ACHILLION PHARMACEUTICALS INC

FORM 10-K
(Annual Report)

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2017

OR

☐ **TRANSITION REPORT PURSUANT TO SECTIONS 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)

Delaware	**52-2113479**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

300 George Street, New Haven, CT 06511
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (203) 724-6000

Securities registered pursuant to Section 12(b) of the Act:

Title of Class	Name of Exchange on Which Registered
Common Stock, $0.001 par value per share	**NASDAQ Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

Large accelerated filer ☒	Accelerated filer ☐
Non-accelerated filer ☐	Smaller reporting company ☐
	Emerging growth company ☐

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

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

The aggregate market value of the voting stock held by non-affiliates of the Registrant on June 30, 2017 was approximately $627,735,767 based on the closing price of such stock as reported by the NASDAQ Global Select Market on June 30, 2017.

As of February 20, 2018, the registrant had 137,894,487 shares of Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III (except for information required with respect to our executive officers, which is set forth under "Part I, Item 1—Business—Executive Officers of the Registrant") have been omitted from this report, as we intend to file with the Securities and Exchange Commission, not later than 120 days after the close of our fiscal year ended December 31, 2017, a definitive proxy statement for our annual meeting of stockholders to be held on May 31, 2018. Such information will appear in our definitive proxy statement and is incorporated by reference into this Annual Report on Form 10-K.

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Cautionary Note Regarding Forward-Looking Information

This Annual Report on Form 10-K 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 with words such as "believe," "expect," "anticipate," "plan," "target," "intend," "may," "predict," "project," "potential," "goals," "will," "would," "could," "should," "continue" and similar expressions) should be considered forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements in this Annual Report on Form 10-K include information with respect to our plans and strategy for our business, the possible achievement of discovery and development goals and milestones, our future discovery and development efforts, and our future operating results and financial position. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery and clinical development programs, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, the ability of our competitors to advance their competing drug candidates, our ability to obtain any necessary financing to conduct our planned activities, our dependence on third parties, and other risk factors. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Please refer to the section entitled "Risk Factors" in Part I—Item 1A of this report for a description of risks and uncertainties relating to our business. Unless required by law, we assume no obligation to update these forward-looking statements to reflect events or circumstances that arise after the date hereof.

PART I

ITEM 1. BUSINESS

Overview

We are a science-driven, patient-focused biopharmaceutical company seeking to leverage our believed strengths across the continuum from discovery through commercialization by discovering and developing small molecule therapeutics to meet the needs of patients with complement-mediated diseases.

We have discovered and developed our complement inhibitor platform, directed at advancing 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 this platform which target complement factor D, an essential protein within the amplification loop of the alternative pathway. We and experts believe the alternative pathway plays a critical role in a number of disease conditions including rare orphan conditions such as C3 glomerulopathy, or C3G, immune complex membranoproliferative glomerulonephritis, or IC-MPGN, both diseases affecting the kidney, and paroxysmal nocturnal hemoglobinuria, or PNH, a blood disorder, as well as several more prevalent indications.

Our lead drug candidate, ACH-4471, has demonstrated preliminary clinical proof-of-concept in patients with C3G and in patients with PNH.

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

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 red blood cells outside of blood vessels, while also 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 suboptimal response to, or who fail to respond to, currently approved treatments for PNH.

We have also generated a platform of additional potent and specific orally-administered compounds that bind to factor D with high affinity, resulting in alternative pathway inhibition. One of these compounds, ACH-5228, is in phase I clinical testing in healthy volunteers, and another compound, ACH-5548, is in late-stage preclinical development. We may seek to advance certain of these factor D inhibitors for oral systemic administration to treat C3G, IC-MPGN, PNH, or other complement mediated diseases.

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 $588.8 million from inception through December 31, 2017 and had an accumulated deficit of $602.7 million as of December 31, 2017, which includes preferred stock dividends recognized until our initial public offering in 2006. Our net losses were $85.2 million, $61.7 million, and $5.0 million for the years ended December 31, 2017, 2016, and 2015, respectively.

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 inhibitor 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 or acceptable to us, if at all. In addition to the risks associated with being an early-stage 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.

