

ACHILLION PHARMACEUTICALS INC  
Form 10-Q  
August 08, 2018  
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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**Washington, D.C. 20549**

**FORM 10-Q**

**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 001-33095**

**ACHILLION PHARMACEUTICALS, INC.**

**(Exact name of registrant as specified in its charter)**

<b>Delaware</b> <b>(State or other jurisdiction of</b>	<b>52-2113479</b> <b>(I.R.S. Employer</b>
<b>incorporation or organization)</b>	<b>Identification No.)</b>
<b>300 George Street, New Haven, CT</b> <b>(Address of principal executive offices)</b>	<b>06511</b> <b>(Zip Code)</b>
<b>(203) 624-7000</b>	
<b>(Registrant's telephone number, including area code)</b>	

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 website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T 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, a smaller reporting company, or 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 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 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

As of August 1, 2018, the registrant had 138,586,070 shares of Common Stock, \$0.001 par value per share, outstanding.



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Table of Contents**PART I. FINANCIAL INFORMATION****ITEM 1. FINANCIAL STATEMENTS****Achillion Pharmaceuticals, Inc.****Balance Sheets****(in thousands, except per share amounts)****(unaudited)**

	<b>June 30, 2018</b>	<b>December 31, 2017</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 35,121	\$ 43,496
Marketable securities	251,624	256,578
Accounts and other receivables	318	60
Prepaid expenses and other current assets	4,842	3,804
Total current assets	291,905	303,938
Marketable securities	7,928	30,511
Fixed assets, net	2,606	2,816
Other assets	198	196
Restricted cash	152	152
Total assets	\$ 302,789	\$ 337,613
<b>Liabilities and Stockholders Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,390	\$ 5,253
Accrued expenses	6,584	7,461
Current portion of long-term debt	153	170
Total current liabilities	8,127	12,884
Long-term debt	53	131
Other long-term liabilities	50	83
Total liabilities	8,230	13,098
Commitments and contingencies (Note 11)		
Stockholders equity:		
Common stock, \$.001 par value; 200,000 shares authorized: 138,586 and 137,894 shares issued and outstanding at June 30, 2018 and December 31, 2017, respectively	139	138

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Additional paid-in capital	935,280	927,420
Accumulated deficit	(640,441)	(602,654)
Accumulated other comprehensive loss	(419)	(389)
Total stockholders' equity	294,559	324,515
Total liabilities and stockholders' equity	\$ 302,789	\$ 337,613

*The accompanying notes are an integral part of these financial statements.*

**Table of Contents****Achillion Pharmaceuticals, Inc.****Statements of Comprehensive Loss****(in thousands, except per share amounts)****(unaudited)**

	<b>Three Months Ended June 30,</b>		<b>Six Months Ended June 30,</b>	
	<b>2018</b>	<b>2017</b>	<b>2018</b>	<b>2017</b>
Revenue	\$	\$	\$	\$
Operating expenses				
Research and development	11,392	18,253	26,142	33,747
General and administrative	7,094	5,363	12,408	11,011
Restructuring charges (Note 4)	75		1,825	
Total operating expenses	18,561	23,616	40,375	44,758
Loss from operations	(18,561)	(23,616)	(40,375)	(44,758)
Other income (expense)				
Interest income	1,370	1,085	2,609	2,092
Interest expense	(8)	(12)	(21)	(29)
Net loss	(17,199)	(22,543)	(37,787)	(42,695)
Basic and diluted net loss per share (Note 5)	(0.12)	(0.16)	(0.27)	(0.31)
Total comprehensive loss (Note 9)	\$ (16,933)	\$ (22,680)	\$ (37,817)	\$ (42,966)
Weighted average number of shares used in computing basic and diluted net loss per share	138,426	136,736	138,221	136,729

*The accompanying notes are an integral part of these financial statements.*

**Table of Contents****Achillion Pharmaceuticals, Inc.****Statements of Cash Flows****(in thousands)****(unaudited)**

	<b>Six Months Ended June 30,</b>	
	<b>2018</b>	<b>2017</b>
<b>Cash flows from operating activities</b>		
Net loss	\$ (37,787)	\$ (42,695)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	571	565
Non-cash stock-based compensation	5,885	5,959
Premium on purchases of marketable securities	(59)	(1,117)
Amortization of premium on marketable securities	160	376
Changes in operating assets and liabilities:		
Accounts and other receivables	(258)	15,027
Prepaid expenses and other assets	(1,040)	(993)
Accounts payable	(3,849)	(3,914)
Accrued expenses and other liabilities	(933)	4,135
Net cash used in operating activities	(37,310)	(22,657)
<b>Cash flows from investing activities</b>		
Purchases of fixed assets	(352)	(334)
Purchases of marketable securities	(124,383)	(208,605)
Maturities of marketable securities	151,789	189,958
Net cash provided by (used in) investing activities	27,054	(18,981)
<b>Cash flows from financing activities</b>		
Proceeds from exercise of stock options	1,874	2
Proceeds from sale of common stock under Employee Stock Purchase Plan	102	127
Payment of deferred financing costs		(175)
Repayments of debt	(95)	(186)
Net cash provided by (used in) financing activities	1,881	(232)
Net decrease in cash and cash equivalents	(8,375)	(41,870)
Cash, cash equivalents and restricted cash, beginning of period	43,648	77,413
Cash, cash equivalents and restricted cash, end of period	\$ 35,273	\$ 35,543

**Supplemental disclosure of cash flow information**



Cash paid for interest	\$	21	\$	30
<b>Supplemental disclosure of non-cash investing activities</b>				
Purchases of fixed assets in accounts payable and accrued expenses	\$	45	\$	86

*The accompanying notes are an integral part of these financial statements.*

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**Achillion Pharmaceuticals, Inc.**

**Notes to Financial Statements**

**(in thousands, except per share amounts)**

**(unaudited)**

**1. Nature of the Business**

Achillion Pharmaceuticals, Inc. (the Company) is a clinical-stage biopharmaceutical company focused on advancing its oral factor D inhibitors into late-stage development and commercialization. The Company focuses its drug development activities on alternative pathway-mediated, rare diseases where there are no approved therapies or where existing therapies are inadequate for patients. The Company's first-generation factor D inhibitor, ACH-4471, has demonstrated preliminary clinical proof-of-concept in patients with C3 glomerulopathy, or C3G, a disease affecting the kidney, and paroxysmal nocturnal hemoglobinuria, or PNH, a blood disorder, and has advanced into phase II clinical trials in both diseases.

The Company incurred net losses of \$17,199 and \$22,543 for the three months ended June 30, 2018 and 2017, respectively, and \$37,787 and \$42,695 for the six months ended June 30, 2018 and 2017, respectively. The Company had an accumulated deficit of \$640,441 at June 30, 2018. The Company has funded its operations primarily through the sale of equity securities.

Based on the Company's current development plan, the Company believes that its existing cash, cash equivalents and marketable securities will be sufficient to meet its current projected operating requirements for at least the next 12 months from the issuance of these financial statements. However, the Company's future capital requirements may change and will depend upon numerous factors, including but not limited to:

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for the Company's drug candidates;

the Company's ability to realize the planned cost savings benefits of the restructuring it implemented in February 2018, which included a significant reduction in its workforce;

the Company's ability to enter into and the terms and timing of any collaborations, licensing or other arrangements that it may establish;

the number of future drug candidates that the Company pursues and their development requirements;

the outcome, timing and costs of seeking regulatory approvals;

the costs of commercialization activities for any of the Company's drug candidates that receive marketing approval to the extent such costs are not the responsibility of any collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

subject to receipt of marketing approval, revenue, if any, received from commercial sales of the Company's drug candidates;

the Company's headcount growth and associated costs as, and when, it seeks to expand its research and development and establish a commercial infrastructure;

the costs involved in preparing, filing, prosecuting, maintaining, enforcing and defending patent and other intellectual property rights and defending against intellectual property-related claims;

the Company's ability to raise debt or equity capital, including any changes in the credit or equity markets that may impact its ability to obtain capital in the future;

the costs associated with, and the outcome of, lawsuits against the Company, if any;

the Company's acquisition and development of new technologies and drug candidates; and

competing technological and market developments, including those currently unknown to the Company.

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**Table of Contents****2. Accounting Standards Updates**

As of January 1, 2018, the Company adopted Accounting Standards Update ( ASU ) No. 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes all existing revenue recognition requirements, including most industry-specific guidance. ASU No. 2014-09 requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. The Company also adopted ASU No. 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations, which clarifies the implementation guidance on principal versus agent considerations as well as ASU No. 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, which clarifies the implementation guidance on identifying performance obligations and licensing. The Company has chosen to adopt ASU No. 2014-09 using a modified retrospective approach. Since the Company did not have any open revenue-generating contracts as of January 1, 2018, there was no cumulative effect upon adoption. Any revenue recognized in prior periods was recognized under Accounting Standards Codification ( ASC ) 605, Revenue Recognition . Should the Company enter into any revenue contracts in the future, it plans to recognize the revenue under ASU No. 2014-09 and include disclosures regarding its related accounting policies based on the nature of the agreement.

As of January 1, 2018, the Company adopted ASU No. 2018-07, Compensation – Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting which was issued in June 2018. ASU No. 2018-07 expands the scope of Topic 718 to include share-based payments issued to nonemployees for goods or services and aligns the accounting for nonemployee share-based payments with the accounting for employee share-based payments. ASU No. 2018-07 is effective for fiscal years beginning after December 15, 2018 and interim periods within those fiscal years. Early adoption is permitted. The Company adopted the provisions of ASU No. 2018-07 effective January 1, 2018 using a modified retrospective approach. Since the Company did not have any nonemployee share-based payment arrangements as of January 1, 2018, there was no cumulative effect upon adoption and there was no material effect on the Company's financial position and results of operations. The Company utilizes the Black-Scholes option pricing model for determining the estimated fair value of stock-based awards and has elected to recognize the effect of nonemployee forfeitures in compensation costs when they occur.

In February 2016, FASB issued ASU No. 2016-02 Leases – Topic 842. ASU No. 2016-02 requires the recognition of lease assets and lease liabilities by lessees for all leases greater than one year in duration and classified as operating leases under previous United States generally accepted accounting principles ( U.S. GAAP ). ASU No. 2016-02 is effective for fiscal years beginning after December 15, 2018, and for interim periods within that fiscal year. The Company is currently evaluating the impact ASU No. 2016-02 will have on its financial position and results of operations. The Company currently expects that most of its operating lease commitments will be subject to the new standard and recognized as operating lease liabilities and right-of-use assets upon its adoption of ASU No. 2016-02.

In August 2016, FASB issued ASU No. 2016-15, Classification of Certain Cash Receipts and Cash Payments. ASU No. 2016-15 eliminates the diversity in practice related to the classification of certain cash receipts and payments in the statement of cash flows by adding or clarifying guidance on eight specific cash flow issues. ASU No. 2016-15 is effective for fiscal years beginning after December 15, 2017 and for interim periods within those fiscal years. The adoption of ASU No. 2016-15 did not have a material effect on the Company's financial position and results of operations.

In November 2016, FASB issued ASU No. 2016-18, Statement of Cash Flows (Topic 230): Restricted Cash. ASU No. 2016-18 requires that the statement of cash flows explain the change during the period in the total of cash, cash equivalents and restricted cash. As a result, restricted cash will be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The new

guidance is effective for fiscal years beginning after December 15, 2017 and for interim periods within those fiscal years. The Company adopted ASU 2016-18 in the first quarter of 2018 and applied the guidance retrospectively to the periods presented. Other than the change in presentation within the statement of cash flows, the adoption of ASU-2016-18 did not have any effect on the Company's financial position and results of operations.

In January 2017, FASB issued ASU No. 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business. ASU 2017-01 adds guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The new guidance is effective for fiscal years beginning after December 15, 2017 and for interim periods within those fiscal years. The adoption of ASU 2017-01 did not have a material effect on the Company's financial position and results of operations.

In May 2017, FASB issued ASU No. 2017-09, Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting which provides clarification on when modification accounting should be used for changes to the terms or conditions of a share-based payment award. ASU No. 2017-09 does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if there is a change to the value, vesting conditions, or award classification. ASU No. 2017-09 is effective for fiscal years beginning after December 15, 2017 and interim periods within those fiscal years. Early adoption is permitted. The adoption of ASU No. 2017-09 did not have a material effect on the Company's financial position and results of operations.

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### **3. Basis of Presentation**

The accompanying unaudited financial statements of the Company should be read in conjunction with the audited financial statements and notes as of and for the year ended December 31, 2017 included in the Company's Annual Report on Form 10-K filed with the SEC on February 22, 2018. The accompanying financial statements have been prepared in accordance with U.S. GAAP for interim financial information, in accordance with the instructions to Form 10-Q and the guidance in Article 10 of Regulation S-X. Accordingly, since they are interim financial statements, the accompanying financial statements do not include all of the information and disclosures required by U.S. GAAP for complete financial statements.

In the opinion of the Company, the accompanying unaudited financial statements contain all adjustments, consisting of only normal recurring adjustments, necessary for a fair statement of its financial position as of June 30, 2018, and its results of operations for the three and six months ended June 30, 2018 and 2017, and cash flows for the six months ended June 30, 2018 and 2017. The balance sheet as of December 31, 2017 was derived from audited annual financial statements but does not contain all of the footnote disclosures from the annual financial statements. Interim results are not necessarily indicative of results for a full year.

The preparation of financial statements in accordance with U.S. GAAP requires management to make estimates and assumptions that affect amounts reported in the financial statements and notes thereto.

