ARDELYX, INC.
Form 10-Q
August 07, 2018
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 10 Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2018

OR

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

FOR THE TRANSITION PERIOD FROM TO

COMMISSION FILE NUMBER: 001 36485

ARDELYX, INC.

(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE	26 1303944
(STATE OR OTHER JURISDICTION OF INCORPORATION OR ORGANIZATION)	(I.R.S. EMPLOYER IDENTIFICATION 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 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 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, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b 2 of the Exchange Act.

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

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

Exchange Act.

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

The number of issued and outstanding shares of the registrant's Common Stock, $0.0001 par value per share, as of August 2, 2018, was 62,053,751.

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ARDELYX, INC.

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PART I. FINANCIAL INFORMATION

ITEM 1. CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

ARDELYX, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share amounts)

	June 30, 2018 (Unaudited)	December 31, 2017 (1)
Assets		
Current assets:		
Cash and cash equivalents	$ 91,751	$ 75,383
Short-term investments	120,980	58,593
Accounts receivable	30	10,796
Unbilled license revenue	5,000	—
Prepaid expenses and other current assets	3,927	4,940
Total current assets	221,688	149,712
Property and equipment, net	6,689	8,032
Other assets	159	159
Total assets	$ 228,536	$ 157,903
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,172	$ 3,933
Accrued compensation and benefits	2,203	3,229
Uncharged license fees	1,000	—
Accrued and other liabilities	9,234	10,709
Total current liabilities	15,609	17,871
Loan payable, long term	48,836	—
Other long-term liabilities	677	720
Total liabilities	65,122	18,591
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized; no shares issued and outstanding as of June 30, 2018 and December 31, 2017, respectively.	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized; 62,053,751 and 47,534,979 shares issued and outstanding as of June 30, 2018 and December 31, 2017, respectively.	6	5
Additional paid-in capital	476,968	417,568
Accumulated deficit	(313,524)	(278,214)
Accumulated other comprehensive loss	(36)	(47)
Total stockholders' equity	163,414	139,312
Total liabilities and stockholders' equity	$ 228,536	$ 157,903

(1)

Derived from the audited consolidated financial statements included in the Company's Annual Report on Form 10 K for the year ended December 31, 2017.

See accompanying notes to Condensed Consolidated Financial Statements.

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ARDELYX, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except share and per share amounts)

(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Revenues:				
Licensing revenue	$ —	$ —	$ 2,320	$ —
Other revenue	30	—	30	—
Total revenues	30	—	2,350	—
Cost of revenue	—	—	464	—
Gross profit	30	—	1,886	—
Operating expenses:				
Research and development	16,046	20,572	$ 29,396	$ 42,960
General and administrative	6,138	5,846	12,329	11,892
Total operating expenses	22,184	26,418	41,725	54,852
Loss from operations	(22,154)	(26,418)	(39,839)	(54,852)
Other income (expense), net	(135)	697	535	1,123
Loss before provision for income taxes	(22,289)	(25,721)	(39,304)	(53,729)
Provision for income taxes	2	—	6	—
Net loss	$ (22,291)	$ (25,721)	$ (39,310)	$ (53,729)
Net loss per common share, basic and diluted	$ (0.42)	$ (0.54)	$ (0.78)	$ (1.13)
Shares used in computing net loss per share - basic and diluted	52,824,483	47,403,243	50,206,470	47,373,404
Comprehensive loss:				
Net loss	(22,291)	(25,721)	$ (39,310)	$ (53,729)
Unrealized (loss) gain on available-for-sale securities, net of tax	55	9	11	31
Comprehensive loss	$ (22,236)	$ (25,712)	$ (39,299)	$ (53,698)

See accompanying notes to Condensed Consolidated Financial Statements.

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ARDELYX, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

(Unaudited)

	Six Months Ended June 30,	
	2018	2017
Operating activities		
Net loss	$ (39,310)	$ (53,729)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	1,343	1,242
Amortization of deferred financing costs	59	325
Amortization of deferred compensation for services	101	91
Amortization of premium on investment securities	(256)	1
Stock-based compensation	5,028	4,899
Non-cash interest expense relating to loan payable	54	—
Changes in operating assets and liabilities:		
Accounts receivable	10,766	—
Prepaid expenses and other assets	1,192	(2,961)
Accounts payable	(706)	(451)
Accrued compensation and benefits	(1,026)	(562)
Accrued and other liabilities	(2,064)	498
Net cash used in operating activities	(24,819)	(50,647)
Investing activities		
Proceeds from maturities of investments	56,050	75,434
Sales and redemptions of investments	850	10,482
Purchases of investments	(119,021)	(44,748)
Purchases of property and equipment	(55)	(1,907)
Net cash (used in) provided by investing activities	(62,176)	39,261
Financing activities		
Proceeds from loan payable, net of issuance costs	49,292	—
Proceeds from underwritten public offering, net of issuance costs	53,770	—
Proceeds from issuance of common stock under stock plans	301	424
Net cash provided by financing activities	103,363	424
Net decrease in cash and cash equivalents	16,368	(10,962)
Cash and cash equivalents at beginning of period	75,383	74,598
Cash and cash equivalents at end of period	$ 91,751	$ 63,636
Supplementary disclosure of non-cash financing information:		
Issuance of derivative in connection with issuance of loan payable	$ 546	$ —

See accompanying notes to Condensed Consolidated Financial Statements.

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ARDELYX, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS

(Unaudited)

NOTE 1. ORGANIZATION AND BASIS OF PRESENTATION

Ardelyx, Inc., or "the Company," is a specialized biopharmaceutical company focused on developing disruptive medicines for the treatment of renal diseases, which affect both the heart and the kidneys. Tenapanor, a first-in-class inhibitor of NHE3, is being evaluated in a second Phase 3 trial for the treatment of hyperphosphatemia in patients with end-stage renal disease, or ESRD, who are on dialysis. The Company is also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia as well as tenapanor for the treatment of people with irritable bowel syndrome with constipation, or IBS-C, for which the Company is preparing to submit a New Drug Application, or NDA, to the United States Food and Drug Administration, or FDA, in the second half of 2018.

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

Basis of Presentation

These unaudited condensed consolidated 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, or 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 consolidated 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 three and six months ended June 30, 2018, are not necessarily indicative of results to be expected for the entire year ending December 31, 2018, or future operating periods.

The accompanying condensed consolidated financial statements and related financial information should be read in conjunction with the audited consolidated financial statements and the related notes thereto for the year ended December 31, 2017, included in the Company's Annual Report on Form 10 K filed with the SEC (the "2017 Form 10 K"). The balance sheet at December 31, 2017, has been derived from the audited consolidated financial statements at that date, as filed with the 2017 Form 10 K.

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

NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates

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

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Accrued Research and Development Expenses

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

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

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

Revenue Recognition

On January 1, 2018 the Company adopted the new standard for Revenue from Contracts with Customers, Topic 606, on a modified retrospective method as an adjustment to the opening balance of retained earnings of the annual reporting period. On January 1, 2018, the Company recorded an increase in current assets of $5.0 million representing a future receivable related to the first milestone under the Company's license agreement with Kyowa Hakko Kirin Co., Ltd., or KHK,, which the Company believes is not materially at risk, an increase in current liabilities of $1.0 million representing a future payable related to the corresponding payment to AstraZeneca AB, or AstraZeneca,, in accordance with the Company's termination agreement with AstraZeneca and a related decrease in its accumulated deficit of approximately $4.0 million as the new standard permits revenue from milestones that possess certain criteria to be recognized earlier of approximately $4.0 million as the new standard contains different recognition criteria related to milestones than under the previous standard, Revenue Recognition, Multiple-Element Arrangements, ASC 605, Licensing revenues.

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

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract;

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

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

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

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

Reclassification

Approximately $0.2 million in the six months ended June 30, 2017, which was previously recorded within “Proceeds from issuance of common stock under stock plans” in Financing activities in the Statement of Cash Flows, has been reclassified as a Changes in operating assets and liabilities item “Prepaid expenses and other assets” within Operating activities.

Recent Accounting Pronouncements

New Accounting Pronouncements - Recently Adopted

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, which amends the guidance for accounting for revenue from contracts with customers. This ASU

supersedes the revenue recognition requirements in Topic 605, Revenue Recognition, and creates a new Topic 606, Revenue from Contracts with Customers. In 2015 and 2016, the FASB issued additional ASUs related to Topic 606 that delayed the effective date of the guidance and clarified various aspects of the new revenue guidance, including principal versus agent considerations, identifying performance obligations, and licensing, and they include other improvements and practical expedients. The Company adopted this new standard on January 1, 2018 using the modified retrospective transition method.

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Impact of Adoption

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

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

As a result of adopting Topic 606 on January 1, 2018, the following financial statement line items in the Company's Condensed Consolidated Balance Sheet at June 30, 2018 and the Condensed Consolidated Statement of Income for the six months ended June 30, 2018 were affected.