Recent Development—Restructuring

In February 2018, we implemented a restructuring plan that will reduce employee headcount by approximately 20% to approximately 70 employees in March 2018. 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 and ACH-5228, and late-stage preclinical compound, ACH-5548. We assessed the staffing levels required to accomplish our revised strategic goals and determined to reduce our staff across several functional areas, while retaining the biology and chemistry core strengths necessary to advance our complement factor D portfolio.

Our Strategy

Our objective is to become a leading biopharmaceutical company by discovering, developing and commercializing small molecule therapies that specifically target the alternative pathway of the human complement system. Specifically, our near-term strategy includes the following efforts:

- ***Advance ACH-4471, the first oral drug candidate to inhibit factor D within the alternative pathway, in clinical development for C3G.*** We believe ACH-4471 is the first small molecule alternative

pathway factor D inhibitor to be tested in humans. We have completed both single-ascending dose and multiple-ascending dose phase I clinical trials designed to understand the safety, pharmacokinetics and pharmacodynamics of the drug candidate after oral administration. We have advanced or plan to advance ACH-4471 in three phase II clinical trials for patients with C3G:

- A 14-day duration trial for which we have announced data from the first two sentinel patients and are continuing to enroll up to eight additional patients. We anticipate reporting data from this trial in the third quarter of 2018.
- A 6-month duration trial which will be double-blind and placebo-controlled and enroll up to 20 patients randomized 1:1 to receive either ACH-4471 or placebo. We anticipate initiating dosing in this trial in the first half of 2018 and reporting data in 2019.
- A 12-month duration trial which will consist of a single open-label arm and in which we expect to enroll up to 20 patients. We anticipate initial dosing in this trial in the first half of 2018 and expect that interim data would be released in the fourth quarter 2018.

- ***Advance ACH-4471 in clinical development for PNH.*** We have advanced or plan to advance ACH-4471 in the following phase II clinical trials in patients with PNH:
  - A monotherapy trial assessing ACH-4471 in patients with PNH from which we announced interim data for the first four patients in August 2017. We continue to enroll PNH patients in this trial, planning to treat a total of eight to twelve PNH patients and report data by the fourth quarter of 2018.
  - An add-on trial assessing ACH-4471 dosed with eculizumab, a therapy for PNH that is marketed by a third party, in patients that are deemed to have a sub-optimal response and continue to experience disease symptoms such as anemia and fatigue despite treatment with eculizumab monotherapy. We anticipate initial dosing in this trial in the first half of 2018, planning to treat a total of eight PNH patients, and releasing interim data in the fourth quarter 2018.
- ***Advance ACH-5228 and ACH-5548, next-generation compounds for oral systemic administration, to treat other complement mediated diseases.*** In addition to advancing ACH-4471, we have advanced ACH-5228 into a phase I, single-ascending dose clinical study in healthy volunteers and have another compound, ACH-5548, in late stage preclinical development. We anticipate that ACH-5548 will enter a phase I, single-ascending dose clinical study in the second quarter of 2018. We expect to report data from the phase I clinical studies of ACH-5228 and ACH-5548 in the fourth quarter 2018. Our objective for these next-generation compounds is to have them advanced either by us for PNH, C3G or other complement diseases, or by potential collaborators for diseases that are not our strategic focus.

Our Complement Factor D Program

The first clinical compound from our complement inhibitor platform is ACH-4471. ACH-4471 is 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.

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

ACH-4471 has exhibited the following characteristics in preclinical studies and clinical trials:

- *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 twice or three times daily. Controlled release formulation systems are also being developed for

ACH-4471 with the objective of optimizing trough exposures and reducing dosing frequency. We initiated a phase I bio-availability assessment of a series of controlled release formulation systems in healthy volunteers in 2017 and plan to complete our feasibility assessment of these formulations in 2018.

- *Safety* . 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. 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 has been 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.

  In an on-going dose ranging phase II clinical trial in PNH patients, doses start at 100mg or 150mg three times daily, or TID, with allowance for intra-patient dose escalation. To date, 225mg TID has been the highest dose administered. In August 2017, we announced that interim data from this trial showed that to date a favorable tolerability profile had been observed with no reports of clinically meaningful increases in liver enzymes. Three of the four patients we reported on in August 2017 continue to be dosed in this phase II clinical trial, including two who have been on therapy with ACH-4471 for longer than nine months and one who has been on therapy for longer than six months, with ACH-4471 showing a good tolerability profile and normal liver enzyme levels.