### **4. Restructuring Plan**

In February of 2018, the Company implemented a restructuring plan that reduced employee headcount by approximately 20% to approximately 70 employees. The restructuring plan was implemented following a strategic assessment of the Company's portfolio. During the assessment, the Company's management team and board of directors concluded that the Company's strategic focus would be on the development of its existing clinical candidates. The Company continues to assess the staffing levels required to accomplish its revised strategic goals and has reduced its staff across several functional areas, while retaining the biology and chemistry core strengths that it believes will be necessary to advance its complement factor D portfolio and also strengthening its clinical development capabilities.

In connection with this restructuring, the Company offered individuals whose employment was terminated a severance package that included severance pay, continuation of benefits and outplacement services. The Company currently estimates that costs related to the restructuring will be approximately \$1,825, of which \$181 relates to non-cash stock-based compensation. Of the \$1,825, \$1,051 was paid out in cash. The remaining \$593 of costs are included in accrued expenses and are expected to be paid out in cash within the next 12 months.

### **5. Earnings (Loss) Per Share**

Basic earnings (loss) per share (EPS) is calculated in accordance with ASC 260, Earnings Per Share, by dividing net income or loss attributable to common stockholders by the weighted average common stock outstanding. Diluted EPS is calculated by adjusting weighted average common shares outstanding for the dilutive effect of common stock options and warrants. In periods in which a net loss is recorded, no effect is given to potentially dilutive securities, since the effect would be antidilutive. Securities that could potentially dilute basic EPS in the future were not included in the computation of diluted EPS because to do so would have been antidilutive. The calculations of basic and diluted net loss per share are as follows:

	<b>Three Months Ended</b>		<b>Six Months Ended</b>	
	<b>June 30,</b>		<b>June 30,</b>	
	<b>2018</b>	<b>2017</b>	<b>2018</b>	<b>2017</b>
Net loss (numerator)	\$ (17,199)	\$ (22,543)	\$ (37,787)	\$ (42,695)
Weighted-average shares, in thousands (denominator)	138,426	136,736	138,221	136,729
Basic and diluted net loss per share	\$ (0.12)	\$ (0.16)	\$ (0.27)	\$ (0.31)

Potentially dilutive securities outstanding as of June 30, 2018 and 2017 are as follows:

	<b>June 30, 2018</b>	<b>June 30, 2017</b>
Stock options	14,240	12,430
Warrants		2,833
<b>Total potentially dilutive securities outstanding</b>	<b>14,240</b>	<b>15,263</b>

**Table of Contents****6. Marketable Securities**

The Company applies the provisions of ASC 820, Fair Value Measurements and Disclosures, for financial assets and liabilities measured on a recurring basis which requires disclosure that establishes a framework for measuring fair value and expands disclosures in the financial statements. The guidance requires that fair value measurements be classified and disclosed in one of the three categories:

Level 1: Quoted prices in active markets for identical assets and liabilities that the reporting entity has the ability to access at the measurement date;

Level 2: Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly; or

Level 3: Unobservable inputs.

The fair value of the Company's marketable securities of \$259,552 and \$287,089 as of June 30, 2018 and December 31, 2017, respectively, is valued based on level 2 inputs. The Company's investments consist mainly of U.S. government and agency securities, government-sponsored bond obligations and certain other corporate debt securities. Fair value is determined by taking into consideration valuations obtained from third-party pricing services. The third-party pricing services utilize industry standard valuation models, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities; issuer credit spreads; benchmark securities; and other observable inputs. The Company has assessed these as level 2 within the fair value hierarchy of ASC 820. The Company classifies its entire investment portfolio as available for sale as defined in ASC 320, Debt and Equity Securities. Securities are carried at fair value with the unrealized gains (losses) reported as a separate component of stockholders' equity within accumulated other comprehensive income.

The unrealized gain (loss) from marketable securities was \$(419) and \$(389) at June 30, 2018 and December 31, 2017, respectively.

As of June 30, 2018 and December 31, 2017, none of the Company's investments were determined to be other than temporarily impaired.

The following table summarizes the Company's investments:

	June 30, 2018				December 31, 2017			
	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Commercial Paper	\$ 41,795	\$ 94	\$ (6)	\$ 41,883	\$ 29,079	\$ 9	(2)	\$ 29,086
Corporate Debt Securities	177,633		(420)	177,213	216,297		(324)	215,973
Government and Agency Securities	40,543		(87)	40,456	42,102		(72)	42,030
Total	\$ 259,971	\$ 94	\$ (513)	\$ 259,552	\$ 287,478	\$ 9	(398)	\$ 287,089

**7. Accrued Expenses and Other Long-Term Liabilities**



Accrued expenses consist of the following:

	<b>June 30, 2018</b>	<b>December 31, 2017</b>
Accrued compensation	\$ 3,430	\$ 4,014
Accrued research and development expenses	1,558	2,384
Accrued professional expenses	693	735
Restructuring	593	
Other accrued expenses	360	411
Total	\$ 6,634	\$ 7,544

Accrued research and development expenses consist of amounts owed to third-party contract research organizations, clinical investigators, laboratories and data managers for research and development work performed on behalf of the Company.

**Table of Contents****8. Stock-Based Compensation**

The Company's Amended and Restated 2015 Stock Incentive Plan (the "2015 Plan"), is administered by the Company's Board of Directors and provides for the grant of incentive stock options, nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights and other stock-based awards. The Company's officers, employees, consultants, advisors and directors are eligible to receive awards under the 2015 Plan; however, incentive stock options may only be granted to employees. Stock option awards are exercisable for a period determined by the Company, but in no event longer than ten years from the date of the grant. Stock option awards generally vest as to 25% of the shares underlying the option on the first anniversary of the date of grant and as to 6.25% of the shares underlying the option quarterly thereafter for the following three years, subject to continued service. In May 2018, the Company's stockholders approved an amendment and restatement of the 2015 Stock Incentive Plan which included an 8,200 increase to the number of shares of common stock that may be issued pursuant to the 2015 Plan. There were 10,559 shares available to be granted under the 2015 Plan as of June 30, 2018.

A summary of the status of the Company's stock option activity for the six months ended June 30, 2018 is presented in the table and narrative below:

	<b>Options</b>	<b>Weighted Average Exercise Price</b>
Outstanding at January 1, 2018	12,160	\$ 6.37
Granted	4,447	3.13
Exercised	(652)	2.87
Forfeited	(855)	4.62
Cancelled	(860)	8.82
Outstanding at June 30, 2018	14,240	\$ 5.47
Options exercisable at June 30, 2018	8,418	\$ 6.51

Weighted-average fair value of options granted during the period	\$ 2.18
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The Company utilizes the Black-Scholes option pricing model for determining the estimated fair value for stock-based awards. The Black-Scholes model requires the use of assumptions which determine the fair value of the stock-based awards. The assumptions used to value options granted to employees are as follows:

	<b>Six Months Ended</b>	
	<b>June 30, 2018</b>	<b>June 30, 2017</b>
Expected term of option	6.0 years	6.0 years
Expected volatility	79% -80%	83%
Risk free interest rate	2.62% - 2.77%	2.08%
Expected dividend yield	0%	0%

Total compensation expense recorded in the accompanying statements of operations associated with stock option grants made to employees was \$3,462 and \$2,766 for the three months ended June 30, 2018 and 2017, respectively, and \$5,775 and \$5,911 for the six months ended June 30, 2018 and 2017, respectively. Total compensation expense recorded in the accompanying statements of operations associated with stock option grants made to consultants was \$72 and \$0 for the three months ended June 30, 2018 and 2017, respectively, and \$72 and \$0 for the six months ended June 30, 2018 and 2017, respectively. The Company recorded no tax benefit related to these stock options since the Company currently maintains a full valuation allowance on its deferred tax assets.

As of June 30, 2018, the intrinsic value of the stock options outstanding was \$167, all of which related to vested stock options. The intrinsic value of stock options is calculated based on the difference between the exercise prices of the underlying common stock and the quoted stock price of the Company's common stock as of the reporting date.

As of June 30, 2018, the total compensation cost related to unvested stock options not yet recognized in the financial statements is approximately \$11,979, net of estimated forfeitures, and the weighted average period over which this amount is expected to be recognized is 2.7 years.

**Table of Contents****9. Comprehensive Loss**

The Company reports and presents comprehensive income (loss) in accordance with ASC 220, Comprehensive Income, which establishes standards for reporting and display of comprehensive income (loss) and its components in a full set of general purpose financial statements. The objective of the statement is to report a measure of all changes in equity of an enterprise that result from transactions and other economic events of the period other than transactions with owners. The Company's other comprehensive income (loss) arises from net unrealized losses on marketable securities and was immaterial for all periods presented.

**10. Stockholders' Equity**

Changes in stockholders' equity for the six months ended June 30, 2018 and 2017 were as follows:

	<b>Six Months Ended</b>	
	<b>June 30,</b>	
	<b>2018</b>	<b>2017</b>
Balance at December 31, 2017 and 2016	\$ 324,515	\$ 399,454
Net loss	(37,787)	(42,695)
Stock-based compensation	5,885	5,959
Exercise of stock options	1,874	2
Change in unrealized loss on marketable securities	(30)	(271)
Issuance of common stock under the Employee Stock Purchase Plan	102	127
Balance at June 30, 2018 and 2017	\$ 294,559	\$ 362,576

**11. Commitments and Contingencies**

From time to time, in the ordinary course of business, the Company is subject to litigation and regulatory examinations as well as information gathering requests, inquiries and investigations. As of June 30, 2018, there were no outstanding matters.

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**ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

*This Quarterly Report on Form 10-Q contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act and Section 21E of the Securities Exchange Act of 1934, as amended, that involve a number of risks and uncertainties. All statements other than statements relating to historical matters including statements to the effect that we believe, expect, anticipate, plan, target, intend and similar expressions should be considered forward-looking statements. Our actual results could differ materially from those discussed in the forward-looking statements as a result of a number of important factors, including factors discussed in this section and elsewhere in this Quarterly Report on Form 10-Q, including those discussed in Item 1A of this report under the heading Risk Factors, and the risks discussed in our other filings with the Securities and Exchange Commission. Readers are cautioned not to place undue reliance on these forward-looking statements, which reflect management's analysis, judgment, belief or expectation only as the date hereof. We assume no obligation to update these forward-looking statements to reflect events or circumstances that arise after the date hereof except as required by law.*

*The following discussion should be read in conjunction with our financial statements and accompanying notes to financial statements in this quarterly report on Form 10-Q and our audited financial statements and related notes included in our Annual Report on Form 10-K for the year ended December 31, 2017.*

**Overview**

We are a clinical-stage biopharmaceutical company focused on advancing our oral factor D inhibitors into late-stage development and commercialization. Each of the drug candidates in our oral factor D portfolio was discovered in our laboratories and is wholly owned by us. We are focusing our drug development activities on alternative pathway-mediated, rare diseases where there are no approved therapies or where existing therapies are inadequate for patients. To advance our investigational drugs into phase III and commercialization, we plan to work closely with key stakeholders including patients, payors, regulators and healthcare professionals.

Our first-generation factor D inhibitor, ACH-4471, has demonstrated preliminary clinical proof-of-concept in patients with C3 glomerulopathy, or C3G, a disease affecting the kidney, and paroxysmal nocturnal hemoglobinuria, or PNH, a blood disorder, and has advanced into phase II clinical trials in both diseases.

In addition to ACH-4471, we have two potent and specific orally-administered second generation factor D inhibitors in phase I clinical trials, ACH-5228 and ACH-5548. We may seek to advance one or both of these compounds into phase II for C3G or PNH pending analysis of the phase I clinical data in the fourth quarter of 2018.

In interim data from the first four patients enrolled in our phase II clinical trial for C3G patients, ACH-4471 demonstrated reductions in the biomarkers associated with the over-activation of the complement alternative pathway characteristic of patients with C3G, as well as significant reductions in proteinuria, a marker of renal dysfunction.

In interim data from the first four patients enrolled in our phase II clinical trial for PNH patients, ACH-4471 demonstrated reductions in lactate dehydrogenase, or LDH, a marker of intravascular hemolysis, increases in hemoglobin, and improvements in fatigue score. We believe that our alternative pathway factor D inhibitor compounds may have a pharmacological advantage by potentially preventing extravascular hemolysis, or the destruction of PNH red blood cells outside of blood vessels, while also potentially preventing intravascular hemolysis, or red blood cell destruction within blood vessels. In addition, we believe our alternative pathway factor D inhibitor compounds may be able to treat the proportion of patients with PNH who have a suboptimal response to, or who fail to respond to, currently approved treatments for PNH.

We have discovered and are developing small molecule compounds that have the potential to be used in the treatment of immune-related diseases associated with the alternative pathway of the complement system. The complement system is a part of the human innate immune system and is believed to be comprised of three pathways: the alternative pathway, the lectin pathway and the classical pathway. We are advancing novel small molecules from our platform which target complement factor D, an essential protein within the amplification loop of the alternative pathway. Experts believe the alternative pathway plays a critical role in a number of disease conditions including rare orphan conditions such as C3G and immune complex membranoproliferative glomerulonephritis, or IC-MPGN, both diseases affecting the kidney, and PNH, a blood disorder, as well as several more prevalent indications.

We were incorporated on August 17, 1998 in Delaware. Since our inception, we have spent substantial research and development funds to develop our drug candidate pipeline and expect to continue to do so for the foreseeable future. We have incurred losses of \$17.2 million and \$22.5 million for the three months ended June 30, 2018 and 2017, respectively, and \$37.8 million and \$42.7 million for the six months ended June 30, 2018 and 2017. As of June 30, 2018, we had an accumulated deficit of \$640.4 million.