	June 30, 2018		
	As Reported	Under Topic 605	Effect of Change
Total current assets	$ 221,688	216,688	$ 5,000
Total current liabilities	15,609	14,609	1,000
Accumulated deficit	(313,524)	(317,524)	4,000

	Six Months Ended June 30, 2018		
	As Reported	Under Topic 605	Effect of Change
Revenue:			
Licensing revenue	$ 2,320	2,320	$ —
Other revenue	30	30	—
Cost of revenue	464	464	—

In May 2017, FASB issued ASU No. 2017-09, Compensation-Stock Compensation (Topic 718) - Scope of Modification Accounting (ASU 2017-09). The amendments included in this update provide guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting. The amendments in this update will be applied prospectively to an award modified on or after the adoption date. On January 1, 2018, we adopted ASU 2017-09 and the adoption of this standard did not have a material impact on the Company's condensed consolidated financial statements.

New Accounting Pronouncements Not Yet Adopted

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842), which replaces most current lease guidance when it becomes effective. This standard update intends to increase the transparency and improve comparability by requiring entities to recognize assets and liabilities on the balance sheet for all leases, with certain exceptions. The new standard states that a lessee will recognize a lease liability for the obligation to make lease payments and a right-of-use asset for the right to use the underlying asset for the lease term. Leases will be classified as either finance or operating, with classification affecting the pattern of expense recognition in the consolidated statements of operations. The new guidance will be effective for the Company starting in the first quarter of fiscal 2019. Early adoption is permitted. The Company plans to adopt the new guidance effective January 1, 2019, and is currently evaluating the effect that this guidance will have on its consolidated financial statements and related disclosures.

In June 2018, the FASB issued ASU No. 2018-07, Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting. ASU 2018-07 is intended to reduce the cost and complexity and to improve financial reporting for nonemployee share-based payments. ASU 2018-07 expands the scope of Topic 718, Compensation-Stock Compensation (which currently only includes share-based payments to employees) to include share-based payments issued to nonemployees for goods or services. Consequently, the accounting for share-based payments to nonemployees and employees will be substantially aligned. ASU 2018-07 supersedes Subtopic 505-50, Equity-Based Payments to Non-

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Employees. ASU 2018-07 is effective for the Company for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year and early adoption is permitted. The Company is currently assessing the impact of this standard on its consolidated financial statements.

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

NOTE 3. CASH, CASH EQUIVALENTS AND INVESTMENTS

Securities classified as cash, cash equivalents and short-term investments as of June 30, 2018 and December 31, 2017, are summarized below (in thousands). Estimated fair value is based on quoted market prices for these investments.

	June 30, 2018			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 2,932	—	—	$ 2,932
Money market funds	67,611	—	—	67,611
Corporate bonds	2,664		—	2,664
Commercial paper	18,544	—	—	18,544
Total cash and cash equivalents	$ 91,751	$ —	$ —	$ 91,751
Short-term investments				
U.S. treasury securities	8,459	1	—	8,460
Corporate bonds	38,788	—	(31)	38,757
Commercial paper	64,642	—	(2)	64,640
Asset-backed securities	9,126	—	(3)	9,123
Total short-term investments	$ 121,015	$ 1	$ (36)	$ 120,980
Total cash equivalents and investments	$ 212,766	$ 1	$ (36)	$ 212,731

	December 31, 2017			
		Gross Unrealized		
	Amortized Cost	Gains	Losses	Fair Value
Cash and cash equivalents:				
Cash	$ 5,882	$ —	$ —	$ 5,882
Money market funds	68,651	—	—	68,651
Commercial paper	850	—	—	850
Total cash equivalents and investments	$ 75,383	$ —	$ —	$ 75,383
Short-term investments				

U.S. treasury securities	$ 3,994	—	(1)	$ 3,993
Corporate bonds	26,853	—	(26)	26,827
Commercial paper	19,584	—	(14)	19,570
Asset-backed securities	8,209	—	(6)	8,203
Total short-term investments	$ 58,640	$ —	$ (47)	$ 58,593
Total cash equivalents and investments	$ 134,023	$ —	$ (47)	$ 133,976

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

All available-for-sale securities held as of June 30, 2018, had contractual maturities of less than one year. The Company's available-for-sale securities are subject to a periodic impairment review. The Company considers a debt security to be impaired when its fair value is less than its carrying cost, in which case the Company would further review the investment to determine whether it is other-than-temporarily impaired. When the Company evaluates an investment for other-than-temporary impairment, the Company reviews factors such as the length of time and extent to which fair value has been below cost basis, the financial condition of the issuer and any changes thereto, intent to sell, and whether it is more likely than not the Company will be required to sell the investment before the recovery of it cost basis. If an investment is other-than-temporarily impaired, the Company writes it down through the statement of operations to its fair value and establishes that value as a new cost basis for the investment. The Company did not identify any of its available-for-sale securities as other-than-temporarily impaired in any of the periods presented. As of June 30, 2018, no investment was in a continuous unrealized loss position for more than one year and the Company believes that is more likely than not the investments will be held until maturity or a forecasted recovery of fair value.

NOTE 4. FAIR VALUE MEASUREMENTS

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

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

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

Level 2 – Valuations based on inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities. Examples of assets and liabilities utilizing Level 2 inputs are corporate bonds, commercial paper, certificates of deposit and over-the-counter derivatives.

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

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

	June 30, 2018			
	Total	Level 1	Level 2	Level 3
Assets:				
Money market funds	$ 67,611	$ 67,611	$ —	$ —
U.S. treasury securities	8,460	8,460	—	—
Corporate bonds	41,421	—	41,421	—
Commercial paper	83,184	—	83,184	—
Asset-backed securities	9,123	—	9,123	—
Total	$ 209,799	$ 76,071	$ 133,728	$ —
Liabilities:				
Derivative liability	$ 546	$ —	$ —	$ 546

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

Where quoted prices are available in an active market, securities are classified as Level 1. The Company classifies money market funds, U.S. treasury securities and U.S. government-sponsored agency bonds 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 corporate bonds, commercial paper and asset-backed securities as Level 2. In certain cases, where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3. There were no transfers between Level 1 and Level 2 during the periods presented.

In May 2018, pursuant to the loan and security agreement with Solar Capital Ltd. and Western Alliance Bank (see Note 5), the Company entered into an Exit Fee Agreement under which the Company agreed to pay $1.5 million in cash, or the Exit Fee, upon any change of control transaction or if the Company obtains FDA approval of tenapanor in the treatment of hyperphosphatemia in ESRD patients on dialysis and FDA approval of tenapanor for the treatment of patients with IBS-C. Notwithstanding the prepayment or termination of the Term Loan, the Company's obligation to pay the Exit Fee will expire 10 years from the Closing Date. The Company evaluated that the Exit Fee is a freestanding derivative which should be accounted for at fair value on a recurring basis. The estimated fair value of the Exit Fee was determined to be $546,000 and is recorded as a derivative liability and included in accrued and other liabilities on the accompanying consolidated balance sheet.

The fair value of the derivative liability was determined using a discounted cash flow analysis, and is classified as a Level 3 measurement within the fair value hierarchy since the Company’s valuation utilized significant unobservable inputs. Specifically, the key assumptions included in the calculation of the estimated fair value of the derivative instrument include: i) the Company’s estimates of both the probability and timing of a potential $1.5 million payment to Solar Capital Ltd. and Western Alliance Bank as a result of the FDA approvals, and ii) a discount rate which was derived from the Company's estimated cost of debt. Generally, increases or decreases in the probability of occurrence would result in a directionally similar impact in the fair value measurement of the derivative instrument and it is estimated that a 10% increase (decrease) in the probability of occurrence would result in a fair value fluctuation of approximately $55,000.

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The carrying amounts reflected in the balance sheets for cash equivalents, short-term investments, accounts receivable, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values at both June 30, 2018 and December 31, 2017, due to their short-term nature.

NOTE 5. BORROWINGS

Solar Capital and Western Alliance Bank Loan Agreement

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

Borrowings under the Term Loan bear interest at a floating per annum rate equal to 7.45% plus the one-month LIBOR. The Company is permitted to make interest-only payments on the Term Loan through December 1, 2020 if the Company achieves its primary endpoint in the Phase 3 study of tenapanor for the treatment of hyperphosphatemia in end-stage renal disease patients on dialysis, prior to June 1, 2020; otherwise, the Company is permitted to make interest-only payments on the Term Loan only through June 1, 2020. Accordingly, beginning on either June 1, 2020 or December 1, 2020, as applicable, through the maturity date, the Company will be required to make monthly payments of interest plus repayment of the Term Loan in consecutive equal monthly installments of principal. The Company paid a closing fee of 1% of the Term Loan, or $0.5 million, upon the closing of the Term Loan. The Company is obligated to pay a final fee equal to 3.95% of the Term Loan upon the earliest to occur of the maturity date, the acceleration of the Term Loan, the prepayment or repayment of the Term Loan or the termination of the Loan Agreement. The Company may voluntarily prepay the outstanding Term Loan, subject to a prepayment premium of (i) 3% of the principal amount of the Term Loan if prepaid prior to or on the first anniversary of the Closing Date, (ii) 2% of the principal amount of the Term Loan if prepaid after the first anniversary of the Closing Date through and including the second anniversary of the Closing Date, or (iii) 1% of the principal amount of the Term Loan if prepaid after the second anniversary of the Closing Date and prior to the maturity date. The Term Loan is secured by substantially all the Company’s assets, except for our intellectual property and certain other customary exclusions. Additionally, in connection with the Term Loan, the Company entered into an Exit Fee Agreement, whereby the Company agreed to pay an exit fee in the amount of 3% of the Term Loan, or the Exit Fee, upon any change of control transaction or FDA approval of tenapanor in the treatment of hyperphosphatemia in ESRD patients on dialysis and FDA approval of tenapanor for the treatment of patients with IBS-C. Notwithstanding the prepayment or termination of the Term Loan, the obligation to pay the Exit Fee will expire 10 years from the Closing Date.