- *Efficacy* . ACH-4471 has been demonstrated to be highly specific for inhibition of factor D, a protein critical to the amplification of the complement system. 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.

  C3G & 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 two patients received an initial dose of 100mg TID for a period of 14 days with a 7-day taper period. Subsequent groups of patients are being dosed at 200 mg 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 this 14-day phase II trial suggest that ACH-4471 may reverse the alternative pathway hyperactivity in C3G based upon the observed improvements in the first two sentinel patients in complement biomarkers and proteinuria following 14 days of treatment with ACH-4471. In both sentinel patients, the primary clinical manifestation was significant proteinuria, or protein in the urine. In both cases, a greater than 50% reduction in proteinuria was observed during the treatment period.

  We also plan to conduct a phase II open-label, 12-month treatment trial for patients with biopsy-confirmed C3G or IC-MPGN 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 will be eligible to continue therapy under this protocol after a wash-out period. We also plan to conduct a phase II randomized, placebo-controlled, double-blinded 6-month trial for patients with biopsy-confirmed C3G. 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. We anticipate initiating each of these trials in the first half of 2018.

  PNH. A phase II clinical trial of ACH-4471 in patients with PNH is on-going and continues to enroll untreated PNH patients. To date, four PNH patients have been treated, three of whom 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. In August 2017, we announced interim data from this trial in which ACH-4471 demonstrated that it mechanistically inhibited factor D, its intended target, and meaningfully improved LDH, hemoglobin, fatigue score, and other measures of response, including PNH clone size.

We also plan to conduct a phase II clinical trial evaluating ACH-4471 in PNH patients currently receiving eculizumab, a therapy for patients with PNH, and 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 initiating this trial in the first half 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.
- *Safety* . We have completed short-term, non-clinical studies in rats and dogs in which ACH-5228 demonstrated tolerability and safety margins supportive of progression into human clinical development.
- *Potency* . 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 are expected to be 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 second half 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.
- *Safety* . We are completing short-term, non-clinical studies in rats and dogs in which ACH-5548 demonstrated tolerability and safety margins supportive of progression into human clinical development.
- *Potency* . 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 anticipate that ACH-5548 will enter phase I clinical development in the second quarter of 2018.

Next Generation Factor D Inhibitors for geographic atrophy. Our research team has selected several compounds from our library for the physicochemical properties that may be advantageous for delivery to the back of the eye for treatment of geographic atrophy, or GA, with the goal of achieving treatment duration of three

months or longer. We had been evaluating several of these compounds, as well as several delivery technologies, to optimize treatment duration. After the announcement that lampalizumab, a product candidate that also targets complement factor D inhibition in GA, was reported to not have met its primary endpoint of reducing GA lesions when compared to a sham treatment, we undertook a reassessment of our factor D preclinical development efforts for GA. This reassessment is ongoing.

The Complement System

The complement system is part of the body's immune system. The immune system protects the body by recognizing and eliminating bacteria, viruses and other infectious agents, referred to as pathogens, and abnormal cells such as cancer cells. The activities of the immune system are undertaken by its two components, the innate immune system and the adaptive immune system. The role of the innate immune system is to provide a rapid nonspecific response to pathogens or abnormal cells in the body and to activate the adaptive immune system. The role of the adaptive immune system is to provide a specific response to pathogens or abnormal cells. Once a pathogen or abnormal cell has been recognized, the adaptive immune system generates immune cells and antibodies that specifically attack that pathogen or abnormal cell.

Complement is activated via three pathways: the alternative pathway, lectin pathway and the classical pathway. At sites of infection, the complement system activates and triggers a series of potent inflammatory responses. There are also many regulatory mechanisms to prevent uncontrolled complement over-activation.