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We have funded our operations primarily through proceeds from the sale of equity securities. Through June 30, 2018, we have received approximately \$932.4 million in aggregate gross proceeds from stock issuances, including convertible preferred stock, our initial public offering, private placements of our common stock, registered offerings of our common stock and an equity investment by a former collaboration partner.

We expect to incur substantial losses for at least the next several years as we seek to continue preclinical and clinical development of certain complement inhibitors drug candidates.

We will need substantial additional financing to obtain regulatory approvals, fund operating losses, and, if deemed appropriate, establish manufacturing and sales and marketing capabilities for our complement inhibitor program, which we will seek to raise through public or private equity or debt financings, collaborative or other arrangements with third parties or through other sources of financing. There can be no assurance that such funds will be available on terms favorable to us, if at all.

In addition to the risks associated with being a drug development company, there can be no assurance that we or any future collaborators will successfully advance or complete our research and development programs, obtain adequate patent protection for our technology, obtain necessary government regulatory approval for drug candidates we develop, find and maintain appropriate collaboration partners or that any approved drug candidates will be commercially viable. In addition, we may not be profitable even if we or any future collaborators succeed in commercializing any of our drug candidates.

## **Restructuring**

In February 2018, we implemented a restructuring plan that will reduce employee headcount by approximately 20% to approximately 70 employees. The restructuring plan was implemented following a strategic assessment of our portfolio. During the assessment, our management team and board of directors concluded that our strategic focus would be on the development of our existing clinical candidates, ACH-4471, ACH-5228, and ACH-5548. We are continuing to assess the staffing levels required to accomplish our revised strategic goals and have reduced our staff across several functional areas, while retaining the biology and chemistry core strengths that we believe will be necessary to advance our complement factor D portfolio and also strengthening our clinical development capabilities.

## **Recent Developments**

In May 2018, Joseph Truitt, our President and Chief Operating Officer, was named Chief Executive Officer to lead the strategic focus on late-stage development and commercialization and was appointed to the Company's Board of Directors. Additionally, Milind S. Deshpande, Ph.D. stepped down from his role as Chief Executive Officer and resigned from the Board of Directors.

In July 2018, we entered into a two-year lease agreement effective August 1, 2018, for additional office space of approximately 3,000 square feet in Blue Bell, Pennsylvania. We anticipate that certain of our officers and employees will be located in this office.

## **Financial Operations Overview**

### ***Revenue***

During the three and six months ended June 30, 2018 and 2017 we did not recognize any revenue. To date, we have not generated any revenue from the sale of any drugs.

***Research and Development***

Our research and development expenses reflect costs incurred for our proprietary research and development projects which consist primarily of salaries and benefits for our research and development personnel, costs of services by clinical research organizations, other outsourced research, materials used during research and development activities, facility-related costs such as rent and utilities associated with our laboratory and clinical development space and operating supplies.

**Our Complement Factor D Program**

The first clinical compound from our complement inhibitor platform is ACH-4471. ACH-4471 is an orally administered compound designed to target and inhibit complement factor D. The next clinical compounds from our complement inhibitor platform that we are focusing on are ACH-5228 and ACH-5548, both of which are next-generation factor D inhibitors that we are seeking to advance for oral administration.



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**ACH-4471.** ACH-4471 is a potent and specific inhibitor of factor D which has demonstrated preliminary proof-of-concept in phase II clinical trials in patients with PNH and C3G. We are currently continuing to conduct phase II clinical trials of ACH-4471, in both indications, and plan to conduct additional trials in patients with PNH and in patients with C3G or IC-MPGN.

*Pharmacokinetics and Metabolism.* Pharmacokinetic results and activity in preclinical studies and clinical trials suggest that ACH-4471 should be explored in clinical development for potential oral dosing three times daily. Controlled release formulation systems were also being developed for ACH-4471 with the objective of optimizing trough exposures and reducing dosing frequency. We completed a phase I bio-availability assessment of a series of preliminary controlled release formulation systems in healthy volunteers and determined that, while half-life and exposure levels in human subjects were improved, additional formulation work would be necessary to achieve less frequent dosing of ACH-4471, however, we are not currently undertaking this work.

*Preclinical.* Six-month and nine-month toxicology studies testing the effects of ACH-4471 in rats and dogs, respectively, have been completed and supported progression of ACH-4471.

*Phase I.* After oral administration of ACH-4471 in phase I clinical trials in healthy volunteers, we noted complete suppression of alternative pathway activity to 24 hours post-dosing. In single-ascending and multi-ascending dose phase I clinical trials in healthy volunteers, at doses ranging from 75mg three times daily to 200mg, 500mg, 800mg, and 1200mg twice daily, ACH-4471 was demonstrated to be generally well tolerated with no treatment-related serious adverse events reported. In the multi-ascending dose 14-day phase I clinical trial, two cases of self-limited alanine aminotransferase, or ALT, elevations (Grade 3 and 4) were observed post-treatment at doses of 500mg and 800mg twice daily, respectively, with neither subject exhibiting signs or symptoms of hepatic decompensation. Both subjects' ALT levels normalized without intervention during follow-up. Further, no treatment-associated fever or infections were observed.

*Phase II.* ACH-4471 has been demonstrated to be highly specific for inhibition of factor D, a protein critical to the amplification of the complement system. In on-going dose ranging phase II clinical trials, doses start at 100mg or 150mg three times daily, or TID, with allowance for intra-patient dose escalation. To date, 250mg TID has been the highest dose administered.

*C3G and IC-MPGN.* We initiated a phase II clinical trial of ACH-4471 in patients with either C3G or IC-MPGN in September 2017 and we continue to add additional clinical trial sites and enroll patients. A sentinel group of patients received dosing of 100mg TID for a period of 14 days with a 7-day taper period, and subsequent groups of patients are being dosed at 200mg TID. This clinical trial is designed to measure C3, a complement protein in blood plasma that is typically low in C3G and IC-MPGN patients, as well as other measures of kidney function or damage characteristic of C3G and IC-MPGN. Preliminary data from four patients with C3G in this 14-day phase II trial suggest that ACH-4471 may reverse the alternative pathway hyperactivity in C3G based upon the observed improvements in complement biomarkers and proteinuria following 14 days of treatment of these four patients. In these patients, the primary clinical manifestation was significant proteinuria, or protein in the urine, which was reduced during the treatment period. Data from this 14-day biomarker study is anticipated to be released in the fourth quarter of 2018.

We have also initiated two longer-term clinical trials in patients with biopsy-confirmed C3G or IC-MPGN. One is a phase II open-label, 12-month treatment trial in which patients will receive treatment with ACH-4471 with periodic assessment of clinical endpoints including proteinuria and estimated glomerular filtration rate, or eGFR. Patients from our 14-day phase II clinical trial in C3G or IC-MPGN will be eligible to continue therapy under this protocol after a wash-out period. Interim data from this open-label trial is anticipated to be released in the fourth quarter of 2018. We have also initiated a phase II randomized, placebo-controlled, 6-month trial. This trial is expected to assess post-treatment renal biopsy findings, as well as changes in complement biomarkers, and clinical endpoints such as proteinuria and eGFR. Data from this clinical trial is anticipated to be released in 2019.

*PNH.* A phase II clinical trial of ACH-4471 in patients with PNH is on-going and continues to enroll untreated PNH patients. Data from the first four PNH patients in this trial was released in 2017. Three of these patients have completed the three-month trial and have entered the long-term extension trial. A fourth patient voluntarily withdrew from the trial on day 41 for reasons unrelated to safety. Interim data from this trial demonstrated that ACH-4471 mechanistically inhibited factor D, its intended target, and meaningfully improved LDH, hemoglobin, fatigue score, and other measures of response, including PNH clone size. We anticipate that interim data from this trial will be released in the fourth quarter of 2018.

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We have also initiated a phase II clinical trial evaluating ACH-4471 in PNH patients currently receiving eculizumab, a therapy for patients with PNH, and who are deemed to be sub-optimal responders who have hemoglobin levels below 10 gm/dL and require transfusions with red blood cells. This trial is designed to evaluate 6 months of treatment with ACH-4471 plus eculizumab with the potential for patients to transition to a long-term treatment extension. We anticipate that interim data from this trial will be released in the fourth quarter of 2018.

**ACH-5228.** ACH-5228 is one of our next-generation factor D inhibitors for oral administration. The compound demonstrated complete inhibition of the complement alternative pathway after repeat, twice-daily dosing in non-human primates over a seven-day period. The compound also has the following characteristics based on our preclinical research to date:

*Pharmacokinetics and Metabolism.* Pharmacokinetic characteristics for ACH-5228 suggest the possibility of less frequent dosing as compared to ACH-4471.

*Preclinical* In short duration, non-clinical studies in rats and dogs ACH-5228 demonstrated tolerability and safety margins supportive of progression into human clinical development. ACH-5228 is also specific for factor D inhibition and demonstrated a two to three-fold greater potency than ACH-4471 in preclinical studies, delivering similar inhibition of the complement alternative pathway at inhibitory concentrations of approximately half that of ACH-4471.

We initiated a first-in-human randomized, placebo-controlled, single-ascending dose phase I study of ACH-5228 administered to healthy volunteers in December 2017. Approximately 28 subjects have been enrolled. The primary endpoint for the trial is the safety and tolerability of ACH-5228. Secondary endpoints include assessments of pharmacokinetics, pharmacodynamics, and evaluation of alternative pathway inhibition in ex vivo laboratory assessments of blood samples from subjects in order to establish a PK/PD relationship for ACH-5228. We expect to report interim data from this study during the fourth quarter of 2018.

**ACH-5548.** ACH-5548 is another of our next-generation factor D inhibitors for oral administration. The compound has the following characteristics based on our preclinical research to date:

*Pharmacokinetics and Metabolism.* Pharmacokinetic characteristics for ACH-5548 suggest the possibility of less frequent dosing as compared to ACH-4471.

*Preclinical.* In short duration, non-clinical studies in rats and dogs ACH-5548 demonstrated tolerability and safety margins supportive of progression into human clinical development. ACH-5548 is also specific for factor D inhibition and demonstrated greater potency than ACH-4471 in preclinical studies, delivering similar inhibition of the complement alternative pathway at inhibitory concentrations four to six-fold lower than that of ACH-4471.

We initiated a first-in-human randomized, placebo-controlled, single-ascending dose phase I study of ACH-5548 administered to healthy volunteers in June 2018. Approximately 28 subjects are expected to be enrolled. The primary endpoint for the trial is the safety and tolerability of ACH-5548. Secondary endpoints include assessments of pharmacokinetics, pharmacodynamics, and evaluation of alternative pathway inhibition in ex vivo laboratory assessments of blood samples from subjects in order to establish a PK/PD relationship for ACH-5548. We expect to

report interim data from this study during the fourth quarter of 2018.

All costs associated with internal research and development, and research and development services for which we have externally contracted, are expensed as incurred. The costs of obtaining patents for our candidates are expensed as incurred as indirect costs. Our research and development expenses for the six months ended June 30, 2018 and 2017 were as follows:

	<b>Six Months Ended</b>	
	<b>June 30,</b>	
	<b>2018</b>	<b>2017</b>
	<b>(in thousands)</b>	
<b>Clinical candidate direct external costs:</b>		
ACH-4471	\$ 10,001	\$ 8,245
ACH-5228	1,648	6,499
ACH-5548	1,192	
Other next generation factor D inhibitors (oral and intravitreal)	1,182	4,041
Other	94	36
	14,117	18,821
Direct internal personnel costs	8,438	10,734
Sub-total direct costs	22,555	29,555
Indirect costs and overhead	3,712	3,927
Research and development tax credit	(125)	265
Total research and development	\$ 26,142	\$ 33,747

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The State of Connecticut provides companies with the opportunity to exchange certain research and development credit carryforwards for cash in exchange for foregoing the carryforward of the research and development credit. The program provides for such exchange of the research and development credit at a rate of 65% of the annual research and development credit. The benefit for such exchange is recorded as a reduction of research and development expenditures.

We expect research and development expenses associated with our complement inhibitor program to be substantial and to increase over time. There are numerous existing factors associated with the development and commercialization, if any, of our complement inhibitor program, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will evolve and therefore are expected to impact the development of our complement inhibitor program and plans over time.

The successful development of our drug candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of our drug candidates. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

the scope, rate of progress and expense of our clinical trials and other research and development activities;

the appropriate endpoints for clinical studies in diseases for which there are no previous regulatory approvals;

the potential benefits of our drug candidates over other therapies;

our ability to market, commercialize and achieve market acceptance for any of our drug candidates that we are developing or may develop in the future;

results of future clinical trials that we may conduct;

results of clinical trials conducted by our competitors;

the terms and timing of any collaborative, licensing and other arrangements that we may establish;

the expense and timing of regulatory approvals; and

the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of any of our drug candidates would significantly change the costs and timing associated with the development of that drug candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required to complete clinical development of a drug candidate, or if we experience significant delays in enrollment in any of our clinical trials, we would be required to expend significant additional financial resources and time on the completion of clinical development.

### ***General and Administrative***

Our general and administrative expenses consist primarily of salaries and benefits for management and administrative personnel, professional fees for legal, accounting and other services, travel costs and facility-related costs such as rent, utilities and other general office expenses.

### **Critical Accounting Policies and Estimates**

Preparation of our financial statements requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses. A summary of our critical accounting estimates is included in the Management's Discussion and Analysis of Financial Condition and Results of Operations section contained in our Annual Report on Form 10-K for the year ended December 31, 2017. We continually review these estimates and their underlying assumptions to ensure they are appropriate for the circumstances. Changes in the estimates and assumptions we use could have a significant impact on our financial results. During the first six months of 2018, there were no significant changes in our estimates or our critical accounting policies.