The Loan Agreement contains customary representations and warranties and customary affirmative and negative covenants. Additionally, if the Company elects to enter into an exclusive license agreement for the use of its intellectual property in the United States (other than for tenapanor for hyperphosphatemia or for our FXR and TGR5

agonist programs) and has not obtained the written consent of the Lenders to enter into such license agreement, the Company has agreed to not allow our unrestricted cash and cash equivalents to be less than $50.0 million, until the Company achieves its primary endpoint in the second Phase 3 study of tenapanor for the treatment of hyperphosphatemia in end-stage renal disease patients on dialysis. As of June 30, 2018, the Company was in compliance with the covenants.

In addition, the Loan Agreement contains customary events of default that entitle the Lender to cause the Company's indebtedness under the Loan Agreement to become immediately due and payable, and to exercise remedies against the Company and the collateral securing the Term Loan, including our cash. Upon the occurrence and for the duration of an event of default, an additional default interest rate equal to 4.0% per annum will apply to all obligations owed under the Loan Agreement. As of June 30, 2018, there were no events of default.

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As of June 30, 2018, assuming the principal payments start on December 1, 2020, the Company's future debt payment obligations towards the principal and final fee, excluding interest payments and exit fee, for the respective fiscal years are as follows (in thousands):

2018	$ —
2019	—
2020	2,083
2021	25,000
2022	24,892
Total principal and final fee payments	51,975
Less: Unamortized discount and debt issuance costs	(1,218)
Less: Unaccreted value of final fee	(1,921)
Loan payable, long term	$ 48,836

NOTE 6. SHAREHOLDERS EQUITY

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

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

NOTE 7. STOCK-BASED COMPENSATION

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Research and development	$ 983	$ 1,414	$ 1,890	$ 2,445
General and administrative	1,620	1,376	3,138	2,454
Total	$ 2,603	$ 2,790	$ 5,028	$ 4,899

In January 2017, the Company granted PRSU awards to certain employees which vest upon the achievement of specified performance conditions, subject to the employees' continued service relationship with the Company. None vested during the three and six months ended June 30, 2018 and 2017. However, the related compensation cost is recognized as an expense over the estimated vesting period when achievement of the milestone is considered probable. The expense recognized for these awards is based on the grant date fair value of the Company's common stock multiplied by the number of units granted. The Company recognized $0.3 million and $0.4 million of related expense during the three and six months ended June 30, 2018, respectively.

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At June 30, 2018, the Company had $14.5 million, $1.6 million, $0.3 million and $0.1 million of total unrecognized compensation expense, net of estimated forfeitures, related to stock option grants, RSU grants, PRSUs and the ESPP, respectively, that will be recognized over an average vesting period of 2.7 years, 1.0 years, 0.3 years and 0.2 years, respectively.

Option Exercises

For the three and six months ended June 30, 2018, zero options were exercised to purchase shares of the Company's common stock, with zero net proceeds to the Company. For the three and six months ended June 30, 2017, 9,025 and 28,326 options, respectively, were exercised to purchase shares of the Company’s common stock, with insignificant net proceeds to the Company.

Restricted Stock Units

For the three and six months ended June 30, 2018, the Company issued zero shares, of its common stock upon vesting of restricted stock units to its employees. For the three and six months ended June 30, 2017, the Company issued zero and 15,188 shares, respectively, of the Company’s common stock due to vesting of restricted stock units resulting in insignificant net proceeds to the Company.

Employee Stock Purchase Plan

In February 2018, the Company sold 68,589 shares under the ESPP. The shares were purchased by employees at a purchase price of $4.38 per share with proceeds to the Company of approximately $0.3 million. In February 2017, the Company sold 42,845 shares under the ESPP. The shares were purchased by employees at a purchase price of $8.77 per share with proceeds to the Company of approximately $0.4 million.

Issuance of Common Stock for Services

For the three and six months ended June 30, 2018, the Company issued 75,183 shares of common stock to members of the board of directors who elected to receive stock in lieu of their cash fees under the Non-Employee Director Compensation Plan. The shares issued were valued at $0.3 million based on the fair value of the common stock on the date of grant. For the three and six months ended June 30, 2017, the Company issued 46,858 shares of common stock to members of the board of directors who elected to receive stock in lieu of their cash fees under the Non-Employee Director Compensation Plan. The shares issued were valued at $0.2 million based on the fair value of the common stock on the date of grant.

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NOTE 8. NET LOSS PER SHARE

Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period, less shares subject to repurchase, and excludes any dilutive effects of stock-based awards and warrants. Diluted net loss per common share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, and unvested restricted common stock and stock units. As the Company had net losses for the three and six months ended June 30, 2018 and 2017, all potential common shares were determined to be anti-dilutive. The following table sets forth the computation of net loss per common share (in thousands, except share and per share amounts):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Numerator:				
Net loss	$ (22,291)	$ (25,721)	$ (39,310)	$ (53,729)
Denominator:				
Weighted average common shares outstanding - basic and diluted	52,824,483	47,403,243	50,206,470	47,373,404
Net loss per share - basic and diluted	$ (0.42)	$ (0.54)	$ (0.78)	$ (1.13)

For the three and six months ended June 30, 2018 the total number of securities that could potentially dilute basic net loss per share in the future that were not included in the computation of diluted net loss per share because the effect would have been antidilutive was 7.9 million and 8.0 million, respectively.

For the three and six months ended June 30, 2017, the total number of securities that could potentially dilute basic net loss per share in the future that were not included in the computation of diluted net loss per share because the effect would have been antidilutive was 6.6 million and 6.4 million, respectively.

NOTE 9. ACCRUED AND OTHER LIABILITIES

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

	June 30, 2018	December 31, 2017
Accrued clinical and non-clinical expenses	$ 5,518	$ 5,447
Accrued contract manufacturing	1,958	3,980
Derivative liability	546	—
Accrued professional and consulting services	368	530
Other	844	752
	$ 9,234	$ 10,709

NOTE 10. COLLABORATION AND LICENSING AGREEMENTS

Kyowa Hakko Kirin Co., Ltd., or KHK

In November 2017, the Company entered into an exclusive license agreement with KHK, or the KHK Agreement, for the development, commercialization and distribution of tenapanor in Japan for cardiorenal indications. The Company assessed these arrangements in accordance with Topic 606 and concluded that the contract counterparty, KHK, is a customer. Under the terms of the KHK Agreement, the Company received $30.0 million in up-front license fees which was recognized as revenue when the agreement was executed. Based on the Company's assessment, it identified that the license and the manufacturing supply services were its material performance obligations at the inception of the agreement, and as such each of the performance obligations are distinct. Additionally, on January 1, 2018, the Company recorded an increase in current assets of $5.0 million as well as in current liabilities of $1.0 million related to the first milestone under the KHK Agreement which the Company believes is not materially at risk, reflecting revenues and cost of revenue,

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respectively, that would have been recognized in the fourth quarter 2017 if the Company had adopted Topic 606 prior to January 1, 2018.

In addition to the up-front license fee of $30.0 million, the Company may be entitled to receive up to $55.0 million in total development milestones and 8.5 billion yen in commercialization milestones, as well as reimbursement of cost plus a reasonable overhead for the supply of product and high-teen royalties on net sales throughout the term of the agreement.

The Company recorded $30,000 of other revenue for manufacturing supply of tenapanor and other materials to KHK for KHK's product development and clinical trials in Japan, in accordance with the Company's agreement with KHK, for the three and six months ended June 30, 2018.

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

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

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

There was no revenue recorded in the three and six month period ended June 30, 2018 related to the Fosun Agreement.

Knight Therapeutics, Inc., or Knight

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

Under the terms of the agreement, the Company is eligible to receive up to CAD 25 million in total payments including an up-front payment and development and sales milestones, reimbursement of supply costs on a schedule specifying cost per tablet, with a reasonable mark up for overhead, as well as double-digit tiered royalties on net sales.

There was no revenue recorded in the three month period ended June 30, 2018 related to the Knight Agreement. In the six month period ended June 30, 2018, there was $2.3 million of revenue recorded related to the Knight Agreement and $0.5 million of cost of revenue pursuant to the AstraZeneca Termination Agreement.