The complement system consists of over 30 small proteins and protein fragments found in the blood, generally synthesized by the liver, and normally circulating in an inactive state. Complement proteins account for about 5% of the globulin portion of blood serum. A number of complement proteins are proteases. When stimulated by one of several triggers, proteases in the system cleave specific proteins and initiate an amplifying cascade of further cleavages. The end-result of this activation cascade is amplification of the response and activation of the pathogen- and cell-killing membrane attack complex, or MAC.

The alternative pathway is one of three complement pathways that opsonize, or prepare a pathogen for destruction, and kill pathogens. The alternative pathway is initiated by the spontaneous hydrolysis, or breaking of protein C3 chemical bonds through the introduction of water. This is sometimes referred to as "tickover" and is the initiation of alternative pathway. Many inflammatory, autoimmune, neurodegenerative and age-related diseases are associated with inefficient complement regulation or excessive activity of the complement system and are believed to be specifically related to the alternative pathway.

Current therapies, including those in development, to treat PNH target other complement proteins such as C5 or C3 that are active "downstream" of factor D within the protein activation cascade of the complement system.

The C3G Market

C3G is a life-threatening, ultra-rare disorder characterized by over-activation of the alternative pathway. The condition includes both dense deposit disease, or DDD, and C3 glomerulonephritis, and is typically characterized by abnormalities in complement protein levels which results in deposits of complement protein C3 fragments within the glomeruli of the kidney, thereby inhibiting proper filtration of the blood, tissue scarring, and ultimately impaired kidney function. The overall prognosis for patients with C3G is poor, with approximately 30% to 50% of C3G patients progressing to end-stage renal disease, or ESRD, within 10 years of diagnosis. Dialysis and renal transplantation are options available for patients who reach ESRD; however, disease recurrence is frequent after transplantation, occurring in more than 50% of patients. Only about 50% of patients have a functioning graft 5 years after transplantation. Based on internal research, we estimate that C3G affects at least 8,000 people in the United States and the major European markets, specifically France, Germany, Italy, Spain and the United Kingdom. There are no approved treatments for patients with C3G.

The PNH Market

PNH is a life-threatening, ultra-rare genetic blood disorder defined by chronic uncontrolled complement activation leading to the destruction of red blood cells, or hemolysis, which can take place both inside, or intravascularly, and outside, or extravascularly, of the circulatory system. Based on internal research, we estimate that PNH affects approximately 10,000 people in the United States and the major European markets. The chronic hemolysis in patients with PNH may be associated with life-threatening thrombotic events, recurrent pain, kidney disease, disabling fatigue, severe anemia, pulmonary hypertension, shortness of breath and intermittent episodes of dark-colored urine or hemoglobinuria. The only currently approved therapy for PNH patients is eculizumab, or Soliris ®, an antibody that inhibits the activity of the complement protein C5, which originally was approved in 2007 and is currently approved in the United States, Europe, Japan and in several other territories. Sales of Soliris ® were reported to be $3.1 billion in 2017.

We estimate that approximately 25% of patients currently treated with eculizumab, the current standard of care for patients with PNH, have suboptimal response in the form of symptomatic extravascular hemolysis due to the accumulation of C3 protein fragments on red blood cells, or due to genetic mutations that prevent binding of eculizumab to C5, the protein target of eculizumab. Patients who respond sub-optimally to eculizumab through extravascular hemolysis often require dosing at higher than recommended levels or greater dosing frequency.

Benefits of Our Approach

We believe that drug candidates advanced from our complement inhibitor platform have distinct potential advantages over currently available therapies.

Focus on the Alternative Pathway

We and experts believe a number of complement-mediated diseases are the direct result of dysregulation of the alternative pathway. While other complement treatments marketed or in development focus on inhibiting the classical, lectin or terminal pathways (the terminal pathway being the final stage of all three complement pathways), these treatments do not affect the complement system at the root of dysregulation. For example, experts believe that C3G results from overproduction of C3 fragments that ultimately deposit in the kidney, impairing renal function. This overproduction of C3 fragments, experts believe, stems from dysregulation of the fluid phase of the alternative pathway. Factor D inhibitors can potentially block or suppress over activation of the alternative pathway, thereby limiting or eliminating excessive C3 fragment formation and subsequent deposition in the kidney. Conversely, other complement inhibitors, such as inhibitors of complement proteins C3 or C5, do not specifically inhibit the alternative pathway.