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Results of operations may vary from period to period depending on numerous factors, including the timing of payments received under existing or future collaborations, strategic alliances, joint ventures or financings, if any, the progress of our research and development projects, technological advances and determinations as to the commercial potential of proposed products.

**Comparison of Three and Six Months Ended June 30, 2018 and 2017****Revenues**

During the three and six months ended June 30, 2018 and 2017 we did not recognize any revenue.

**Comparison of Three and Six Months Ended June 30, 2018 and 2017**

*Research and Development Expenses.* Research and development expenses, exclusive of restructuring charges, were \$11.4 million and \$18.3 million for the three months ended June 30, 2018 and 2017, respectively, and \$26.1 million and \$33.7 million for the six months ended June 30, 2018 and 2017, respectively. The decrease for the three and six months ended June 30, 2018 was primarily due to decreased non-cash stock compensation and personnel costs due to fewer employees, including fewer executives, combined with decreased manufacturing and formulation costs related to ACH-5228 and decreased discovery research costs related to our intravitreal factor D inhibitors. These amounts were partially offset by increased clinical trial costs related to ACH-4471 and preclinical costs related to ACH-5548. We expect research and development expenses will increase somewhat during the second half of the year. Research and development expenses for the three and six months ended June 30, 2018 and 2017 are comprised as follows:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2018	2017	Change	Change	2018	2017	Change	Change
	(in thousands)							
				%				%
Personnel costs	\$ 3,174	\$ 3,947	\$ (773)	(20)%	\$ 6,987	\$ 8,063	\$ (1,076)	(13)%
Stock-based compensation	743	1,277	(534)	(42)%	1,452	2,671	(1,219)	(46)%
Outsourced research and supplies	4,884	10,798	(5,914)	(55)%	11,852	17,658	(5,806)	(33)%
Professional and consulting fees	1,388	1,175	213	18%	3,589	2,804	785	28%
Facilities costs	939	779	160	21%	1,898	1,631	267	16%
Travel and other costs	324	352	(28)	(8)%	489	655	(166)	(25)%
Research and development tax credit	(60)	(75)	15	(20)%	(125)	265	(390)	(147)%
Total	\$ 11,392	\$ 18,253	\$ (6,861)	(38)%	\$ 26,142	\$ 33,747	\$ (7,605)	(23)%

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*General and Administrative Expenses.* General and administrative expenses, exclusive of restructuring charges, were \$7.1 million and \$5.4 million for the three months ended June 30, 2018 and 2017, respectively, and \$12.4 million and \$11.0 million for the six months ended June 30, 2018 and 2017, respectively. The increase for the three and six months ended June 30, 2018 was primarily due to increased personnel and non-cash stock-based compensation charges related to the transition of our former chief executive officer, partially offset by decreased consulting fees. We expect general and administrative expenses for the second half of the year to be consistent with the first half of the year. General and administrative expenses for the three and six months ended June 30, 2018 and 2017 are comprised as follows:

	Three Months Ended June 30,				Six Months Ended June 30,			
	2018	2017	Change	%	2018	2017	Change	%
Personnel costs	\$ 2,462	\$ 1,544	\$ 918	59%	\$ 4,218	\$ 3,221	\$ 997	31%
Stock-based compensation	2,806	1,506	1,300	86%	4,252	3,288	964	29%
Professional and consulting fees	932	1,364	(432)	(32)%	2,121	2,777	(656)	(24)%
Facilities costs	357	329	28	9%	752	670	82	12%
Travel and other costs	537	620	(83)	(13)%	1,065	1,055	10	1%
Total	\$ 7,094	\$ 5,363	\$ 1,731	32%	\$ 12,408	\$ 11,011	\$ 1,397	13%

*Other Income (Expense).* Interest income was \$1.4 million and \$1.1 million for the three months ended June 30, 2018 and 2017, respectively. The \$0.3 million, or 27%, increase was primarily due to a greater return on investments during the three months ended June 30, 2018. Interest expense was \$8,000 and \$12,000 for the three months ended June 30, 2018 and 2017, respectively.

Interest income was \$2.6 million and \$2.1 million for the six months ended June 30, 2018 and 2017, respectively. The \$0.5 million, or 24% increase was primarily due to a greater return on investments during the six months ended June 30, 2018. Interest expense was \$20,000 and \$29,000 for the six months ended June 30, 2018 and 2017, respectively.

**Liquidity and Capital Resources**

Since our inception, we have financed our operations primarily through proceeds from the sale of equity securities. Through June 30, 2018, we have received approximately \$932.4 million in aggregate gross proceeds from stock issuances, including convertible preferred stock, our initial public offering, private placements of our common stock, registered offerings of our common stock and an equity investment by a former collaboration partner.

In October 2014, we entered into a Master Security Agreement for a \$1.0 million Capital Expenditure Line of Credit, or the 2014 Credit Facility, with Webster Bank, National Association, or Webster. In May 2016, we entered into an amendment to the Master Security Agreement. The amendment provided for a line of credit for equipment loan advances of \$1.4 million, of which approximately \$400,000 reflected the outstanding balance as of the date of the amendment, under the Master Security Agreement, dated October 2014 and extended the period during which we were entitled to draw down equipment loan advances through May 26, 2017. In July 2017, Webster agreed to further extend the period during which we were entitled to draw down under the facility through May 28, 2018. Under the facility, purchased equipment serves as collateral for any advances. Each drawdown under the facility is payable over



a three-year term and bears interest at a fixed rate, determined at the time of each borrowing, equal to the Three Year Federal Home Loan Bank of Boston Classic Advance rate plus 4.75%. In October 2016, Webster advanced \$443,000 to us under the facility.

As of June 30, 2018, our debt balance due to borrowings was \$206,000 with a weighted average interest rate of 6.01%.

In February 2017, we filed a universal shelf registration on Form S-3 with the U.S. Securities and Exchange Commission, or SEC, which was declared effective by the SEC on April 28, 2017, to register for sale from time to time up to \$250.0 million of common stock, preferred stock, warrants and/or units in one or more registered offerings. Further, in February 2017, we entered into a sales agreement with Cantor Fitzgerald & Co., or Cantor, as sales agent in an at-the-market sales arrangement pursuant to which, from time to time, we may offer and sell shares of our common stock having an aggregate offering price of up to \$75.0 million through Cantor pursuant to such universal shelf registration statement.

We had \$294.7 million and \$330.6 million in cash, cash equivalents and marketable securities as of June 30, 2018 and December 31, 2017, respectively, and \$152,000 of restricted cash as of June 30, 2018 and December 31, 2017, respectively. We regularly review our investments and monitor the financial markets. As of June 30, 2018, our cash, cash equivalents and marketable securities included high-quality financial instruments, primarily money market funds, government sponsored bond obligations and other corporate debt securities which we believe are subject to limited credit risk.

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Cash used in operating activities was \$37.3 million for the six months ended June 30, 2018 and was primarily attributable to our \$37.8 million net loss, combined with a \$3.9 million decrease in accounts payable and a \$1.0 million increase in prepaid expenses. This amount was partially offset by \$5.9 million in non-cash stock-based compensation. Cash used in operating activities was \$22.7 million for the six months ended June 30, 2017 and was primarily attributable to our \$42.7 million net loss, combined with a \$3.9 million decrease in accounts payable. This amount was partially offset by a \$15.0 million decrease in accounts receivable, primarily related to the receipt of the Janssen milestone payment in January 2017, combined with \$5.9 million in non-cash stock-based compensation and a \$4.1 million increase in accrued expenses.

Cash provided by investing activities was \$27.1 million for the six months ended June 30, 2018 and was primarily attributable to \$151.8 million in maturities of marketable securities partially offset by \$124.4 million in purchases of marketable securities. Cash used in investing activities was \$19.0 million for the six months ended June 30, 2017 and was primarily attributable to \$208.6 million in purchases of marketable securities partially offset by \$190.0 million in maturities of marketable securities.

Cash provided by financing activities was \$1.9 million for the six months ended June 30, 2018 and was primarily attributable to \$1.9 million in proceeds from the exercise of stock options. Cash used in financing activities was \$232,000 for the six months ended June 30, 2017 and was primarily attributable to the payment of deferred financing costs related to the universal shelf registration on Form S-3 filed in February 2017 and our entry into the sales agreement with Cantor, combined with repayments of debt, offset by proceeds received from our Employee Stock Purchase Plan.

We do not expect our existing capital resources to be sufficient to fund the completion of the development of our complement inhibitor program. As a result, we may need to raise additional funds prior to, among other things, being able to further the development of our complement inhibitor program, market any drug candidates associated with that program, obtain regulatory approvals, fund operating losses, and if deemed appropriate, establish manufacturing and sales and marketing capabilities. We may need to raise such additional financing through a combination of public or private equity or debt financings, collaborations, partnerships or other arrangements with third parties or other sources of financing.

We believe that our existing cash, cash equivalents and marketable securities will be sufficient to meet our current projected operating requirements for at least the next 12 months. However, our future capital requirements may change and will depend upon numerous factors, including but not limited to:

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our drug candidates;

our ability to enter into and the terms and timing of any collaborations, licensing or other arrangements that we may establish;

the number of future drug candidates that we pursue and their development requirements;

the outcome, timing and costs of seeking regulatory approvals;

the costs of commercialization activities for any of our drug candidates that receive marketing approval to the extent such costs are not the responsibility of any collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

subject to receipt of market approval, revenue, if any, received from commercial sales of our drug candidates;

our headcount growth and associated costs as, and when, we seek to expand our research and development and establish a commercial infrastructure;

the costs involved in preparing, filing, prosecuting, maintaining, enforcing and defending patent and other intellectual property rights and defending against intellectual property-related claims;

our ability to raise debt or equity capital, including any changes in the credit or equity markets that may impact our ability to obtain capital in the future;

the costs associated with, and the outcome of, lawsuits against us, if any;

our acquisition and development of new technologies and drug candidates; and

competing technological and market developments, including those currently unknown to us.

Furthermore, in February 2018, we implemented a restructuring plan that reduced employee headcount by approximately 20% across several functional areas to approximately 70 employees. We may not realize the planned or expected cost savings benefits of the restructuring, which could adversely affect our estimate of the period for which our cash, cash equivalents and marketable securities will be sufficient to fund our projected operating requirements.

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We may augment our cash balance through financing transactions, including through a combination of public and private equity offerings, debt financings and collaboration, strategic alliance and licensing arrangements. For example, in February 2017, we entered into an agreement with Cantor pursuant to which, from time to time, we may offer and sell up to \$75.0 million of shares of our common stock at the market through Cantor pursuant to a universal shelf registration statement that we filed with the SEC in February 2017. In connection with capital raising activities, we may be required to dilute the ownership interests of our existing stockholders substantially. There can be no assurance that we will be able to obtain adequate levels of additional funding on favorable terms, if at all. If we are unable to obtain adequate levels of additional funding, we may be required to:

delay, reduce the scope of, or eliminate research and development programs, including our complement inhibitor program;

obtain funds through arrangements with collaborators or others on terms that may be unfavorable to us or that may require us to relinquish rights to certain drug candidates that we might otherwise seek to develop or commercialize independently; and/or

pursue merger or acquisition strategies.

If our operating plan changes, we may need additional funds sooner than planned. Such additional financing may not be available when we need it or may not be available on terms that are favorable to us. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis, or at all, we may be required to terminate or delay preclinical studies, clinical trials or other development activities for one or more of our drug candidates. We may seek additional financing through a combination of private and public equity offerings, debt financings and collaboration, strategic alliance and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing stockholders will be diluted, and the terms may include adverse liquidation or other preferences that adversely affect stockholders' rights.

## **Off-Balance Sheet Arrangements**

We did not have any off-balance sheet arrangements as of June 30, 2018.

## **Recently Issued Accounting Standards**

For a discussion of the recent accounting pronouncements relevant to our business operations, see Note 2, Accounting Standards Updates under Part I, Item 1. Financial Statements.

## **ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

*Interest Rate Risk.* Our exposure to market risk is confined to our cash, cash equivalents and marketable securities. We regularly review our investments and monitor the financial markets. We invest in high-quality financial instruments, primarily money market funds, U.S. government and agency securities, government-sponsored bond obligations and certain other corporate debt securities, with the effective duration of the portfolio less than twelve months and no

security with an effective duration in excess of twenty-four months, which we believe are subject to limited credit risk. We currently do not hedge interest rate exposure. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe that an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We do not believe that we have any material exposure to interest rate risk or changes in credit ratings arising from our investments.

*Capital Market Risk.* We currently have no product revenues and depend on funds raised through other sources. One source of funding is through future debt or equity offerings. Our ability to raise funds in this manner depends upon, among other things, capital market forces affecting our stock price, and on the state of the capital markets generally.

#### **ITEM 4. CONTROLS AND PROCEDURES**

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2018. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well

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designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of June 30, 2018, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the fiscal quarter ended June 30, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**PART II. OTHER INFORMATION****ITEM 1A. RISK FACTORS**

*The following risk factors and other information included in this Quarterly Report on Form 10-Q should be carefully considered. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not currently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations. These risk factors restate and supersede in their entirety the risk factors previously disclosed in Part I, Item 1A. Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2017.*

**Risks Related to the Discovery and Development of Our Drug Candidates**

**Our approach to the discovery and development of drug candidates that target complement alternative pathway factor D inhibition is unproven, and we do not know whether we will be able to develop any products of commercial value.**

We are focused on the research and development of our complement inhibitor platform, pursuant to which we are initially targeting complement factor D, an essential protein of the complement alternative pathway that is a part of the human innate immune system. Our complement inhibitor platform is focused on advancing small molecule compounds that inhibit the alternative pathway and have the potential to be used in the treatment of immune-related diseases where the complement pathway plays a critical role. We anticipate that our complement inhibitor platform may play a role in addressing needs of patients with paroxysmal nocturnal hemoglobinuria, or PNH, including patients who have suboptimal response to, or who fail to respond to, currently approved treatments for PNH, and C3 glomerulopathy, or C3G, and immune complex membranoproliferative glomerulonephritis, or IC-MPGN, both kidney diseases, as well as the needs of patients with other complement-mediated diseases where the alternative pathway may play a significant role.