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AstraZeneca

In June 2015, the Company entered into a termination agreement with AstraZeneca, or the Termination Agreement, pursuant to which the Company remains liable to pay AstraZeneca license fees for (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by the Company or its licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should the Company elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, up to a maximum of $75.0 million in aggregate for (i) and (ii). To date in aggregate, the Company has recognized $9.9 million of the $75.0 million, recorded as cost of revenue comprising (i) $6.0 million and $2.4 million related to the KHK Agreement and Fosun Agreement, respectively, recorded in 2017 (ii) $1.0 million related to the KHK Agreement associated with a future milestone which the Company believes is not materially at risk for which the Company recorded an increase in current liabilities in the six month period ended June 30, 2018 reflecting the future payable to AstraZeneca and (iii) $0.5 million related to the Knight Agreement recorded in the six month period ended June 30, 2018.

NOTE 11. CONTINGENCIES

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

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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 consolidated 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, 2017. 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 specialized biopharmaceutical company focused on developing first-in-class, disruptive medicines for the treatment of renal diseases, which affect both the heart and the kidneys. This includes patients with end-stage renal disease, or ESRD, who suffer from elevated serum phosphorus, or hyperphosphatemia; and patients with chronic kidney disease, or CKD, and/or heart failure who have elevated serum potassium, or hyperkalemia. We have also developed a number of programs directed toward treating gastrointestinal, or GI, disorders, including the treatment of irritable bowel syndrome with constipation, or IBS-C.

Our portfolio is led by the development of tenapanor, a first-in-class inhibitor of NHE3. In our renal pipeline, tenapanor is being evaluated in a second Phase 3 trial for the treatment of hyperphosphatemia in patients with ESRD who are on dialysis. We are also advancing a small molecule potassium secretagogue program, RDX013, for the potential treatment of hyperkalemia.

We have also developed tenapanor for the treatment of people with irritable bowel syndrome with constipation, or IBS-C. In 2017, we completed the T3MPO program for this indication, including two Phase 3 studies, both of which achieved statistical significance for the primary endpoint, and a long-term safety extension study. Based on the results of the T3MPO clinical program in IBS-C, we currently plan to submit our first NDA to FDA in the second half of 2018 for tenapanor for the treatment of IBS-C.

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

Since commencing operations in October 2007, substantially all our efforts have been dedicated to our research and development activities, including developing our clinical product candidate tenapanor and developing our proprietary drug discovery and design platform. We have not generated any revenues from product sales and have no products approved for commercialization.

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

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

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We expect to incur operating losses for the foreseeable future as we prepare for the development and commercialization of tenapanor, including costs associated with completing the on-going Phase 3 development program for tenapanor for the treatment of hyperphosphatemia in patients with ESRD on dialysis, as well as the advancement of our research programs into the preclinical stage and the progression of our early stage research. To date, we have funded our operations from the sale and issuance of common stock, convertible preferred stock, funds from our former collaboration partnerships with AstraZeneca AB, or AstraZeneca, and Sanofi SA, or Sanofi, and funds from our recent license agreements with Kyowa Hakko Kirin Co., Ltd., or KHK, Shanghai Fosun Pharmaceutical Industrial Development Co. Ltd., or Fosun Pharma, and Knight Therapeutics Inc., or Knight.

Financial Operations Overview

Revenue

We have not generated any revenue from product sales. Our past revenue performance is not necessarily indicative of results to be expected for the entire year ending December 31, 2018, or future operating periods. Our non-product revenue cannot always be predicted since it is dependent upon achievement of certain milestones. See “NOTE 2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES” for further detail.

During the first quarter of 2018, we executed license agreements with Knight for the development, commercialization and distribution of tenapanor for hyperphosphatemia and IBS-C in Canada. Under the terms of the Knight license agreements, the Company received a nonrefundable payment of CAD 3 million, or U.S. $2.3 million, in up-front license fees, which was recorded as revenue when the contracts were executed. The agreement also provides for development and commercialization milestone payments, which will be recorded as revenue when we achieve the underlying milestone.

On January 1, 2018 we adopted the new standard for Revenue from Contracts with Customers, Topic 606, on a modified retrospective method as an adjustment to the opening balance of retained earnings of the annual reporting period. On January 1, 2018, we recorded an increase in current assets of $5.0 million reflecting a future receivable related to the first milestone under our license with KHK, which we believe is not materially at risk, an increase in current liabilities of $1.0 million reflecting a future payable related to the corresponding payment to AstraZeneca, in accordance with our termination agreement with AstraZeneca and a related decrease in its accumulated deficit of approximately $4.0 million as the new standard permits revenue from certain milestones to be recognized earlier of approximately $4.0 million as the new standard contains different recognition criteria related to milestones than under the previous standard, Topic 605.

Cost of Revenue

Cost of revenue currently represents payments due to AstraZeneca, who under the terms of a termination agreement entered into in 2015 are entitled to (i) future royalties at a royalty rate of 10% of net sales of tenapanor or other NHE3 products by us or our licensees, and (ii) 20% of non-royalty revenue received from a new collaboration partner should we elect to license, or otherwise provide rights to develop and commercialize tenapanor or another NHE3 inhibitor, up to a maximum of $75.0 million in aggregate for (i) and (ii). We recognize these expenses as cost of revenue when we recognize the revenue that generates our liability for these license payments. To date in aggregate, we have recognized $9.9 million of the $75.0 million, recorded as cost of revenue comprising (i) $6.0 million and $2.4 million related to the KHK Agreement and Fosun Agreement, respectively, recorded in 2017 (ii) $1.0 million related to the KHK Agreement associated with a future milestone which we believe is not materially at risk for which we recorded an increase in current liabilities in the six month period ended June 30, 2018 reflecting the future payable to AstraZeneca and (iii) $0.5 million related to the Knight Agreement recorded in the six month period ended June 30, 2018.

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Research and Development Expenses

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

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

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

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

General and Administrative

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

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

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Provision for Income Taxes

The provision for income taxes was insignificant for the three and six months ended June 30, 2018 and zero for the three and six months ended June 30, 2017. We expect to generate a net loss for the year ending December 31, 2018. Our deferred tax assets continue to be fully offset by a valuation allowance.

The Tax Cuts and Jobs Act ("TCJA") makes broad and complex changes to the U.S. tax code, including, but not limited to, reducing the U.S. federal corporate tax rate from 35% to 21%, effective January 1, 2018. The Company was able to determine a reasonable estimate of certain effects of the TCJA and has therefore recognized the provisional tax impacts related to the revaluation of deferred tax assets and liabilities. The Securities and Exchange Commission has provided accounting and reporting guidance that allows the Company to report provisional amounts within a measurement period of up to one year from the date of enactment due to the complexities inherent in adopting the TCJA. The ultimate impact may differ from provisional amounts, possibly materially, due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of the TCJA. As of June 30, 2018, the Company still considers its accounting for the impacts of the new law to be provisional and will continue to assess the impact of the recently enacted tax law on its business and condensed consolidated financial statements over the next six months.

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 consolidated 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 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 research and development expense, accruals and stock-based compensation to be critical policies. Other than the implementation of Topic 606 there have been no changes to our critical accounting policies since we filed our 2017 Form 10-K with the SEC on March 14, 2018. For a description of our critical accounting policies, please refer to our Form 10-K we filed with the SEC on March 14, 2018.

RESULTS OF OPERATIONS

Three and six months ended June 30, 2018 and 2017

Revenue

Revenue for the three and six months ended June 30, 2018, 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,	
	2018	2017	2018	2017

Licensing revenue	$ —	$ —	$ 2,320	$ —
Other revenue	30	—	30	—
Total revenues	30	—	2,350	—
Dollar change from prior year	30		2,350	
Percent change from prior year	*		*	—

* not meaningful

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Revenue was $30,000 for the three months ended June 30, 2018, an increase of $30,000, compared to zero for the three months ended June 30, 2017. The increase in revenue of $30,000 was related to the manufacturing supply of tenapanor and other materials to KHK for KHK's product development and clinical trials in Japan in accordance with our agreement with KHK.

Revenue was $2.4 million for the six months ended June 30, 2018, an increase of $2.4 million, compared to zero for the six months ended June 30, 2017. The increase in revenue was primarily from the licensing revenue of $2.3 million related to the license fees payment we received.

Cost of revenue

Cost of revenue for the three and six months ended June 30, 2018, 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,	
	2018	2017	2018	2017
Cost of revenue	$ —	$ —	$ 464	$ —
Dollar change from prior year	—		464	
Percent change from prior year	*		*	

* not meaningful

Cost of revenue was negligible for the three months ended June 30, 2018 and June 30, 2017.

Cost of revenue was $0.5 million for the six months ended June 30, 2018, an increase of $0.5 million, compared to zero for the six months ended June 30, 2017. The increase in cost of revenue of $0.5 million was due to the license fees paid to AstraZeneca pursuant to the Termination Agreement, corresponding to the revenue realized.