Targeting Factor D

Factor D is a catalytic enzyme that has one of the lowest concentrations in blood serum of all the complement proteins, several times lower than the targets of other complement therapies including C5 and C3. Factor D, therefore, has the potential to provide a highly specific target for drug intervention while, we believe, limiting off-target effects. Our expertise in synthetic chemistry has allowed our scientists to utilize crystal structures with high resolution in order to synthesize compounds that bind specifically to factor D. Further, because factor D is rate-limiting in activation of the alternative pathway, targeting factor D effectively shuts down the amplification loop that can lead to indiscriminate activation of the complement system.

Small Molecule Inhibitors

All our complement factor D inhibitor compounds for the potential treatment of rare diseases are orally-available small molecule compounds. This is in contrast to biologic compounds that require intravenous or subcutaneous dosing. The current FDA-approved therapy for PNH is dosed intravenously, requiring routine

hospital or infusion center visits. We believe that oral dosing could provide a more convenient regimen for patients and their care-givers. We have also designed a number of small molecule compounds to be optimized for ophthalmic administration. These small molecule compounds may have dosing advantages in ophthalmological complement-mediated diseases such as GA, with the potential for dosing intervals of every three months or longer.

Collaboration with Janssen Pharmaceuticals, Inc.

On September 9, 2017, we received notice from Janssen Pharmaceuticals, Inc., or Janssen, of Janssen's termination, effective as of November 8, 2017, of our exclusive collaboration and license agreement with them, which we refer to as the Janssen Agreement. Under the terms of the Janssen Agreement, we had granted Janssen exclusive worldwide rights to develop and commercialize products that contained one or more of our drug candidates for the treatment of chronic hepatitis C virus, or HCV, namely odalasvir, a second-generation NS5A inhibitor, ACH-3422, a NS5B HCV nucleoside polymerase inhibitor, and sovaprevir, a NS3/4A HCV protease inhibitor.

Janssen terminated the Janssen Agreement under section 14.6 of the Janssen Agreement, which allows for unilateral termination at Janssen's discretion upon 60 days' written notice to us at any time prior to the submission of the first application for marketing approval for a licensed product in any of the major market countries specified in the Janssen Agreement. Pursuant to its notice of termination, 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 that we licensed to Janssen under the Janssen Agreement. Following the termination, all licenses granted by either party to the other under the Janssen Agreement terminated, except to the extent necessary to allow either party to perform any obligations or exercise rights that survive the termination.

As a result of the termination of the Janssen Agreement, we will not receive any future milestone-based or royalty payments under that agreement, and Janssen will not bear the future costs of developing and commercializing our HCV portfolio. We currently have no plans to advance the HCV program on our own.

Competition

The development and commercialization of new drug products is highly competitive. We expect that we, and 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. 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 complement-mediated disease 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.

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. In addition to currently approved products, our competitors also may obtain additional FDA or other marketing approvals 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.

Intellectual Property

Our strategy is to pursue patents, developed internally and licensed from third parties, and other means to protect our technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets that may be important to the development of our business.

Our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for the technology, inventions, improvements and know-how we consider important to our business;
- defend and enforce our patents;
- preserve the confidentiality of our trade secrets; and
- operate without infringing the valid and enforceable patents and proprietary rights of third parties.

We hold issued patents and pending patent applications in the United States, and in foreign countries we deem appropriate, covering intellectual property developed as part of our research and development programs.

As of December 31, 2017, our complement inhibitor patent portfolio included a large number of pending U.S. applications, international applications filed under the Patent Cooperation Treaty, referred to as the PCT, and applications that have been entered into the national phase of prosecution in foreign countries. These patents and patent applications, if issued, will expire in 2035 or 2036, without regard to possible patent term extensions to account for regulatory delay to market our drugs, or any patent term adjustment. These applications include claims directed to composition of matter, pharmaceutical composition and their methods of use to treat complement factor D related disorders, including C3G, PNH, and macular age-related degeneration.