Our approach to the discovery and development of drug candidates that target the alternative pathway is unproven. We are currently only in the early clinical testing stages for our most advanced drug candidates under this program. We may not successfully develop any medicines that target alternative pathway inhibition, and even if we are successful in early development, any medicines that we develop may not effectively inhibit the alternative pathway or provide a clinical benefit. Even if we are able to develop a product candidate that effectively inhibits complement factor D in preclinical studies, we may not succeed in demonstrating safety and efficacy of the product candidate in human clinical trials. For example, although lampalizumab, a product candidate that was in clinical development with another company that targeted complement factor D inhibition in geographic atrophy, or GA, was reported to have

demonstrated safety, tolerability and evidence of activity in a phase II trial, the trial's sponsor announced that in two phase III trials of the product candidate in GA did not meet its primary endpoint of reducing GA lesions when compared to a sham treatment, and the program was discontinued. Our focus on using our proprietary technology to identify drug candidates targeting the alternative pathway may not result in the discovery and development of commercially viable medicines to treat human disease.

**If we are unable to develop, obtain marketing approval for or successfully commercialize drug candidates, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be materially harmed.**

We currently have no products approved for sale and are investing substantially all of our efforts and financial resources on the development of our complement inhibitor platform. Our prospects are substantially dependent on our ability, or that of any future collaborator we may have to develop, obtain marketing approval for, and successfully commercialize at least one drug candidate in one or more disease indications based upon our programs.

The success of our complement inhibitor platform, will depend on several factors, including the following:

initiation, successful enrollment and completion of clinical trials;

safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;

timely receipt of marketing approvals from applicable regulatory authorities;

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the performance of any future collaborators;

the extent of any required post-marketing approval commitments to applicable regulatory authorities;

establishment of supply arrangements with third party raw materials suppliers and manufacturers;

establishment of arrangements with third party manufacturers to obtain finished drug products that are appropriately packaged for sale;

obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally;

protection of our rights in our intellectual property portfolio;

successful commercial launch following any marketing approval;

a continued acceptable safety profile following any marketing approval; and

commercial acceptance of our products or those of our collaborators, if and when approved, by patients, the medical community and third-party payors;

The success of our complement inhibitor platform also depends on our ability to compete with other marketed therapies for complement-mediated diseases such as those from Alexion Pharmaceuticals, Inc., and other potential therapies in development by Akari Therapeutics PLC, Amgen Inc., Amyndas Pharmaceuticals S.A., Apellis Pharmaceuticals, Inc., ChemoCentryx, Inc., Genentech, Inc., Novartis AG, Omeros Corporation, Ra Pharmaceuticals, Inc., and Regeneron Pharmaceuticals, Inc.

Many of the factors on which our success is dependent are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborators. If we or our collaborators are unable to develop, receive marketing approval for and successfully commercialize products based on our technologies, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

**Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.**

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. In addition, changes to formulations



of drug candidates may result in delays and requirements for additional clinical testing. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the drug candidates. Even if we, or any future collaborators, believe that the results of clinical trials for our drug candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our drug candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same drug candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, variability of the disease being studied, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our drug candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced drug candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

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

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable drug candidates. For example, we are currently focusing our efforts in developing ACH-4471 and certain next generation compounds for both C3G and PNH. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the drug candidate.

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### **We recently implemented a plan to reduce our staff levels and eliminate certain personnel and other costs, which could significantly adversely affect our ability to continue to discover and develop new compounds.**

In February 2018, we implemented a restructuring plan that reduced employee headcount by approximately 20% to approximately 70 employees. The restructuring plan was implemented following a strategic assessment of our portfolio. During the assessment, our management team and board of directors concluded that our strategic focus would be on the development of our existing clinical candidates, ACH-4471, ACH-5228, and ACH-5548. We are assessing the staffing levels required to accomplish our revised strategic goals and have reduced our staff across several functional areas.

Our restructuring efforts may disrupt our staff and our business, and we may not be successful in advancing our existing clinical candidates or in discovering or developing new compounds as a result of lower staffing levels and a reduction in our spending plan.

### **Clinical drug development involves a lengthy and expensive process with an uncertain outcome.**

Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our drug candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a drug candidate may not continue development or is not approvable. It is possible that even if one or more of our drug candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of any clinical trials. Conversely, as a result of the same factors, any clinical trials may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any. Similarly, in any clinical trials we may fail to detect toxicity of or intolerability caused by our drug candidates, or mistakenly believe that our drug candidates are toxic or not well tolerated when that is not in fact the case.

Additional factors that may negatively impact our clinical development efforts include:

delay or failure in obtaining approval by institutional review board or similar reviewing entities to conduct a clinical trial at each site;

delay or failure in reaching agreement on acceptable terms with prospective contract research organizations, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different contract research organizations and trial sites;

clinical sites and investigators deviating from trial protocol, failing to conduct the trial in accordance with regulatory requirements, or dropping out of a trial;

slow patient enrollment, particularly in rare diseases being studied;

competition with other sponsors for patients;

delay or failure in having patients complete a trial or return for post-treatment follow-up;

disruption of clinical supply or clinical operations at our clinical trial sites;

adverse medical events or side effects in treated patients, and the threat of legal claims and litigation alleging injuries;

lack of effectiveness or safety of the product candidate being tested; and

decisions by regulatory authorities, the institutional review board, ethics committee, or us, or recommendation by a data safety monitoring board, to suspend or terminate clinical trials at any time for safety issues or for any other reason.

Our failure to successfully initiate and complete clinical trials of our drug candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our drug candidates would significantly harm our business.

**If clinical trials of our drug candidates fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or may ultimately be unable to complete, the development and commercialization of these drug candidates.**

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any drug candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements. We, and any future collaborators, may never receive such approvals. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our drug candidates in humans before we, or they, will be able to obtain these approvals.

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Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. In addition, our interest in developing potential therapies for rare diseases for which there is no currently available treatment, such as C3G, makes the difficulty in study design and outcome more challenging, as the appropriate endpoints for obtaining approval from regulatory authorities have not been previously defined. Additionally, the clinical course of C3G is highly variable and it may be difficult to identify appropriate patients for clinical studies. PNH and C3G are chronic conditions and regulatory authorities may require clinical trials for longer periods than anticipated by us. Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if (1) we, or any future collaborators, are required to conduct additional clinical trials or other testing of our drug candidates beyond the trials and testing that we, or they contemplate, (2) we, or any future collaborators, are unable to successfully complete clinical trials of our drug candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or (4) there are unacceptable safety concerns associated with our drug candidates, we, or any future collaborators, in addition to incurring additional costs, may:

be delayed in obtaining marketing approval for our drug candidates;

not obtain marketing approval at all;

obtain approval for indications or patient populations that are not as broad as intended or desired;

obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;

be subject to additional post-marketing testing or other requirements; or

be required to remove the product from the market after obtaining marketing approval.

**Adverse events or undesirable side effects caused by, or other unexpected properties of, any of our drug candidates may be identified during development that could delay or prevent their marketing approval or limit their use.**

Adverse events or undesirable side effects caused by, or other unexpected properties of, our drug candidates could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our drug candidates and could result in a more restrictive label or FDA requirement for a risk evaluation and mitigation strategy, or REMS, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. For example, treatment with complement inhibitors, like each of our factor D inhibitors, may decrease the body's ability to fend off infection by certain types of pathogens. Treatment with the marketed complement C5 inhibitor, eculizumab (Soliris®), is associated with increased risk for certain types of infection, including meningococcal infection. For this reason, patients treated with complement inhibitors, including patients treated in our future clinical trials, may be vaccinated for pathogens known to have increased risk of infection with complement deficiency or inhibition and may also be treated with prophylactic antibiotics in an effort to reduce

the risk of an adverse event resulting from an infection. However, there is a risk that vaccination and/or prophylactic antibiotics will not prevent or reduce the risk of infections, including meningococcal infection.

Other adverse events may occur. In our phase I multiple ascending dose study of ACH-4471 in healthy volunteers, two cases of self-limited, ALT elevations (Grade 3 and 4) were observed post-treatment in the two highest dose groups, with neither subject exhibiting signs or symptoms of liver decompensation. Both subjects' ALT levels normalized without intervention during follow up. Further, no treatment-associated fever or infections were observed. ALT is a liver enzyme measure to see whether a liver is damaged or diseased. There is a risk that increases in ALT will be seen in other healthy subjects or patients in our clinical studies dosed with ACH-4471. To date, ACH-4471 has been dosed in few patients and for limited durations, the longest being approximately one year, and there is a risk that in longer dosing durations planned for our clinical trials, patients may experience increases in ALT or other adverse events. There is also a risk that doses of ACH-4471 which we believe can be safely administered to patients may not be effective in treating complement mediated diseases such as PNH or C3G.

If any of our drug candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that drug candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

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**If we, or any future collaborators, experience any of a number of possible unfavorable events in connection with clinical trials of our drug candidates, potential marketing approval or commercialization of our drug candidates could be delayed or prevented.**

We, or any future collaborators, may experience numerous unfavorable events during, or as a result of, clinical trials that could delay or prevent marketing approval or commercialization of our drug candidates, including:

clinical trials of our drug candidates may produce unfavorable or inconclusive results;

we, or any future collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;

the number of patients required for clinical trials of our drug candidates may be larger than we, or any future collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any future collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate;

the cost of planned clinical trials of our drug candidates may be greater than we anticipate;

our third-party contractors or those of any future collaborators, including those manufacturing our drug candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any future collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any future collaborators in a timely manner or at all;

regulators or institutional review boards may not authorize us, any future collaborators, or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

we, or any future collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;

we, or any future collaborators, may have to delay, suspend or terminate clinical trials of our drug candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the drug candidate;

regulators or institutional review boards may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the drug candidate or findings of undesirable effects caused by a chemically or mechanistically similar drug or drug candidate;

the FDA or comparable foreign regulatory authorities may disagree with our, or any future collaborators, clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;

the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we, or any future collaborators, enter into agreements for clinical and commercial supplies;

the supply or quality of raw materials or manufactured drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; 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 to obtain marketing approval.

Product development costs for us, or any future collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our drug candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize our drug candidates or allow our competitors, or the competitors of any future collaborators, to bring products to market before we, or any future collaborators, do and impair our ability, or the ability of any future collaborators, to successfully commercialize our drug candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our drug candidates.

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**If we, or any future collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our or their receipt of necessary regulatory approvals could be delayed or prevented.**

We, or any future collaborators, may not be able to initiate or continue clinical trials for any of our drug candidates if we, or they, are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. We are investigating our drug candidates in PNH, C3G and IC-MPGN, all of which are rare diseases. Arranging for investigative sites and recruiting patients for our clinical trials in these diseases may be very difficult. In addition, other companies are currently investigating their investigational products in PNH and C3G which may make it more difficult to enroll eligible patients into our clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

the size and nature of the patient population, particularly for rare diseases such as PNH, C3G and IC-MPGN;

the severity of the disease under investigation;

the proximity of patients to clinical sites;

the eligibility criteria for the trial;

the design of the clinical trial;

efforts to facilitate timely enrollment;

competing clinical trials; and

clinicians and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

Our inability, or the inability of any future collaborators, to enroll a sufficient number of patients for our, or their, clinical trials could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in our, or their, clinical trials may result in increased development costs for our drug candidates, delay or halt the development of and approval processes for our drug candidates and jeopardize our, or any future collaborators', ability to commence sales of and generate revenues from our drug candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

**If any of our drug candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any future collaborators, to market the drug could be compromised.**



Clinical trials of our drug candidates are expected to be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a drug candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a drug candidate, we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

regulatory authorities may withdraw their approval of the drug;

we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;

additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;

we may be subject to fines, injunctions or the imposition of civil or criminal penalties;

regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;

we, or any future collaborators, could be sued and held liable for harm caused to patients;

the drug may become less competitive; and

our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

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**Even if one of our drug candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third party payors, health authorities and others in the medical community necessary for commercial success and the market opportunity for the drug candidate may be smaller than we estimate.**

We have never commercialized a product. Even if one of our drug candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient, or even any, market acceptance by physicians, patients, third party payors, health authorities and others in the medical community. For example, physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of our drug candidates may require significant resources and may not be successful. If any of our drug candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

the efficacy and safety of the product;

the potential advantages of the product compared to alternative treatments;

the prevalence and severity of any side effects;

the clinical indications for which the product is approved;

whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy;

limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling;

our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;

the product's convenience and ease of administration compared to alternative treatments;

the willingness of the target patient population to try, and of physicians to prescribe, the product;

the strength of sales, marketing and distribution support;

the approval of other products for the same indications;

changes in the standard of care for the targeted indications for the product;

the timing of market introduction of our approved products as well as competitive products;

availability and amount of reimbursement from government payors, managed care plans and other third-party payors;

adverse publicity about the product or favorable publicity about competitive products; and

potential product liability claims.

**If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any drug candidates that we develop if and when those drug candidates are approved.**

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to use a combination of focused in-house sales and marketing capabilities and third-party collaboration, licensing and distribution arrangements to sell any of our products that receive marketing approval.