Research and Development

Research and development expenses for the three and six months ended June 30, 2018, 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,	
	2018	2017	2018	2017
Research and development	$ 16,046	$ 20,572	$ 29,396	$ 42,960
Dollar change from prior year	(4,526)		(13,564)	
Percent change from prior year	(22) %		(32) %	

Research and development expenses were $16.1 million for the three months ended June 30, 2018, a decrease of $4.5 million, or 22%, compared to $20.6 million for the three months ended June 30, 2017. The decrease consisted of a $2.4 million decrease in our external program costs and a $2.1 million decrease in our internal program costs.

The decrease in our external program costs of $2.4 million included a $2.2 million decrease related to discontinuation of the RDX7675 program and a $1.0 million decrease related to the reduction of activities associated with the RDX8940 program that was partially offset by $0.8 million primarily related to an increase in expense due to the start of our second tenapanor hyperphosphatemia Phase 3 study.

The decrease in our internal costs of $2.1 million was primarily due to a decrease in personnel costs, including stock-based compensation costs as a result of a reduction in force during the third quarter of 2017, and a related decrease in research and development activities.

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Research and development expenses were $29.4 million for the six months ended June 30, 2018, a decrease of $13.6 million, or 32%, compared to $43.0 million for the six months ended June 30, 2017. The decrease consisted of a $9.4 million decrease in our external program costs and a $4.2 million decrease in our internal program costs.

The decrease in our external program costs of $9.4 million included a $5.5 million decrease related to discontinuation of the RDX7675 program, a $1.6 million decrease related to the reduction of activities associated with the RDX8940 program and a net $2.3 million decrease in expense primarily for clinical development activities related to the completion of our tenapanor IBS-C Phase 3 clinical program as well as our first tenapanor hyperphosphatemia Phase 3 clinical trial that was partially offset by an increase in expenses incurred related to the start of our second tenapanor hyperphosphatemia Phase 3 study.

The decrease in our internal costs of $4.2 million was primarily due to a decrease in personnel costs, including stock-based compensation costs, as a result of a reduction in force during the third quarter of 2017, and a related decrease in research and development activities.

General and Administrative

General and administrative expenses for the three and six months ended June 30, 2018, 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,	
	2018	2017	2018	2017
General and administrative	$ 6,138	$ 5,846	$ 12,329	$ 11,892
Dollar change from prior year	292		437	
Percent change from prior year	5 %		4 %	

General and administrative expenses were $6.1 million for the three months ended June 30, 2018, an increase of $0.3 million, or 5%, compared to $5.8 million for the three months ended June 30, 2017. The increase was primarily due to an increase in professional services and stock-based compensation expense, partially offset by a reduction in personnel costs due to reduction in force during the third quarter of 2017.

General and administrative expenses were $12.3 million for the six months ended June 30, 2018, an increase of $0.4 million, or 4%, compared to $11.9 million for the six months ended June 30, 2017. The increase was primarily due to an increase in professional services and stock-based compensation expense, partially offset by a reduction in personnel costs due to reduction in force during the third quarter of 2017.

Liquidity and Capital Resources

The following table displays a summary of our cash, cash equivalents and short-term investments as of June 30, 2018 and December 31, 2017 (in thousands):

	June 30, 2018	December 31, 2017
Cash and cash equivalents	$ 91,751	$ 75,383
Short-term investments	120,980	58,593

Total liquid funds	$ 212,731	$ 133,976

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

On May 25, 2018, we completed an underwritten public offering of 12,500,000 shares of our common stock at a price to the public of $4.00 per share, that were purchased by the Underwriters from the Company at a price of $3.76 per Share,

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

Our primary sources of cash have been primarily from past equity financings, debt financings and collaboration partnerships, including past collaboration partnerships with AstraZeneca and Sanofi and more recent collaboration partnerships with KHK, Fosun Pharma, and Knight. 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, 2018 will be sufficient to meet our projected operating requirements for at least the next 12-months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Further, our operating plan can change, and we may require significant additional capital to fund our operations, including to support the development, commercialization and manufacturing efforts for tenapanor. We may seek to obtain such additional capital through debt financings, credit facilities, additional equity offerings and/or strategic collaborations. We currently have no unutilized credit facility or committed sources of capital, and there can be no assurances that such sources of capital will be available to us when needed or on acceptable terms. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we may enter into additional collaboration partnerships with third-parties to participate in their development and commercialization, our future funding requirements will depend on many factors, including the following:

- the progress, timing, scope, results and costs of our Phase 3 clinical trial programs evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, the submission of an NDA with the FDA to request marketing authorization for tenapanor for the treatment of IBS-C, as well as our decision whether or not to pursue other indications for tenapanor;
- our ability to identify a collaboration partner and negotiate acceptable terms for a collaboration partnership for the commercialization of tenapanor in IBS-C in the United States;
- our ability to successfully commercialize tenapanor, either alone or with one or more collaboration partners;
- the manufacturing costs of tenapanor, and the availability of one or more suppliers for tenapanor at reasonable costs;
- the selling and marketing costs associated with tenapanor, including the cost and timing of building our sales and marketing capabilities;
- our ability to maintain our existing collaboration partnerships and to establish additional collaboration partnerships, in-license/out-license, joint ventures or other similar arrangements and the financial terms of such agreements;
- the timing, receipt, and amount of sales of, or royalties on, tenapanor, if any;
- the sales price and the availability of adequate third-party reimbursement for tenapanor;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of research 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;

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- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates: and
- requirements to pay the interest and principal of our Loan Agreement and the restrictions, penalties and covenants therein.

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

	Six Months Ended June 30,	
	2018	2017
Cash used in operating activities	$ (24,819)	$ (50,647)
Cash (used in) provided by investing activities	(62,176)	39,261
Cash provided by financing activities	103,363	424
Net increase (decrease) in cash and cash equivalents	$ 16,368	$ (10,962)

Cash Flows from Operating Activities

Net cash used in operating activities during the six months ended June 30, 2018, was approximately $24.8 million. The net loss of $39.3 million was adjusted for non-cash charges of $1.3 million related to depreciation amortization and non-cash interest expense and $5.0 million for stock-based compensation, and an increase to cash of $8.2 million related to other working capital items associated with changes in our net operating assets and liabilities primarily related to a decrease of receivables related to the Fosun Agreement offset by working capital related to clinical development and manufacturing of tenapanor.

Net cash used in operating activities during the six months ended June 30, 2017 was approximately $50.6 million. The net loss of $53.7 million was adjusted for non-cash charges of $1.7 million for depreciation and amortization and $4.9 million for stock-based compensation, and a decrease to cash of $3.5 million related to other working capital items associated with changes in our net operating assets and liabilities, primarily related to a decrease in pre-payments to vendors for clinical development and manufacturing activities, and a decrease of accounts payable and accrued liabilities primarily due to expenses for the activities for tenapanor, RDX7675 and RDX8940.

Cash Flows from Investing Activities

Net cash used in investing activities was $62.2 million for the six months ended June 30, 2018, primarily due to purchases of investments of $119.0 million offset by maturities of investments of $56.0 million and redemptions of investments of $0.8 million.

Net cash provided by investing activities was $39.3 million for the six months ended June 30, 2017 and was primarily due to maturities and sales of investments of $85.9 million. This was offset by purchases of investments of $44.7 million and acquisition of property and equipment of $1.9 million 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, 2018, was $103.4 million, primarily due to net proceeds of $53.8 million, after deducting the underwriting discounts and commissions and offering expenses from an underwritten public offering of our common stock in May 2018, net proceeds of $49.3 million, after

deducting the closing fee, legal expenses and issuance cost from the term loan provided by Solar Capital Ltd. and Western Alliance Bank, and net proceeds of $0.3 million from issuance of common stock under the employee stock purchase plan, or ESPP.

Net cash provided by financing activities for the six months ended June 30, 2017 was $0.4 million and was due to proceeds from issuance of common stock under ESPP.

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Off-Balance Sheet Arrangements

None.

Recent Accounting Pronouncements

Refer to Note 2 in the notes to our unaudited interim condensed consolidated financial statements in Part I, Item 1 of this Quarterly Report on Form 10 Q, 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 2017 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, 2018. 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, 2018, our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended June 30, 2018, 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.

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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, 2018, there is no litigation pending that would reasonably be expected to have a material adverse effect on our results of operations and financial condition.

ITEM 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 tenapanor and developing our proprietary drug discovery and design platform. To date, we have not commercialized any products or generated any revenue from the sale of products.

We are not profitable and have incurred losses in each year since our inception in October 2007, and we do not know whether or when we will become profitable. We have only a limited operating history upon which to evaluate our business and prospects. We continue to incur significant research, development and other expenses related to our ongoing operations. As of June 30, 2018, we had an accumulated deficit of $313.5 million.

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

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

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

ownership changes that have occurred previously and additional limitations may be applicable as a result of ownership changes that could occur in the future.