Our complement inhibitor patent portfolio includes several families of published patents and patent applications. Our first family of complement inhibitor patent filings, which consists of eight subfamilies, is based on a priority provisional application filed in February 2014. Our second family of complement inhibitor patent filings, which consists of nine subfamilies, is based on priority provisional applications filed in August 2015. Our third family of complement inhibitor patent filings, which also consists of nine subfamilies, is also based on priority provisional applications filed in August 2015.

Our first family of complement inhibitor patent applications includes nine issued U.S. patents. We have received an issued U.S. patent covering the composition of matter on our lead drug candidate, ACH-4471, and its medical use (U.S. Patent No. 9,796,741). We have also received eight additional U.S. patents covering other Factor D inhibitors (U.S. Patent Nos. 9,758,537, 9,598,446, 9,663,543, 9,732,104, 9,695,205, 9,828,396, 9,732,103, and 9,643,986). All eight of the subfamilies of patent applications are currently pending in at least the United States.

Several of the subfamilies of the first family of complement inhibitor patent applications were entered into the international phase with PCT applications in February 2015 and then entered into the national phase of prosecution in the United States and in foreign countries in August 2016. Two of the subfamilies are currently pending in a number of foreign jurisdictions including the major market countries (China, Australia, Canada, Japan and South Korea) and three regional patent offices (European Patent Office (EPO), African Regional Patent Office (ARIPO), and Eurasian Patent Office (EAPO)).

Our second family of patent applications was entered into the international phase with PCT applications in August 2016. United States patent applications are pending in five of the subfamilies, and two additional subfamilies will enter the United States in February 2018. One of the subfamilies will be filed in foreign jurisdictions in February 2018. This subfamily covers several of our most advanced complement D inhibitors, including ACH-5228.

Our third family of complement inhibitor patent filings was entered into the international phase with PCT applications in August 2016. In February 2018, we expect to file some of these applications in the United States, and in Europe.

In September 2017, the Janssen HCV collaboration was terminated and the intellectual property rights we had exclusively licensed to Janssen under the Janssen Agreement were returned to us. As a result of the Janssen collaboration, we also have several U.S. and PCT applications that we own jointly with Janssen. We currently have no plans to advance the HCV program on our own. We are in the process of evaluating our HCV intellectual property portfolio and may discontinue most of the patents and patent applications that comprise that portfolio.

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. In order 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.

Manufacturing and Supply

We currently rely on contract manufacturers to produce drug substances and drug products required for our clinical trials under current good manufacturing practices (cGMP), with oversight by our internal managers. We plan to continue to rely upon contract manufacturers and collaboration partners to manufacture commercial quantities of our drug candidates if and when approved for marketing by the FDA. We currently rely on a limited number of manufacturers for the preclinical or clinical supplies of each of our drug candidates we are developing and do not currently have relationships for redundant supply or a second source for any of these drug candidates. We believe that there are alternate sources of supply that can satisfy our clinical trial requirements without significant delay or material additional costs.

Sales and Marketing

We intend to establish our own sales and marketing capabilities if and when we obtain regulatory approval of our drug candidates. In North America and Western Europe, patients in the markets for our drug candidates are largely managed by medical specialists in the areas of immunology, nephrology, and hematology. Historically, companies have experienced substantial commercial success through the deployment of specialized sales forces which can address a majority of key prescribers. Therefore, we expect to utilize a specialized sales force in North America for the sales and marketing of drug candidates that we may successfully develop. We currently have no marketing, sales or distribution capabilities. In order to participate in the commercialization of any of our drugs, we must develop these capabilities on our own or in collaboration with third parties. We may also choose to hire a third party to provide sales personnel instead of developing our own staff.

Outside of North America, and in situations or markets where a more favorable return may be realized through licensing commercial rights to a third party, we may license a portion or all of our commercial rights in a territory to one or more third parties in exchange for one or more of the following: up-front payments, research funding, development funding, milestone payments and royalties on drug sales.

Regulatory Matters

Government Regulation and Product Approvals

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, sales, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory requirements, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, requesting marketing for one or more proposed indications;
- review of the candidate product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and

- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and potentially post-market requirement, or PMR, and commitment, or PMC, studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of the IND application, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the submission of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin (or resume if the clinical trial had been ongoing at the time a clinical hold was imposed).