We generally plan to seek to retain full commercialization rights in the United States for products that we can commercialize with a small specialized sales force in certain rare diseases. The development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

We generally plan to collaborate with third parties for commercialization in the United States of any products that we cannot commercialize with a small sales force and that require a large sales, marketing and product distribution infrastructure. We also plan to commercialize our drug candidates outside the United States through collaboration, licensing and distribution arrangements with third



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parties. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our drug candidates that receive marketing approval.

### **We face substantial competition from other pharmaceutical and biotechnology companies, and our operating results may suffer if we fail to compete effectively.**

The development and commercialization of new drug products is highly competitive. We expect that we and our future collaborators, if any, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any of our drug candidates that we, or they, may seek to develop or commercialize in the future. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of drug candidates for the treatment of the key complement-mediated disease indications. For example, Alexion Pharmaceuticals, Inc. s eculizumab (Soliris<sup>®</sup>) is a marketed therapy for the treatment of PNH and atypical hemolytic uremic syndrome. Akari Therapeutics PLC, Amgen Inc. Amyndas Pharmaceuticals S.A., Apellis Pharmaceuticals, Inc., ChemoCentryx, Inc., Genentech, Inc., Novartis AG, Omeros Corporation, Ra Pharmaceuticals, Inc., and Regeneron Pharmaceuticals, Inc. have complement inhibitor therapies in development for other hematologic or nephritic diseases. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, have fewer or more tolerable side effects or are less costly than any drug candidates that we are currently developing or that we may develop, which could render our drug candidates obsolete and noncompetitive.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we, or any future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we, or any future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any future collaborators, are able to enter the market.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

**If the FDA or comparable foreign regulatory authorities approve generic versions of any of our products that receive marketing approval, or such authorities do not grant our products appropriate periods of data exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.**

Once a new drug application, or NDA, is approved, the product covered thereby becomes a reference-listed drug in the FDA's publication, *Approved Drug Products with Therapeutic Equivalence Evaluations*. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical studies. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

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Competition that our products may face from generic versions of our products could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those drug candidates.

**Even if we, or any future collaborators, are able to commercialize any drug candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third party payor reimbursement practices or healthcare reform initiatives that could harm our business.**

The commercial success of our drug candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our drug candidates will be paid by third party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize our drug candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third party payors and coverage and reimbursement for products can differ significantly from payor to payor.

There is significant uncertainty related to third party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any of our drug candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third party payors. Third party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our drug candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates

may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any drug candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our drug candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.



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Spurred by examples of large price increases for certain drugs, political candidates and others have raised media attention to the issue of pharmaceutical price regulation. For example, recently announced plans have included elements such as patient spending caps, requirements for drug makers to spend a defined portion of their profits on research and development, allowing Americans to import lower-priced drugs from other countries and addressing specialty pharmaceuticals which tend to have higher prices than other drugs. If greater regulation of pharmaceutical pricing is approved, we may not be able to receive adequate reimbursement for our drug therapies or may be forced to accept pricing at levels lower than that which would make us profitable. We cannot predict the political or regulatory climate that may result in enhanced drug pricing regulations.

**Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop.**

We face an inherent risk of product liability claims as a result of the clinical testing of our drug candidates despite obtaining appropriate informed consents from any clinical trial participants. We will face an even greater risk if we or any future collaborators commercially sell any product that we may, or they may, develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical 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 or 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 drug candidates. Regardless of the merits or eventual outcome, liability claims may result in:

decreased demand for our drug candidates or products that we may develop;

injury to our reputation and significant negative media attention;

withdrawal of clinical trial participants;

significant costs to defend resulting litigation;

substantial monetary awards to trial participants or patients;

loss of revenue;

reduced resources of our management to pursue our business strategy; and

the inability to commercialize any products that we may develop.

Although we maintain general liability insurance and clinical trial/products liability insurance, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even

if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin selling any drug candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our drug candidates, which could adversely affect our business, financial condition, results of operations and prospects.

**Our business and operations would suffer in the event of system failures or security breaches.**

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our product development programs and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liabilities and the further development of our drug candidates may be delayed.

Additionally, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to 20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for

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damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with any European activities.

### **Risks Related to our Financial Position and Need for Additional Capital**

**We have incurred significant losses since inception, expect to incur significant and accumulating losses for at least the next several years, and we may never achieve or maintain profitability.**

We have incurred significant annual net operating losses since our inception. We expect to continue to incur significant and accumulating net operating losses for at least the next several years. Our net losses were \$17.2 million and \$22.6 million for the three months ended June 30, 2018 and 2017, respectively, and \$37.8 million and \$42.7 million for the six months ended June 30, 2018 and 2017, respectively. We had an accumulated deficit of \$640.4 million at June 30, 2018. We have not generated any revenues from product sales, have not completed the development of any drug candidate and may never have a drug candidate approved for commercialization. We are currently only in the early clinical testing stages for our most advanced drug candidate under our complement inhibitor platform and expect that it will be many years, if ever, before we have a drug candidate ready for commercialization.

We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and our clinical development programs. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

continue clinical development efforts for our factor D inhibitor drug candidates, including ACH-4471, ACH-5228 and ACH-5548;

seek regulatory and marketing approvals for our drug candidates that successfully complete clinical trials, if any;

establish sales, marketing, distribution and other commercial infrastructure to commercialize various products for which we may obtain marketing approval, if any;

contract for the manufacture of larger quantities of drug candidates for clinical development and potentially commercialization;

maintain, expand and protect our intellectual property portfolio; and

hire and retain additional personnel, such as clinical, quality control and regulatory personnel. Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or any future collaborator is, able to obtain marketing approval for, and successfully commercialize, products based on our programs. This will require success in a range of challenging activities, including completing clinical trials of our drug candidates, obtaining marketing approval for these drug candidates, manufacturing, marketing and selling those products for which we, or any future collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of increased expenses, and if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and adversely impact our stock price and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of drug candidates or continue our operations.

**We will need additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.**

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate clinical trials of, initiate new research and preclinical development efforts for and seek marketing approval for, our drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator. Accordingly, we will need to obtain additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

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We will be required to expend significant funds in order to advance the development of our complement factor D inhibitor drug candidates. In addition, while we may seek one or more collaborators for future development of our drug candidates, we may not be able to enter into a collaboration for any of our drug candidates on suitable terms or at all. In any event, our existing cash, cash equivalents and marketable securities will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our drug candidates.

Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. Furthermore, as a result of the termination of our exclusive license and collaboration agreement with Janssen Pharmaceuticals, Inc., or Janssen, which we refer to as the Janssen Agreement, we will not receive any future milestone-based or royalty payments under that arrangement.

We believe that our existing cash, cash equivalents and marketable securities as of June 30, 2018, will enable us to fund our current projected operating requirements for at least the next 12 months from the issuance of these financial statements. Our estimate as to how long we expect our existing cash, cash equivalents and marketable securities to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our drug candidates;

our ability to realize the planned cost savings benefits of the restructuring we implemented in February 2018, which included a significant reduction in our workforce;

our ability to enter into and the terms and timing of any collaborations, licensing or other arrangements that we may establish;

the number of future drug candidates that we pursue and their development requirements;

the outcome, timing and costs of seeking regulatory approvals;

the costs of commercialization activities for any of our drug candidates that receive marketing approval to the extent such costs are not the responsibility of any collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

subject to receipt of marketing approval, revenue, if any, received from commercial sales of our drug candidates;

our headcount growth and associated costs as we seek to expand our research and development and establish a commercial infrastructure;

the costs involved in preparing, filing, prosecuting, maintaining, enforcing and defending patent and other intellectual property rights and defending against intellectual property-related claims;

our ability to raise debt or equity capital, including any changes in the credit or equity markets that may impact our ability to obtain capital in the future;

the costs associated with, and the outcome of, lawsuits against us, if any;

our acquisition and development of new technologies and drug candidates; and

competing technological and market developments, including those currently unknown to us.

**Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or drug candidates.**

We expect that we will need additional capital in the future to continue our planned operations. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interests of our stockholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of a common stockholder. In February 2017, we entered into a sales agreement with Cantor Fitzgerald & Co., or Cantor, as sales agent, pursuant to which, from time to time, we may offer and sell shares of our common stock having an aggregate offering price of up to \$75,000,000 through Cantor pursuant to a universal shelf registration statement that we filed with the Securities and Exchange Commission, or SEC, in February 2017. Sales of our common stock, if any, under the agreement with Cantor may be made in sales deemed to be an at-the-market offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended, or the Securities Act. Sales of substantial amounts of shares of our common stock or other securities could cause dilution to our stockholders and lower the market price of our common stock.

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In addition, debt financing, if available, could result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our drug candidates.

If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or drug candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

**As a result of the termination of the Janssen Agreement, we will not receive any future milestone-based or royalty payments from Janssen relating to our HCV program, and we have no plans to advance the HCV program on our own.**

In May 2015, we entered into the Janssen Agreement with Janssen. On September 9, 2017, Janssen provided us with notice that Janssen was unilaterally terminating the Janssen Agreement in its entirety and discontinuing their development program for JNJ-4178, a three-drug combination regimen that contained one of our chronic hepatitis C virus, or HCV, product candidates licensed to Janssen. The termination became effective on November 8, 2017. We had previously granted Janssen exclusive worldwide rights to develop and commercialize our portfolio of drug candidates for the treatment of HCV infection. We currently have no plans to advance the program on our own. As such, we do not expect to derive any further value from the HCV program.

**The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.**

On December 22, 2017, President Trump signed into law new legislation that significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income, limitation on the amount of research and development expenses deductible per year, and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

**Our effective tax rate may fluctuate, and we may incur additional tax obligations.**

We are subject to taxation in a number of U.S. states. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different

than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability, if any, from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in additional tax obligations.

**Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.**

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a company undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. For example, we completed a review of our changes in ownership through December 31, 2015 and determined that we had four ownership changes since inception. The changes of ownership resulted in net operating loss and research and development credit carryforwards expiring unutilized. If additional limitations were to apply, utilization of a portion of our net operating loss and tax credit carryforwards could be further limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.



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**If the estimates we make and the assumptions on which we rely in preparing our financial statements prove inaccurate, our actual results may vary significantly.**

Our financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses. Such estimates and judgments include revenue recognition, stock-based compensation expense, the valuation of investments, accrued expenses and deferred tax assets and liabilities. We base our estimates and judgments on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. However, these estimates and judgments, or the assumptions underlying them, may change over time. Accordingly, our actual financial results may vary significantly from the estimates contained in our financial statements.

### **Risks Related to Our Dependence on Third Parties**

**We may enter into collaborations with third parties for the development and commercialization of our drug candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these drug candidates.**

We may in the future seek third-party collaborators for the development and commercialization of product candidates based on our complement inhibitor platform. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our drug candidates. Our ability to generate revenues from any future collaboration or license agreement will depend on the collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any collaborators may have the right to abandon research or development projects and terminate applicable agreements, including any funding obligations, prior to or upon the expiration of the agreed upon terms. For example, on September 9, 2017, we received notice from Janssen that the Janssen Agreement, pursuant to which we granted Janssen exclusive worldwide rights to develop and commercialize our portfolio of HCV drug candidates, would be terminated effective November 8, 2017. As a result of the termination, we will not receive any future milestone-based or royalty payments under the Janssen Agreement, our HCV drug candidates will not be developed or commercialized by Janssen and our HCV drug candidates may never be developed or commercialized.

Collaborations involving our drug candidates pose a number of risks, including the following:

collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

collaborators may not perform their obligations as expected;

collaborators may not pursue development and commercialization of our drug candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus, changes in the competitive environment, available funding or external factors, such as an acquisition, that divert resources or create competing priorities. For example, pursuant to the

notice of termination of the Janssen Agreement, Janssen informed us that with an increasing number of effective therapies addressing medical need in hepatitis C, Janssen had made a strategic decision to discontinue the development of JNJ-4178, a three-drug combination regimen that contained one of our HCV product candidates licensed to Janssen;

collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;

a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;

disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of drug candidates, might lead to additional responsibilities for us with respect to drug candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

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collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable drug candidates.

Collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any drug candidate licensed to it by us.

**We may seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.**

Our drug development programs and the potential commercialization of our drug candidates will require substantial additional cash to fund expenses. For some of our drug candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those drug candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the potential differentiation of our drug candidate from competing drug candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the drug candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our drug candidate.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. In addition, any collaboration agreements that we enter into in the future may contain, restrictions on our ability to enter into potential collaborations or to otherwise develop specified compounds.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate product revenue.

**We have and intend to continue to rely on third parties to conduct any clinical trials. If they do not perform satisfactorily, our business could be materially harmed.**

We have and intend to continue to rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct clinical trials and expect to rely on these third parties to conduct clinical trials of any drug candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new contract research organization begins work. As a result, delays would likely occur, which could materially impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, our reliance on these third parties for clinical development activities limits our control over these activities, but we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our drug candidates, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in any clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our drug candidates, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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Furthermore, the third parties that we intend to engage to conduct clinical trials on our behalf are not our employees, and except for remedies available to us under agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct any clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our drug candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our drug candidates. In such an event, our financial results and the commercial prospects for any drug candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

We also intend to rely on other third parties to store and distribute drug supplies for any clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our drug candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

**We have and intend to continue to contract with third parties for the manufacture and distribution of any drug candidates for clinical trials in connection with our future development and commercialization efforts. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.**

We currently have no manufacturing facilities and limited personnel with manufacturing experience. We have and intend to continue to rely on contract manufacturers to produce both drug substance and drug product required for any clinical trials. We also intend to rely upon contract manufacturers, and potentially collaboration partners, to manufacture commercial quantities of our products, if approved. Reliance on such third-party contractors entails risks, including:

manufacturing delays if our third-party contractors give greater priority to the supply of other products over our drug candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;

the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;

the possible breach by the third-party contractors of our agreements with them;

the failure of third party contractors to comply with applicable regulatory requirements;

the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;

the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and

the possible misappropriation of our proprietary information, including our trade secrets and know-how. We currently rely, and expect to continue to rely, on a small number of third party contract manufacturers to supply active pharmaceutical ingredient and required finished product for our preclinical studies and clinical trials. We do not have long-term agreements with any of these third parties. If any of our existing manufacturers should become unavailable to us for any reason, we may incur some delay in identifying or qualifying replacements.