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

We have no products approved for sale and have never generated any revenue from product sales. Our ability to generate revenue from product sales and achieve profitability depends on our ability to successfully complete the development of and obtain the regulatory and marketing approvals necessary to commercialize tenapanor for one or more indications, either on our own, or with one or more collaboration partners. We do not anticipate generating revenue from product sales for the foreseeable future. Our ability to generate future revenue from product sales or pursuant to milestone payments depends heavily on many factors, including but not limited to:

- the successful completion of nonclinical and clinical development of tenapanor;
- obtaining regulatory approvals for tenapanor, either on our own, or with one or more collaboration partners;
- our ability to identify a collaboration partnership and negotiate acceptable terms for a collaboration partnership for the commercialization of tenapanor in IBS-C in the United States;
- our ability to successfully commercialize tenapanor, either on our own, or with one or more collaboration partners;
- developing a sustainable and scalable manufacturing process for tenapanor and establishing and maintaining supply and manufacturing relationships with third parties that can provide an adequate (in amount and quality) supply of product to support the market demand for tenapanor, if approved;
- obtaining market acceptance of tenapanor, if approved, as a viable treatment option for the indications for which it is approved;
- addressing any competing technological and market developments;
- identifying, assessing, acquiring, in-licensing and/or developing new product candidates;
- negotiating favorable terms in any collaboration partnership, licensing or other arrangements into which we may enter;
- maintaining, protecting, and expanding our portfolio of intellectual property rights, including patents, trade secrets, and know-how, and our ability to develop, manufacture and commercialize our product candidates and products without infringing intellectual property rights of others; and
- attracting, hiring, and retaining qualified personnel.

In cases where we are successful in obtaining regulatory approvals to market tenapanor for one or more indications, our revenue will be dependent, in part, upon the size of the markets in the territories for which regulatory approval is granted, the accepted price for the product, the ability to get reimbursement at any price and whether we are commercializing the product or the product is being commercialized by a collaboration partner, and in such case, whether we have royalty and/or co-promotion rights for that territory. If the number of patients suitable for tenapanor is not as significant as we estimate, the indications approved by regulatory authorities are narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from the sale of tenapanor, even if approved. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to generate revenue from product sales would likely depress our market value and could impair our ability to raise capital, expand our business, discover or develop other product candidates or continue our operations. A decline in the value of our common stock could cause our stockholders to lose all or part of their investment.

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

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

Additionally, we may be required to repay the outstanding indebtedness under the loan facility if an event of default occurs under the loan and security agreement. Under the loan and security agreement, an event of default will occur if, among other things, we fail to make payments under the loan and security agreement; we breach any of our covenants under the loan and security agreement, subject to specified cure periods with respect to certain breaches; the Lenders determines that a material adverse change has occurred; we or our assets become subject to certain legal proceedings, such as bankruptcy proceedings; we are unable to pay our debts as they become due; or we default on contracts with third parties which would permit the Lenders to accelerate the maturity of such indebtedness or that could have a material adverse change on us. We may not have enough available cash or be able to raise additional funds through equity or debt financings to repay such indebtedness at the time any such event of default occurs. In this case, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts or grant to others' rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. The Lenders could also exercise their rights as collateral agent to take possession of and to dispose of the collateral securing the term loans, which collateral includes substantially all of our property (excluding intellectual property, which is subject to a negative pledge). Our business, financial condition and results of operations could be materially adversely affected as a result of any of these events.

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

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

· the progress, timing, scope, results and costs of our Phase 3 clinical trial programs evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis, the submission of an NDA with the FDA to request marketing authorization for tenapanor for the treatment of IBS-C, as well as our decision whether or not to pursue other indications for tenapanor;

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- our ability to identify a collaboration partner and negotiate acceptable terms for a collaboration partnership for the commercialization of tenapanor in IBS-C in the United States;
- our ability to successfully commercialize tenapanor, either alone or with one or more collaboration partners;
- the manufacturing costs of our product candidates, and the availability of one or more suppliers for our product candidates at reasonable costs, both for clinical and commercial supply;
- the selling and marketing costs associated with tenapanor, including the cost and timing of building our sales and marketing capabilities, should we elect to do so;
- our ability to maintain our existing collaboration partnerships and to establish additional collaboration partnerships, in-license/out-license, joint ventures or other similar arrangements and the financial terms of such agreements;
- the timing, receipt, and amount of sales of, or royalties on, tenapanor, if any;
- the sales price and the availability of adequate third-party reimbursement for tenapanor, if approved;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the number and scope of preclinical and discovery programs that we decide to pursue or initiate, and any clinical trials we decide to pursue for other product candidates;
- the time and cost necessary to respond to technological and market developments;
- the costs of filing, prosecuting, maintaining, defending and enforcing any patent claims and other intellectual property rights, including litigation costs and the outcome of such litigation, including costs of defending any claims of infringement brought by others in connection with the development, manufacture or commercialization of tenapanor or any of our product candidates; and
- the payment of interest and principal related to our loan and security agreement entered into during May 2018.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research activities, preclinical and clinical trials for our product candidates and our establishment and maintenance of sales and marketing capabilities or other activities that may be necessary to commercialize tenapanor, either alone or with collaboration partners. Additionally, our inability to access capital on a timely basis and on terms that are acceptable to us may force us to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor or certain of our product candidates through the use of alternative structures.

Risks Related to Our Business

We are substantially dependent on the success of our lead product candidate, tenapanor, which may not be successful in further 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. The clinical and commercial success of tenapanor will depend on a number of factors, including the following:

- our ability to, in a timely manner and under terms that are acceptable to us, establish a collaboration partnership for the commercialization of tenapanor for the treatment of IBS-C in the United States;

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- the ability of the third-party manufacturers we contract with to successfully execute and scale up the manufacturing processes for tenapanor, which has not yet been demonstrated, and to manufacture supplies of tenapanor and to develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMP, requirements;
- whether the FDA or foreign regulatory authorities require additional nonclinical and/or clinical studies, which could delay the commercialization of tenapanor;
- whether the FDA or foreign regulatory authorities require us to conduct clinical trials in addition to 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;
- acceptance of tenapanor as safe, effective and well-tolerated by patients and the medical community;
- our ability, alone or with collaboration partners, to manage the complex pricing and reimbursement negotiations associated with marketing the same product at different doses for separate indications, if tenapanor is approved for marketing and sale by the FDA or foreign regulatory authorities for both IBS-C and hyperphosphatemia in dialysis patients;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of tenapanor compared to alternative and competing treatments;
- obtaining and sustaining an adequate level of coverage and reimbursement for tenapanor by third-party payors;
- enforcing intellectual property rights in and to tenapanor;
- avoiding third-party interference, opposition, derivation or similar proceedings with respect to our patent rights, and avoiding other challenges to our patent rights and patent infringement claims; and
- a continued acceptable safety and tolerability profile of tenapanor following approval.

As tenapanor is a first-in-class drug, there is a higher likelihood that approval may not be attained as compared to a class of drugs with approved products. While tenapanor met the primary endpoint in two Phase 3 clinical studies evaluating tenapanor for the treatment of patients with IBS-C, there can be no assurance that our NDA that we plan to submit for this indication, once submitted, will be accepted by FDA or that we will receive marketing authorization from FDA. Although tenapanor met the primary endpoint in the first Phase 3 clinical trial for the treatment of hyperphosphatemia in ESRD patients on dialysis, there can be no assurances that the second Phase 3 trial of tenapanor in this indication will achieve the primary endpoint, or that tenapanor will receive regulatory approval for this indication. Further, it may not be possible

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or practicable to demonstrate, or if approved, to market tenapanor on the basis of certain of the benefits we believe tenapanor possesses. If the number of patients in the market for tenapanor or the price that the market can bear is not as significant as we estimate, 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 Phase 3 clinical study of tenapanor for the treatment of hyperphosphatemia. Furthermore, results of earlier studies and trials may not be predictive of future trial results.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical and clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. An unexpected adverse event profile, or the results of drug-drug interaction studies, may present challenges for the future development and commercialization of a product candidate for a particular condition despite receipt of positive efficacy data in a clinical study. Although tenapanor met the primary endpoint in the first Phase 3 clinical trial for the treatment of hyperphosphatemia in ESRD patients on dialysis, there can be no assurances that the second Phase 3 trial results of tenapanor in that indication will show the desired safety and efficacy. 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 Phase 3 program for tenapanor for the treatment of hyperphosphatemia is completed, and despite the completion of our Phase 3 program for tenapanor for IBS-C, the results for one or both indications may not be sufficient to obtain regulatory approval for tenapanor, or if such regulatory approval is obtained, the content of the label approved by regulatory authorities may materially and adversely impact our ability to commercialize the product for the approved indication.