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical trial under an IND. When a foreign clinical trial is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical trial is not conducted under an IND, the sponsor must ensure that the trial complies with certain FDA regulatory requirements in order to use the trial as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP

requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical trials, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct a continuing review and reapprove the trial at least annually. The IRB must review and approve, among other things, the trial protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data monitoring committee, or DMC. DMCs may be charged with monitoring efficacy, safety, and/or study conduct. A DMC provides a recommendation for whether or not a clinical trial should move forward at designated check points based on available data from the trial. A recommendation by a DMC to suspend or terminate development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in four sequential phases, which may overlap or be combined:

- ***Phase 1.*** The drug is initially introduced into a small number of healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition (e.g., cancer) and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- ***Phase 2.*** The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- ***Phase 3.*** These clinical trials are commonly referred to as "pivotal" studies, which denote a study that presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a drug. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, identify adverse effects, establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.
- ***Phase 4 .*** Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials conducted under the IND must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA or the sponsor or the data monitoring committee may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee which typically increases each year. The annual program fee for fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to certain performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the date of filing, and most applications for "priority review" products are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing such as active pharmaceutical ingredients, finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. The

FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain drug applications, including applications for drugs in a shortage or drugs for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA may refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Improvement Act. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's review clock goal for taking action on a marketing application from ten months to six months. For new chemical entities, or NCEs, the review clock starts after the NDA is filed with a total clock of twelve and eight months, respectively.

Finally, with passage of the 21st Century Cures Act, or Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy (as defined in the Cures Act) that is intended to treat, modify, reverse or cure a serious or life- threatening disease or condition and preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements,

including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Requirements

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, condition of NDA approval may include sponsor agreement to PMR or PMC studies, which are designed to further assess drug safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, or complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, healthcare professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level and set minimum standards for the regulation of drug distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples, and the DSCA imposes requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on

the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are "abbreviated" because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, the strength of the drug and the conditions of use of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if "the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug." Upon approval of an ANDA, the FDA indicates whether the generic product is "therapeutically equivalent" to the RLD in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE 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, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The new legislation also authorizes FDA to expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive the approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another orphan drug under certain circumstances, including if a subsequent product with the same drug for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. New legislation has clarified that the Orphan Drug Act does not require the FDA to recognize orphan exclusivity if another drug candidate demonstrates clinical superiority.

In the fourth quarter of 2017, we were granted orphan drug designation for ACH-4471 for the treatment of PNH and for the treatment of C3G in the United States.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the Food and Drug Administration Safety and Innovation Act or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time. For drugs intended to treat a serious or life-threatening disease or condition, the FDA must,

upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with drug sponsors. The legislation requires FDA to meet with drug sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless and until FDA promulgates a regulation stating otherwise, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product is effective in the pediatric population studied, rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

The 21 st Century Cures Act

On December 13, 2016, President Obama signed the Cures Act into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, or PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that

end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

Review and Approval of Drug Products Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the EU

Requirements for the conduct of clinical trials in the European Union including GCP are set forth in the Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the E.U. member states. Under this system, approval must be obtained from the competent national authority of each E.U. member state in which a study is planned to be conducted. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

In April 2014, the EU passed the new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new E.U. clinical trials legislation was passed as a regulation that is directly applicable in all E.U. member states. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. According to the current plans of EMA, the new Clinical Trials Regulation will become applicable in 2019. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the E.U. portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I is assessed jointly by all member states

concerned, and Part II is assessed separately by each member state concerned); strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products (CHMP) or Committee for Advanced Therapies (CAT) are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization

To obtain marketing approval of a product under European Union regulatory systems, an applicant must submit a marketing authorization application, or MAA, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. The centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the European Medicines Agency, or EMA, is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure is available to applicants who wish to market a product in various European Union member states where such product has not received marketing approval in any European Union member states before. The decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state designated by the applicant, known as the reference member state. Under this procedure, an applicant submits an application based on identical dossiers and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment report and drafts of the related materials within 210 days after receipt of a valid application. Within

90 days of receiving the reference member state's assessment report and related materials, each concerned member state must decide whether to approve the assessment report and related materials.