Any manufacturing problem or the loss of a contract manufacturer could be disruptive to our operations, delay any clinical trials and, if our products are approved for sale, result in lost sales. Additionally, we intend to rely on third parties to supply the raw materials needed to manufacture any drug candidates. Any reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to future contract manufacture caused by problems at suppliers could delay shipment of our drug candidates, increase our cost of goods sold and result in lost sales.

If any of our future drug candidates are approved by any regulatory agency, we plan to enter into agreements with third party contract manufacturers for the commercial production and distribution of those products. It may be difficult for us to reach agreement with a contract manufacturer on satisfactory terms or in a timely manner. In addition, we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under current good manufacturing practices, or cGMPs, that are capable of manufacturing our drug candidates. Consequently, we may not be able to reach agreement with third party manufacturers on satisfactory terms, which could delay our commercialization efforts.

Third party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the drug candidate. Similar regulations apply to manufacturers of our drug candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable

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regulatory requirements for the manufacture of our drug candidates. If our manufacturers cannot successfully manufacture material that conforms to our specifications or the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable drug candidate.

In addition, our manufacturers are subject to ongoing periodic inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements both prior to and following the receipt of marketing approval for any of our drug candidates. Some of these inspections may be unannounced. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our drug candidates and have a material adverse impact on our business, financial condition and results of operations.

Our current and anticipated future dependence upon others for the manufacture of our drug candidates may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

## **Risks Related to Our Intellectual Property**

**If our patent position does not adequately protect our drug candidates, others could compete against us more directly, which would harm our business.**

We own or hold exclusive licenses to a number of U.S. issued patents, pending U.S. provisional and non-provisional patent applications, as well as pending Patent Cooperating Treaty, or PCT, applications and associated foreign patents and patent applications. Our success depends in large part on our ability to obtain and maintain patent protection both in the United States and in other countries for our drug candidates. Our ability to protect our drug candidates from unauthorized or infringing use by third parties depends in substantial part on our ability to obtain and maintain valid and enforceable patents. Due to evolving legal standards relating to the patentability, validity and enforceability of patents covering pharmaceutical inventions and the scope of claims made under these patents, our ability to maintain, obtain and enforce patents is uncertain and involves complex legal and factual questions. Accordingly, rights under any issued patents may not provide us with sufficient protection for our drug candidates or provide sufficient protection to afford us a commercial advantage against competitive products or processes. We cannot guarantee that any patents will issue from any pending or future patent applications owned by or licensed to us.

Patent applications in the United States are maintained in confidence for up to 18 months after their filing. In some cases, however, patent applications remain confidential in the U.S. Patent and Trademark Office, which we refer to as the U.S. Patent Office, for the entire time prior to issuance as a U.S. patent. Similarly, publication of discoveries in the scientific or patent literature often lags behind actual discoveries. Consequently, we cannot be certain that we or our licensors or co-owners were the first to invent, or the first to file patent applications on, our drug candidates or their intended uses. Furthermore, we may not have identified all U.S. and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market or patentability, or all prior art that could be considered relevant to our patent claims.

The claims of any patents which have already issued or may issue in the future and are owned or controlled by us, may not confer on us significant commercial protection against competing products. Additionally, our patents may be challenged by third parties, resulting in the patent being deemed invalid, unenforceable or narrowed in scope, or the

third party may circumvent any such issued patents. The cost of these procedures could be substantial, and it is possible that our efforts would be unsuccessful resulting in a loss of our U.S. patent position. Also, our pending patent applications may not issue, and we may not receive any additional patents. Our patents might not contain claims that are sufficiently broad to prevent others from utilizing our technologies. For instance, the issued patents relating to our drug candidates may be limited to a particular molecule or a related group of molecules. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property. To the extent a competitor can develop similar products using a different molecule, our patents may not prevent others from directly competing with us.

The Leahy-Smith America Invents Act, or the America Invents Act, was signed into law in September 2011, and many of the substantive changes became effective in March 2013. The America Invents Act revised United States patent law in part by changing the standard for patent approval from a first to invent standard to a first to file standard and developing a post-grant review system. This legislation changes United States patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 2013. For example, if we are the first to invent a new drug or its use, but another party is the first to file a patent application on this invention, under the new law the other party may be entitled to the patent rights on the invention.



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The America Invents Act created for the first-time new procedures to challenge issued patents in the United States, including post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with a priority date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent was filed prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with a priority date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of challenge, whereas inter partes review proceedings can only be brought to raise a challenge based on published prior art. These adversarial actions at the U.S. Patent Office review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent cancelled in a Patent Office post-grant review or inter partes review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a U.S. patent office proceeding, there is no guarantee that we or our licensors will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed. For example, we could become a party to foreign opposition proceedings, such as at the European Patent Office, or patent litigation and other proceedings in a foreign court. If so, uncertainties resulting from the initiation and continuation of such proceedings could have a material adverse effect on our ability to compete in the market place. The cost of foreign adversarial proceedings can also be substantial, and in many foreign jurisdictions, the losing party must pay the attorney fees of the winning party.

Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any of our drug candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization of our drug candidates, thereby reducing any advantages of the patent. To the extent our drug candidates based on that technology are not commercialized significantly ahead of the date of any applicable patent, or to the extent we have no other patent protection on such drug candidates, those drug candidates would not be protected by patents, and we would then rely solely on other forms of exclusivity, such as regulatory exclusivity provided by the FDCA or trade secret protection.

**If we infringe or are alleged to infringe intellectual property rights of third parties, our business could be harmed.**

Our research, development or commercialization activities, including any drug candidates or products resulting from these activities, may infringe or be claimed to infringe patents or other proprietary rights owned by third parties and to which we do not hold licenses or other rights. We may not be aware of third party patents that a third party might assert against us. For example, there may be third party applications that have been filed but not published that, if issued, could be asserted against us. If a patent infringement suit were brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or drug candidate that is the subject of the suit. Further, if we are found to have infringed a third-party patent, we could be obligated to pay royalties and/or other payments to the third party for the sale of our product, which may be substantial, or we could be enjoined from selling our product. We could also incur substantial litigation costs.

**Litigation regarding patents, intellectual property, and other proprietary rights may be expensive and time consuming. If we are involved in such litigation, it could cause delays in bringing drug candidates to market and harm our ability to operate.**

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Although we are not currently aware of any litigation or other proceedings or third-party claims of intellectual property infringement against us related to our drug candidates, the pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may obtain patents in the future and allege that the use of our technologies infringes these patent claims or that we are employing their proprietary technology without authorization. Likewise, third parties may challenge or infringe upon our existing or future patents. Proceedings involving our patents or patent applications or those of others could result in adverse decisions regarding:

the patentability of our inventions relating to our drug candidates; and/or

the enforceability, validity or scope of protection offered by our patents relating to our drug candidates. Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may:

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incur substantial monetary damages;

encounter significant delays in bringing our drug candidates to market; and/or

be precluded from participating in the manufacture, use or sale of our drug candidates or methods of treatment requiring licenses.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

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

Filing, prosecuting and defending patents on our drug candidates in all countries throughout the world would be prohibitively expensive. The requirements for patentability may differ in certain countries, particularly in developing countries. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, may not favor the enforcement of our patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. A number of foreign countries have stated that they are willing to issue compulsory licenses to patents held by innovator companies on approved drugs to allow the government or one or more third party companies to sell the approved drug without the permission of the innovator patentee where the foreign government concludes it is in the public interest. India, for example, has used such a procedure to allow domestic companies to make and sell patented drugs without innovator approval. There is no guarantee that patents covering any of our drugs will not be subject to a compulsory license in a foreign country, or that we will have any influence over if or how such a compulsory license is granted. Further, in at least Brazil, the country allows its regulatory agency ANVISA to participate in the decision of whether to grant a drug patent in that country, including based not on whether the patent meets the requirements for a patent but whether such a patent is deemed in the country's interest. In addition, several other countries have created laws that make it more difficult to enforce drug patents than patents on other kinds of technologies. Further, under the treaty on the Trade-Related Aspects of Intellectual Property (TRIPS) as interpreted by the Doha Declaration, countries in which drugs are manufactured are required to allow exportation of the drug to a developing country that lacks adequate manufacturing capability. Therefore, our drug markets in the U.S. or foreign countries may be affected by the influence of current public policy on patent issuance, enforcement or involuntary licensing in the healthcare area.

**We rely on our ability to stop others from competing by enforcing our patents, however some jurisdictions may require us to grant licenses to third parties. Such compulsory licenses could be extended to include some of our**

**drug candidates, which may limit our potential revenue opportunities.**

Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties, in certain circumstances. For example, compulsory licensing, or the threat of compulsory licensing, of life-saving products and expensive products is becoming increasingly popular in developing countries, either through direct legislation or international initiatives. Compulsory licenses could be extended to include some of our drug candidates, if they receive marketing approval, which may limit our potential revenue opportunities. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may also use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in major markets for our products where such patent rights exist, 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.

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In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief and may be unable to enjoin infringement if a government is the infringer, which could materially diminish the value of the patent.

### **The rights we rely upon to protect our unpatented trade secrets may be inadequate.**

We rely on unpatented trade secrets, know-how and technology, which are difficult to protect, especially in the pharmaceutical industry, where much of the information about a product must be made public during the regulatory approval process. We seek to protect trade secrets, in part, by entering into confidentiality agreements with employees, consultants and others. These parties may breach or terminate these agreements or may refuse to enter into such agreements with us, and we may not have adequate remedies for such breaches. Furthermore, these agreements may not provide meaningful protection for our trade secrets or other proprietary information or result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized use or disclosure of confidential information or other breaches of the agreements. Despite our efforts to protect our trade secrets, we or our collaboration partners, board members, employees, consultants, contractors or scientific and other advisors may unintentionally or willfully disclose our proprietary information to competitors.

If we fail to maintain trade secret protection, our competitive position may be adversely affected. Competitors may also independently discover our trade secrets. Enforcement of claims that a third party has illegally obtained and is using trade secrets is expensive, time consuming and uncertain. If our competitors independently develop equivalent knowledge, methods and know-how, we would not be able to assert our trade secrets against them and our business could be harmed.

### **Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information and may not adequately protect our intellectual property.**

We rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. To protect our proprietary technology and processes, we also rely in part on confidentiality and intellectual property assignment agreements with our corporate partners, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information nor result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information or other breaches of the agreements. In addition, others may independently discover our trade secrets and proprietary information, and in such case, we could not assert any trade secret rights against such party. Enforcing a claim that a party illegally obtained and is using our trade secrets is difficult, expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States may be less willing to protect trade secrets. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

### **Risks Related to Employee Matters and Managing Growth**

#### **If we are not able to attract and retain key management, scientific personnel and advisors, we may not successfully develop our drug candidates or achieve our other business objectives.**

We depend upon our senior management and scientific staff for our business success. All of our employment agreements with our senior management employees are terminable without notice by the employee. The loss of the service of any of the key members of our senior management may significantly delay or prevent the achievement of

drug development and other business objectives. For example, we recently announced the departure of Milind Deshpande, our former CEO. Our ability to attract and retain qualified personnel, consultants and advisors, including senior leadership with the requisite qualifications and experience to lead our research and development programs and lead our company, is critical to our success. We face intense competition for qualified individuals, particularly those experienced in discovering and developing complement inhibitor drug candidates, from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions. In addition, as a result of our restructuring in February 2018, we may face additional challenges in recruiting and retaining key personnel. We may be unable to attract and retain these individuals, and our failure to do so would adversely affect our business.

**If we acquire or license technologies, resources or drug candidates, we will incur a variety of costs and may never realize benefits from the transaction.**

If appropriate opportunities become available, we may license or acquire technologies, resources, drugs or drug candidates. We may never realize the anticipated benefits of such a transaction. In particular, due to the risks inherent in drug development, we may not successfully develop or obtain marketing approval for the drug candidates we acquire. Future licenses or acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, the creation of contingent liabilities, material impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

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**In the future, we may grow our organization, and as a result, we may encounter difficulties in managing any such growth, which could disrupt our operations.**

In the future, we may experience growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, regulatory affairs and sales, marketing and distribution. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a disproportionate amount of its attention to managing these growth activities. We may not be able to effectively manage the expansion of our operations or identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Any growth in the future could also require significant capital expenditures and may divert financial resources from other projects. If we are unable to effectively manage our growth in the future, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our drug candidates.

## **Risks Related to Regulatory Approval and Marketing of Our Drug Candidates and Other Legal Compliance Matters**

**Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates. If we or any future collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize our drug candidates, and our ability to generate revenue will be materially impaired.**

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries. Failure to obtain marketing approval for a drug candidate will prevent us from commercializing the drug candidate. We have not received approval to market any of our drug candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the drug candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our drug candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval

process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a drug candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Accordingly, if we or any future collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our drug candidates, the commercial prospects for our drug candidates may be harmed and our ability to generate revenues will be materially impaired.

**Failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed in such jurisdictions.**

In order to market and sell our medicines in the European Union and many other jurisdictions, we or any future collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that



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required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before the product can be approved for sale in that country. We or any future collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

**We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our drug candidates in United States, European Union or other markets and, even if we do, that exclusivity may not prevent the FDA, EMA or other regulatory authorities from approving other competing products.**

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We, or any future collaborators, may seek orphan drug designations for other drug candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a drug candidate, we, or they, may not be able to obtain orphan drug exclusivity for that drug candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Additionally, in the European Union, the orphan designation for a drug is reevaluated at the time of request for marketing authorization to verify whether it can maintain its status as an orphan drug and there is a risk that any orphan designation may not be maintained. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

**Fast track designation by the FDA or other regulatory acceleration options may not actually lead to a faster development or regulatory review or approval process and does not assure approval.**

If a drug is intended for the treatment of a serious or life threatening condition and the drug demonstrates the potential to address unmet medical need for this condition, the drug sponsor may apply for FDA fast track designation. However, fast track designation does not ensure that the drug sponsor will receive marketing approval or that approval will be granted within any particular timeframe. We may seek fast track designation for one or more of our drug candidates. If we do seek fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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**Priority review designation by the FDA or similar classifications by other regulatory authorities may not lead to a faster regulatory review or approval process and, in any event, does not assure approval.**

If the FDA determines that a drug candidate offers major advances in treatment or provides a treatment where no adequate therapy exists, the FDA may designate the drug candidate for priority review. For all new molecular entity (NME) new drug applications, a priority review designation means that the goal for the FDA to act on the NDA is 8 months from the date of submission, rather than the standard 12 months. For subsequent applications (e.g., sNDAs), a priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our drug candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a drug candidate, so even if we believe a particular drug candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster regulatory review process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the eight-month or six-month clock or thereafter.

**Even if we, or any future collaborators, obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our products may limit how we, or they, manufacture and market our products, which could materially impair our ability to generate revenue.**

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. 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 labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or any future collaborators, receive marketing approval for one or more of our drug candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

**Any drug candidate for which we or any future collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our drug candidates, when and**

**if any of them are approved.**

Any drug candidate for which we or any future collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to

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enforcement action for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

restrictions on such products, manufacturers or manufacturing processes;

restrictions on the labeling or marketing of a product;

restrictions on distribution or use of a product;

requirements to conduct post-marketing studies or clinical trials;

warning letters or untitled letters;

withdrawal of the products from the market;

refusal to approve pending applications or supplements to approved applications that we submit;

recall of products;

damage to relationships with any potential collaborators;

unfavorable press coverage and damage to our reputation;

fining, restitution or disgorgement of profits or revenues;

suspension or withdrawal of marketing approvals;

refusal to permit the import or export of our products;

product seizure;

injunctions or the imposition of civil or criminal penalties; and

litigation involving patients using our products.

Non-compliance with U.S. and European Union requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

**Under the CURES Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.**

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

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. An under-staffed FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a Regulatory Reform Officer and establish a Regulatory Reform Task Force to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations, however it is difficult to predict how these requirements 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 the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.



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**Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.**

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$10,781 to \$21,563 per false claim;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to annually report to CMS (i) payments and other transfers of value to physicians and teaching hospitals, and (ii) certain physician ownership or investment interests; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by third party payors, including private insurers.



Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to other healthcare providers and healthcare entities, or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, individual imprisonment, integrity obligations, and the curtailment or restructuring of our operations. Any penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from funded healthcare programs, or curtailment or restructuring of our operations could adversely affect our financial results. We are developing and implementing a corporate compliance program designed to ensure that we will market and sell any future products that we successfully develop from our drug candidates in compliance with all applicable laws and regulations, but we cannot guarantee that this program will protect us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be

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subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, integrity obligations, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs.

**Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of our other drug candidates and affect the prices we, or they, may obtain.**

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;

extension of manufacturers' Medicaid rebate liability;

expansion of eligibility criteria for Medicaid programs;

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

new requirements to report certain financial arrangements with physicians and teaching hospitals;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a "skinny" version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

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The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction (CSR) payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the individual mandate. The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop commercialize product candidates.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired. In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

Moreover, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by the

United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent drug labeling and post-marketing testing and other requirements.

**Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.**

If we expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

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Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and drug candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

### **If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.**

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts, which could adversely affect our business, financial condition, results of operations or prospects. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

### **Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.**

In some countries, such as the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we, or any future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or

limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

**Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.**

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, provide accurate information to the FDA or comparable non-U.S. regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve 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 employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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**Risks Related to Our Common Stock**

**Our executive officers, directors and principal stockholders have the ability to significantly influence all matters submitted to our stockholders for approval, which could have the effect of delaying, deferring or preventing a change in control of us and entrenching our management or board of directors.**

As of August 1, 2018, our directors, executive officers and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, beneficially owned, in the aggregate, greater than approximately 30% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation, sale of all or substantially all of our assets or similar transaction, as well as our management and affairs. The interests of this group of stockholders may not always coincide with our corporate interests or the interest of other stockholders, and they may act in a manner with which you may not agree or that may not be in the best interests of other stockholders. This concentration of voting power may have the effect of delaying, deferring or preventing a change in control of our company on terms that other stockholders may desire and entrenching our management or board or directors.

**Our stock price has been and may in the future be volatile, and the market price of our common stock may decline in value in the future.**

The market price of our common stock has fluctuated in the past and is likely to fluctuate in the future. During the period from January 1, 2009 to June 30, 2018, our stock price has ranged from a low of \$0.70 to a high of \$16.87. Market prices for securities of early stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

the results of current and planned clinical trials of our drug candidates including our complement factor D drug candidates;

the results of clinical trials conducted by others on drugs that would compete with our drug candidates;

the announcements of those data, particularly at high profile medical meetings, and the investment community's perception of and reaction to those data;

the entry into, modification of, or termination of collaborations and other key agreements;

market expectations about the timeliness of our entry into, failure to enter to, or termination of, collaboration arrangements with third parties;

the results of regulatory reviews and actions relating to the approval of our drug candidates;



our failure to obtain patent protection for any of our drug candidates or the issuance of third-party patents that cover our drug candidates;

the initiation of, material developments in, or conclusion of litigation;

failure of any of our drug candidates, if approved, to achieve commercial success;

general and industry-specific economic conditions that may affect our business, financial condition and operations, including without limitation research and development expenditures;

the launch of drugs by others that would compete with our drug candidates;

the benefits of, and market reaction to, any restructurings we undertake;

the failure or discontinuation of any of our research programs;

issues in manufacturing our drug candidates or any approved products;

the introduction of technological innovations or new commercial products by us or our competitors;

changes in estimates or recommendations by securities analysts, if any, who cover our common stock;

future sales, or the anticipation of future sales, of our common stock by us, our insiders or other stockholders;

changes in the structure of health care payment systems;

period-to-period fluctuations in our financial results;

low trading volume of our common stock; and

the other factors described in this **Risk Factors** section.

In addition, if we fail to reach an important research, development or commercialization milestone or result by a publicly expected deadline, even if by only a small margin, there could be significant impact on the market price of our common stock. Additionally, as we approach the announcement of important clinical data or other significant information and as we announce such results and information, we expect the price of our common stock to be particularly volatile, and negative results would have a substantial negative impact on the price of our common stock.



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The stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may adversely affect the trading price of our common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our business operations and reputation. For example, we, and certain of our current and former officers, were named as defendants in a consolidated class action lawsuit following our announcements regarding the FDA's clinical hold related to sovalprevir, our clinical-stage drug candidate for the treatment of chronic HCV infection. On May 5, 2014, without any settlement payment by us, any individual defendant or any third party on their behalf, the lead plaintiffs in the consolidated class action lawsuit voluntarily dismissed all of their claims without prejudice.

### **Sales of a substantial number of shares of our common stock in the public market could cause the market price of our common stock to drop significantly.**

Certain stockholders hold a substantial number of shares of our common stock. If such 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. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 under the Securities Act of 1933 and, in any event, we have filed registration statements permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline. Future sales by other stockholders may also have a material adverse effect on the trading price of our common stock.

### **Unstable market and economic conditions may have serious adverse consequences on our business.**

Our general business strategy may be adversely affected by economic downturns and volatile business environments and continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive difficult economic times, which would directly affect our ability to attain our operating goals on schedule and on budget.

### **Our management is required to devote substantial time and incur additional expense to comply with public company regulations. Our failure to comply with such regulations could subject us to public investigations, fines, enforcement actions and other sanctions by regulatory agencies and authorities and, as a result, our stock price could decline in value.**

As a public company, the Sarbanes-Oxley Act of 2002 and the related rules and regulations of the SEC, as well as the rules of the Nasdaq Global Select Market, have required us to implement additional corporate governance practices and adhere to a variety of reporting requirements and complex accounting rules. Compliance with these public company obligations places significant additional demands on our limited number of finance and accounting staff and on our financial, accounting and information systems.

In particular, as a public company, our management is required to conduct an annual evaluation of our internal control over financial reporting and include a report of management on our internal controls in our Annual Reports on Form

10-K. If we are unable to continue to conclude that we have effective internal control over financial reporting or, if our independent registered public accounting firm is unable to provide us with an attestation and an unqualified report as to the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, which could result in a decrease in the value of our common stock.

**Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be stockholders' sole source of gain.**

We have never declared or paid cash dividends on our capital stock. We anticipate that we will retain our earnings, if any, for future growth and therefore do not anticipate paying cash dividends in the future. As a result, only appreciation of the price of our common stock will provide a return to stockholders.

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**Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.**

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which a stockholder might otherwise receive a premium for his or her shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

establish a classified board of directors such that all members of the board are not elected at one time;

allow the authorized number of our directors to be changed only by resolution of our board of directors;

limit the manner in which stockholders can remove directors from the board;

establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

limit who may call a special meeting of stockholder meetings;

authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders.

**ITEM 5. OTHER INFORMATION.**

**Approval of Amended and Restated 2015 Stock Incentive Plan**

At our annual meeting of stockholders held on May 31, 2018, our stockholders approved our Amended and Restated 2015 Stock Incentive Plan, or the Amended and Restated 2015 Plan, which was adopted by our board of directors on March 22, 2018, subject to stockholder approval. The Amended and Restated 2015 Plan amends and restates the 2015 Stock Incentive Plan which was adopted by our board of directors on March 19, 2015 and approved by our stockholders on June 2, 2015. The Amended and Restated 2015 Plan, among other things, reserves an additional 8,200,000 shares of our common stock for issuance under the plan, modifies provisions regarding performance awards, places limits on stock and cash awards to non-employee directors, prohibits grants of stock appreciation rights, or SARs, containing provisions for automatic grant of additional SARs in connection with exercise of a SAR and dividend equivalents with respect to SARs, and subjects awards under the Amended and Restated 2015 Plan to any of our clawback policies.

The material terms of the Amended and Restated 2015 Plan are summarized on pages 15 through 25 of our definitive proxy statement on Schedule 14A filed with the Securities and Exchange Commission on April 20, 2018, which description is attached hereto as exhibit 99.1 and incorporated herein by reference. The description of the Amended and Restated 2015 Plan is qualified in its entirety by reference to the full text of the Amended and Restated 2015 Plan, a copy of which is attached hereto as Exhibit 10.3 and is incorporated herein by reference.

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<b>Exhibit No.</b>	<b>Exhibit</b>
10.1	<u>Second Amended and Restated Employment Agreement, dated May 1, 2018, by and between the Registrant and Joseph Truitt (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 2, 2018).</u>
10.2	<u>Consulting Agreement, dated May 18, 2018, by and between the Registrant and Milind Deshpande.</u>
10.3	<u>Amended and Restated 2015 Stock Incentive Plan.</u>
10.4	<u>Letter Agreement, dated May 23, 2018, by and between the Registrant and Milind Deshpande.</u>
31.1	<u>Certification of President and Chief Executive Officer of Achillion Pharmaceuticals, Inc. pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.</u>
31.2	<u>Certification of Chief Financial Officer of Achillion Pharmaceuticals, Inc. pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.</u>
32.1	<u>Certification of President and Chief Executive Officer of Achillion Pharmaceuticals, Inc. pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.</u>
32.2	<u>Certification of Chief Financial Officer of Achillion Pharmaceuticals, Inc. pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.</u>
99.1	<u>Text of PROPOSAL 3 APPROVAL OF AMENDMENT AND RESTATEMENT OF OUR 2015 STOCK INCENTIVE PLAN from the Registrant's definitive proxy statement on Schedule 14A filed with the Securities and Exchange Commission on April 20, 2018.</u>
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Label Linkbase Document
101.PRE	XBRL Taxonomy Presentation Linkbase Document

Attached as Exhibit 101 to this report are the following formatted in XBRL (Extensible Business Reporting Language): (i) Balance Sheets at June 30, 2018 and December 31, 2017 (unaudited), (ii) Statements of Comprehensive Loss for the three and six months ended June 30, 2018 and 2017 (unaudited), (iii) Statements of Cash Flows for the six months ended June 30, 2018 and 2017 (unaudited), and (iv) Notes to Financial Statements (unaudited).

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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.

ACHILLION PHARMACEUTICALS, INC.

Date: August 8, 2018

/s/ Joseph Truitt  
President and Chief Executive Officer  
(Principal Executive Officer)

Date: August 8, 2018

/s/ Mary Kay Fenton  
Chief Financial Officer  
(Principal Financial and Accounting Officer)