital fund associated with one of our directors, collectively beneficially hold approximately 36.6% of our capital stock, including warrants exercisable for shares of our common stock, and NEA together with our executive officers and directors beneficially owned approximately 37.2% of our capital stock, including warrants exercisable for shares of our common stock. Therefore, these stockholders may be able to determine all matters requiring stockholder approval, and the entities affiliated with New Enterprise Associates alone, will have significant ability to influence decisions through their ownership position. 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.

As of July 18, 2016, the date of the closing of our private placement of equity securities, entities affiliated with NEA, collectively beneficially hold approximately 31.8% of our capital stock, including warrants exercisable for shares of our common stock, and NEA together with our executive officers and directors beneficially owned approximately 32.3% of our capital stock, including warrants exercisable for shares of our common stock. Therefore, these stockholders may be able to determine all matters requiring stockholder approval, and the entities affiliated with NEA alone, will have significant ability to influence decisions through their ownership position. For example, these stockholders may be able to 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.

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 June 30, 2016, we had 34,650,266 shares of common stock outstanding. Of those shares, approximately 12.0 million, were held by current directors, executive officers and other affiliates, or may otherwise be subject to Rule 144 under the Securities Act of 1933, or the Securities Act. As of July 18, 2016, we had 47,250,496 shares of common stock outstanding. Of those shares, approximately 14.3 million, were held by current directors, executive officers and other affiliates, or may otherwise be subject to Rule 144 under the Securities Act of 1933, or the Securities Act.

In addition, as of June 30, 2016, approximately 2.5 million 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. In addition, approximately 2.2 million shares that are subject to outstanding warrants are eligible for sale in the public market. 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 5.6 million shares of our outstanding common stock as of June 30, 2016, are entitled to rights with respect to the registration of their shares under the Securities Act. The holders of approximately 18.2 million shares of our outstanding common stock as of July 18, 2016, are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

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

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;

Table of Contents

no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;

the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;

the required approval of at least 66 $^{2}/_{3}$% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;

the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;

the ability of our board of directors to alter our bylaws without obtaining stockholder approval;

the required approval of at least 66 $^{2}/_{3}$% of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;

a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;

the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and

advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror s own slate of directors or otherwise attempting to obtain control of us.

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

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

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

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

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

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

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

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

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

Table of Contents

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 Sales of Equity Securities

On July 14, 2016, we entered into a Securities Purchase Agreement, or the Purchase Agreement, with the purchasers named therein, or the Purchasers. Pursuant to the Purchase Agreement, on July 18, 2016 we sold an aggregate of 12,600,230 shares of common stock, or the Shares, for aggregate gross proceeds of approximately $110.0 million. The purchase price for each share was $8.73, which was equal to the consolidated closing bid price on the NASDAQ Global Market on the day of pricing, July 14, 2016.

In connection with the Purchase Agreement, we entered into a Registration Rights Agreement, or the Registration Rights Agreement, with the Purchasers. Pursuant to the Registration Rights Agreement, we agreed to prepare and file a registration statement with the SEC, by September 1, 2016 for purposes of registering the resale of the Shares We also agreed, among other things, to indemnify the selling holders under the registration statements from certain liabilities and to pay all fees and expenses (excluding underwriting discounts and selling commissions and all legal fees of any selling holder) incident to our obligations under the Registration Rights Agreement.

The issue and sale of the Shares pursuant to the Purchase is exempt from registration pursuant to the exemption for transactions by an issuer not involving any public offering under Section 4(a)(2) the Securities Act of 1933, as amended, and Regulation D under the Securities Act of 1933, as amended.

Use of Proceeds

Not applicable.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

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	
10.1	Securities Purchase Agreement by and among Ardelyx, Inc. and the purchasers signatory thereto, dated July 14, 2016.				X
10.2	Registration Rights Agreement by and among Ardelyx, Inc. and the investors signatory thereto, dated July 14, 2016.				X
10.3	Third Amendment to Lease by and between Ardelyx, Inc. and 34175 Ardenwood venture, LLC, dated as of April 28, 2016.				X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.				
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 June 30, 2016 and December 31, 2015, (ii) Condensed Statements of Operations and Comprehensive (Loss) Income for the three and six months ended June 30, 2016 and 2015; (iii) Condensed Statements of Cash Flows for the six months ended June 30, 2016 and 2015; 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: August 8, 2016

By: /s/ Mark Kaufmann
Mark Kaufmann

Chief Financial Officer

(Principal Accounting and Financial Officer)