We do not know whether our second Phase 3 clinical trial for tenapanor for the treatment of hyperphosphatemia will 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:

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

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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 our Phase 3 clinical trial is suspended or terminated by us, by the IRBs of the institutions in which the trial is being conducted, or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

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

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

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

- with respect to tenapanor for IBS-C in the United States, our ability to obtain a collaboration partner for commercialization and the strength of such collaboration partner's marketing and distribution organizations;
- the efficacy demonstrated in clinical trials;
- the prevalence and severity of any side effects and overall safety and tolerability profile of the product;
- the clinical indications for which it is approved;
- advantages over new or traditional or existing therapies, including recently approved therapies or therapies that the physician community anticipate will be approved;
    - acceptance by physicians, major operators of clinics and patients of tenapanor as a safe, effective and well-tolerated treatment;
- relative convenience and ease of administration of tenapanor;
- the potential and perceived advantages of tenapanor over current treatment options or alternative treatments, including future alternative treatments;

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- the cost of treatment in relation to alternative treatments and willingness to pay for tenapanor, if approved, on the part of physicians and patients;
- the availability of alternative products and their ability to meet market demand; and
- the quality of our relationships with patient advocacy groups; and

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

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

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

If we are unable to enter collaborative relationships a timely manner, or on acceptable terms, and/or we fail or are delayed in the development of our internal sales, marketing and distribution capabilities, we may choose to delay the commercialization of our products and/or the commercialization of our products could be adversely impacted, and we may not be able to successfully commercialize our product candidates.

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

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

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

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may select candidates for development, yet we may fail to advance product candidates to clinical development for many reasons, including the following:

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

Even if we are successful in continuing to expand our pipeline, through our own research and development efforts, the potential product candidates that we identify or for which we acquire rights may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize a product pipeline, we may not be able to generate revenue from product sales in future periods or ever achieve profitability.

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

We have developed a proprietary drug discovery and design platform to enable the identification, screening, testing, design and development of new product candidates, and have developed APECCS as a component of this of this platform. We have utilized APECCS in the design of our small molecules and to identify new and potentially novel targets in the GI tract. However, there can be no assurance that APECCS will be able to identify new targets in the GI tract or that any of these potential targets or other aspects of our proprietary drug discovery and design platform will yield product candidates that could enter clinical development and, ultimately, be commercially valuable. In addition, as we focus our efforts on the discovery and design of therapies for the treatment of renal diseases, we may need to further develop our proprietary drug discovery and design platform to enhance its usefulness in the identification, screening, testing, design and development of new product candidates for the treatment of renal diseases. There can be no assurances that we will be successful in such additional development of our platform or that our platform will yield product candidates for the treatment of renal diseases.

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We rely on third parties to conduct some of our nonclinical studies and all of our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize our product candidates.

We do not have the ability to independently conduct clinical trials and, in some cases, nonclinical studies. We rely on medical institutions, clinical investigators, contract laboratories, and other third parties, such as CROs, to conduct clinical trials on our product candidates. The third parties with whom we contract for execution of the clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we control only certain aspects of their activities and have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely, and will continue to rely, on these third parties to conduct some of our nonclinical studies and all of our clinical trials, we remain responsible for ensuring that each of our studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on third parties does not relieve us of our regulatory responsibilities. We, and these third parties are required to comply with current GLPs for nonclinical studies, and good clinical practices, or GCPs, for clinical studies. GLPs and GCPs are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our products in nonclinical and clinical development, respectively. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors fail to comply with applicable regulatory requirements, including GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the European Medicines Agency, or EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurance that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

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

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

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

could occur, including:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or a collaboration partner, may be required to recall the product;

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- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof, including the imposition of a Risk Evaluation and Mitigation Strategies, or REMS, plan that may require creation of a Medication Guide outlining the risks of such side effects for distribution to patients, as well as elements to assure safe use of the product, such as a patient registry and training and certification of prescribers;
- we, or a collaboration partner, may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer

Any of the foregoing events could prevent us, or a collaboration partner, from achieving or maintaining market acceptance of a particular product candidate, if approved, and could result in the loss of significant revenue to us, which would materially and adversely affect our results of operations and business.

We face substantial competition and our competitors may discover, develop or commercialize products faster or more successfully than us.

The biotechnology and pharmaceutical industries are highly competitive, and we face significant competition from companies in the biotechnology, pharmaceutical and other related markets that are researching and marketing products designed to address diseases that we are currently developing products to treat. If approved for marketing by the FDA or other regulatory agencies, tenapanor, as well as our other product candidates, would compete against existing treatments.

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

- Calcium carbonate (many over-the-counter brands including Tums and Caltrate)
- Calcium acetate (several prescription brands including PhosLo and Phoslyra)
- Lanthanum carbonate (Fosrenol marketed by Shire)
- Sevelamer hydrochloride (Renagel, marketed by Sanofi)
- Sevelamer carbonate (Renvela, marketed by Sanofi)
- Sucroferric oxyhydroxide (Velphoro, marketed by Vifor Fresenius)
- Ferric citrate (Auryxia, marketed by Keryx)

The hydrochloride form of sevelamer, Renagel, was launched in the United States by Genzyme Corporation in 1998 prior to its acquisition by Sanofi, and the carbonate form, Renvela, was launched in 2008. Sanofi booked €802 million ($0.98 billion) in worldwide sales of sevelamer during 2017. Generic sevelamer carbonate has been approved in certain jurisdictions in Europe since 2015 and in the U.S. market since June 2017. In addition to the currently marketed phosphate binders, we are aware of at least two other binders in development, including fermagate (Alpharen), an iron-based binder

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in Phase 3 being developed by Opko Health, Inc., and PT20, an iron-based binder in Phase 3 being developed by Shield Therapeutics.

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

We are also aware of three prescription products marketed for IBS-C: (i) Linzess (linaclotide), marketed by Ironwood Pharmaceuticals and Allergan, (ii) Amitiza (lubiprostone), marketed by Takeda and Sucampo, a wholly-owned subsidiary of Mallinckrodt, and (iii) Trulance (plecanatide), marketed by Synergy Pharmaceuticals.

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 may experience difficulties in managing our current activities and growth given our level of managerial, operational, financial and other resources.

While we have continued to work to optimize our management composition, personnel and systems to support our current activities for future growth, these resources may not be adequate for this purpose. Our need to effectively execute our business strategy requires that we:

- manage our clinical trials effectively, including the Phase 3 trial of tenapanor which is being conducted at multiple trial sites;
- manage our internal research and development efforts effectively while carrying out our contractual obligations to licensors, contractors, collaborators, government agencies and other third parties;
- continue to improve our operational, financial and management controls, reporting systems and procedures; and
- retain and motivate our remaining employees and potentially identify, recruit, and integrate additional employees.

If we are unable to maintain or expand our managerial, operational, financial and other resources to the extent required to manage our development and pre-commercialization activities, our business will be materially adversely affected.

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We rely completely on third parties to manufacture our nonclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of tenapanor, if approved. Our business would be harmed if those third parties fail to obtain approval of the FDA, 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 tenapanor or any of other our product candidates on a commercial scale, or to manufacture our drug supplies for use in the conduct of our nonclinical and clinical studies. The facilities used by our contract manufacturers to manufacture 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 and certain processes, such as spray drying, that we use to manufacture our drugs, and there may be a need to identify alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical studies, and, if approved, ultimately for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials or processes by our manufacturers. Although we generally do not begin a clinical study unless we believe we have on hand, or will be able to manufacture, a sufficient supply of a product candidate to complete such study, any significant delay or discontinuity in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical study due to the need to replace a third-party manufacturer could considerably delay completion of our clinical studies, product testing, and potential regulatory approval of our product candidates, which could harm our business and results of operations.

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

The pricing, coverage and reimbursement of our product candidates, if approved, must be adequate to support a commercial infrastructure. The availability and adequacy of coverage and reimbursement by governmental and private payors are essential for most patients to be able to afford treatments such as ours, assuming approval. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid for by health maintenance, managed care, pharmacy benefit, and similar healthcare management organizations, or reimbursed by government authorities, private health insurers, and other third-party payors. If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about coverage and reimbursement for new drugs are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S.

Department of Health and Human Services responsible for administering the Medicare program, as CMS decides whether and to what extent a new drug will be covered and reimbursed under Medicare. Private payors tend to follow the

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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 extended this implementation date to January 1, 2024. Additionally, section 204 of the Stephen Beck, Jr., Achieving a Better Life Experience Act of 2014, or ABLE, provides that payment for oral-only ESRD drugs cannot be made under the ESRD Prospective Payment System prior to January 1, 2025. As a result of the recent legislation, beginning in 2025, oral-only ESRD-related drugs may be included in the bundle and separate Medicare reimbursement will no longer be available for such drugs, as it is today under Medicare Part D. While it is too early to project the full impact that bundling may have on the industry, the impact could potentially cause dramatic price reductions for tenapanor, if approved. We may be unable to sell tenapanor, if approved, to dialysis providers on a profitable basis if third-party payors reduce their current levels of payment, or if our costs of production increase faster than increases in reimbursement levels.

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

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, these caps may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend 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;

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- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize or co-promote our product candidates.

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

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

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer data security breaches, which could adversely affect our business.

Our business is increasingly dependent on critical, complex and interdependent information technology systems to support business processes as well as internal and external communications. Despite the implementation of security measures, the size and complexity of our internal computer systems, and those of our CROs and other contractors, make them 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

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recover or reproduce the data. 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.

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 $1.07 billion, (3) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (4) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

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.

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We have formed in the past, and may form in the future, collaboration partnerships, joint ventures and/or licensing arrangements, and we may not realize the benefits of such collaborations.

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

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

We may consider strategic transactions, such as acquisitions of companies, asset purchases, and or in-licensing of products, product candidates or technologies. In addition, if we are unable to access capital on a timely basis and on terms that are acceptable to us, we may be forced to restructure certain aspects of our business or identify and complete one or more strategic collaborations or other transactions in order to fund the development or commercialization of tenapanor or certain of our product candidates through the use of alternative structures. Additional potential transactions that we may consider include a variety of different business arrangements, including spin-offs, spin outs, collaboration partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction may require us to incur non-recurring or other charges, may increase our near- and long-term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including:

- up-front, milestone and royalty payments, equity investments and financial support of new research and development candidates including increase of personnel, all of which may be substantial;
- exposure to unknown liabilities;

- disruption of our business and diversion of our management's time and attention in order to develop acquired products, product candidates or technologies;
- incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions;

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- 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.

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

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

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· business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

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

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

We may be adversely affected by the global economic environment.

Our ability to attract and retain collaboration partners or customers, invest in and grow our business and meet our financial obligations depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, presidential elections, other political influences and inflationary pressures. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The 2008 global financial crisis caused extreme volatility and disruptions in the capital and credit markets. We cannot anticipate all the ways in which the global economic climate and global financial market conditions could adversely impact our business in the future.

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

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

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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
- 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.

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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.

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

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

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

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

- warning letters, fines or holds on clinical trials;
- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- injunctions or the imposition of civil or criminal penalties;
- suspension or revocation of existing regulatory approvals;
- suspension of any of our ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications submitted by us;
- restrictions on our or our contract manufacturers' operations; or
- product seizure or detention, or refusal to permit the import or export of products.

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

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may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these Executive Orders will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

All entities involved in the preparation of product candidates for clinical studies or commercial sale, including our existing contract manufacturers for our product candidates are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with cGMP regulations. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of an NDA or comparable regulatory filing on a timely basis and must adhere to cGMP regulations enforced by the FDA and other regulatory agencies through their facilities inspection programs. The facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. Although we oversee the contract manufacturers, we cannot control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the products may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

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

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

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production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

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

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

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

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

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a qui tam suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

If approved, tenapanor and our other product candidates may cause or contribute to adverse medical events that we are required to report to regulatory agencies and if we fail to do so we could be subject to sanctions that would materially harm our business.

Some participants in clinical studies of tenapanor have reported adverse effects after being treated with tenapanor, including diarrhea, nausea, flatulence, abdominal discomfort, abdominal pain, abdominal distention and changes in electrolytes. If we are successful in commercializing any products, FDA and foreign regulatory agency regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse

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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 comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

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

In order to market any product in the EEA (which is composed of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, separate regulatory approvals are required. In the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. Before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

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

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

Although we do not currently have any products on the market, once we begin commercializing our products, we and our collaboration partners may be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. The laws that may affect our ability to operate as a commercial organization include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;
- the federal physician sunshine requirements under the Affordable Care Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to 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 pricing information and marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- 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

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statutes. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to market our products and adversely impact our financial results.

Legislative or regulatory healthcare reforms in the United States may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates and to produce, market and distribute our products after clearance or approval is obtained.

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

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

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

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

We currently expect that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation, and we currently expect that the current Presidential Administration and U.S. Congress will seek to modify, or repeal all, or certain provisions of, the Affordable Care Act. There is still uncertainty with respect to any regulatory changes, and such regulatory changes could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were otherwise authorized by the Affordable Care Act. However, we cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any drug products for which we may obtain regulatory approval, our

ability to set a price that we believe is fair for our products, our ability to obtain coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

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Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. These new laws, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year that will remain in effect through 2025 unless additional action is taken by Congress, additional specific reductions in Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and an increase in the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, individual states have become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing. Recently, there has also been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

Risks Related to Intellectual Property

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

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

We may be subject to third-party patent infringement claims in the future against us or our that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing a third party's patents. We may be required to indemnify future collaboration partners against such claims. We are not aware of any threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If a patent infringement suit were brought against us we could be forced to stop or delay research, development, manufacturing or 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, we may be unable to maintain such licenses and the rights may be nonexclusive, which would give our competitors access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or forced to redesign it, or to

cease our use of APECCS or some other aspect of our business operations if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms, or unable to maintain such licenses when granted. Even if we are successful in defending against such claims, such litigation can be expensive and time consuming to litigate and would divert management's attention from our core business. Any of these events could harm our business significantly.

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

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in the United States Patent and Trademark Office, or the USPTO, to determine which party is entitled to a patent on the disputed invention. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights with respect to our products and technology. Since patent applications are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates.

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

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

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

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

intellectual property, and some of our competitors have substantially greater intellectual property portfolios than we do.

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

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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.

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

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the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties.

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

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

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

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

Risks Related to Our Common Stock

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 Phase 3 clinical trial for tenapanor for hyperphosphatemia;
- the success of our efforts to establish a collaboration partnership for the commercialization of tenapanor for IBS-C in the United States;

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- our ability, alone or with collaboration partners, to commercialize or obtain regulatory approval for tenapanor, or delays in commercializing or obtaining regulatory approval;
- announcements of regulatory approval, a complete response letter or a refuse to file letter to tenapanor, or specific label restrictions or patient populations for its use, or changes or delays in the regulatory review process;
- announcements relating to our current or future collaboration partnerships;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory agencies with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to our product candidates;
- the success of our testing and clinical trials;
- failure to meet any of our projected timelines or goals with regard to the clinical development of any of our product candidates, including the Phase 3 clinical trial for tenapanor for hyperphosphatemia;
- failure to meet any of our projected timelines with regard to the filing of the NDA for tenapanor for IBS-C;
- 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;

sales of debt securities and sales or licensing of assets;

- general economic and market conditions and overall fluctuations in the United States equity markets; and
- the loss of any of our key scientific or management personnel.

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In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

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

As of June 30, 2018, entities affiliated with New Enterprise Associates, or NEA, a venture capital fund associated with one of our directors, collectively beneficially owned approximately 26.4% of our common stock, and NEA together with our executive officers and directors beneficially owned approximately 29.0% of our capital stock, including outstanding restricted stock units that will vest within 60 days of June 30, 2018, and warrants and stock options exercisable for shares of our common stock within 60 days of June 30, 2018. Therefore, these stockholders may be able to determine all matters requiring stockholder approval, and the entities affiliated with NEA alone will have significant ability to influence decisions through their ownership position. For example, these stockholders may be able to influence or control elections of directors, amendments to our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that certain stockholders may feel are in their best interest as one of our stockholders.

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

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any 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, 2018, we had 62,053,751 shares of common stock outstanding. Of those shares, approximately 15.7 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 June 30, 2018, approximately 0.6 million shares of common stock issuable upon vesting of outstanding restricted stock units and approximately 5.1 million shares of common stock issuable upon exercise of outstanding options were eligible for sale in the public market to the extent permitted by the provisions of the applicable vesting schedules, and Rule 144 and Rule 701 under the Securities Act. In addition, as of June 30, 2018, approximately 2.2 million shares of common stock issuable upon exercise of outstanding warrants were eligible for sale in the public market. If these additional shares of common stock are issued and sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

As of June 30, 2018, the holders of approximately 5.6 million shares of our outstanding common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

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

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least two-thirds of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

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

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

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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.
- 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

Effective May 16, 2018, we entered into a loan and security agreement pursuant to which the Lenders agreed to provide us a $50.0 million term loan facility. Covenants in the loan and security agreement limit our ability to pay dividends or make other distributions. For additional information refer to Note 5 in the notes to our unaudited interim condensed consolidated financial statements in Part I, Item 1 of this Quarterly Report on Form 10 Q.

Unregistered Sales of Equity Securities

None.

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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.

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ITEM 6. Exhibits

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
10.1	Loan and Security Agreement, dated May 16, 2018, by and between the Company and Solar Capital Ltd. and Western Alliance Bank.				X
10.2	Exit Fee Agreement, dated May 16, 2018, by and between the Company and Solar Capital Ltd. and Western Alliance Bank.				X
10.3 #	Transition and Separation Agreement dated July 8, 2018, by and between the Company and Reginald Seeto, MBBS.				X
31.1	Certification of Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1	Certification of Chief Executive Officer and Chief Financial Officer Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101	The following financial statements, formatted in XBRL: (i) Condensed Consolidated Balance Sheets as of June 30, 2018 and December 31, 2017, (ii) Condensed Consolidated Statements of Operations and Comprehensive Loss for the three and six months ended June 30, 2018 and 2017, (iii) Condensed Consolidated Statements of Cash Flows for the six months ended June 30, 2018 and 2017; and (iv) Notes to Unaudited Condensed Consolidated Financial Statements.				X

#Indicates a management contract or compensatory plan or arrangement.

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SIGNATURES

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

Ardelyx, Inc.

Date: August 7, 2018 By: /s/ Mark Kaufmann
Mark Kaufmann
Chief Financial Officer
(Principal Financial and Accounting Officer)