If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the European Commission, whose decision is binding on all member states.

Within this framework, manufacturers may seek approval of hybrid medicinal products under Article 10(3) of Directive 2001/83/EC. Hybrid applications rely, in part, on information and data from a reference product and new data from appropriate pre-clinical tests and clinical trials. Such applications are necessary when the proposed product does not meet the strict definition of a generic medicinal product, or bioavailability studies cannot be used to demonstrate bioequivalence, or there are changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration of the generic product compared to the reference medicinal product. In such cases the results of tests and trials must be consistent with the data content standards required in the Annex to the Directive 2001/83/EC, as amended by Directive 2003/63/EC.

Hybrid medicinal product applications have automatic access to the centralized procedure when the reference product was authorized for marketing via that procedure. Where the reference product was authorized via the decentralized procedure, a hybrid application may be accepted for consideration under the centralized procedure if the applicant shows that the medicinal product constitutes a significant therapeutic, scientific or technical innovation, or the granting of a community authorization for the medicinal product is in the interest of patients at the community level.

A marketing authorization may be granted only to an applicant established in the EU. Regulation No. 1901/2006 provides that prior to obtaining a marketing authorization in the EU, an applicant must demonstrate compliance with all measures included in a Pediatric Investigation Plan, or PIP, approved by the Pediatric Committee of the EMA, or PDCO, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the PIP. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the marketing authorization is obtained in all Member States of the EU and study results are included in the product information, even when negative, the product is eligible for six months' supplementary protection certificate extension. For orphan-designated medicinal products, the 10-year period of market exclusivity is extended to 12 years.

Regulatory Data Exclusivity in the European Union

In the European Union, innovative medicinal products authorized in the EU on the basis of a full marketing authorization application (as opposed to an application for marketing authorization that relies on data available in the marketing authorization dossier for another, previously approved, medicinal product) are entitled to eight years of data exclusivity. During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to ten years' market exclusivity. During this ten-year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is held to bring a significant clinical benefit in comparison with

existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Orphan Drug Designation and Exclusivity in the EU

Regulation (EC) No 141/2000 and Regulation (EC) No. 847/2000 provide that a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of: (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives the medicinal product is unlikely to be developed. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. The criteria required to obtain orphan status will be reevaluated at the time of MAA review and must still be met in order to retain orphan status.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and, in addition, a range of other benefits during the development and regulatory review process, including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom (U.K.) voted in favor of leaving the European Union (commonly referred to as “Brexit”). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the U.K. from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the U.K. provides a notice of withdrawal pursuant to the E.U. Treaty. Since the regulatory framework for pharmaceutical products in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including

government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, ensuring adequate coverage and payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities can extend well beyond the receipt of regulatory marketing approval for a product and may require a clinical trial that compares the cost effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue

after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching physicians, patient privacy laws and regulations, and other healthcare laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, 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 their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, which may apply to healthcare items or services that are 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 in addition

to requiring drug manufacturers to report information related to payments and transfers of value to other health care providers and health care 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.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare.

In March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
    - expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
    - expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
    - addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
    - expanded the types of entities eligible for the 340B drug discount program;
    - established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
    - a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
    - the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
    - established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted since the PPACA 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 will stay in effect through 2024 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.

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 for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which 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.

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.

Segment Reporting

We are engaged solely in the discovery and development of innovative small molecule drug therapies for immune system disorders. Accordingly, we have determined that we operate in one operating segment.

Revenue

We had no revenue for the year ended December 31, 2017. For the years ended December 31, 2016 and 2015, payments of $15.0 million and $66.1 million from Janssen represented 100% and 100% of our revenue, respectively, all of which were related to payments under the Janssen Agreement and its exclusive license of worldwide rights to develop and commercialize products that contain one or more of our drug candidates for the treatment of HCV.

Research and Development Expense

For the years ended December 31, 2017, 2016 and 2015, company-sponsored research and development expenses were $65.0 million, $59.2 million and $56.6 million, respectively.

Employees

As of February 20, 2018, we had 88 full-time employees, 35 of whom hold doctoral degrees. Approximately 62 of our employees are engaged in research and development, with the remainder engaged in administration, finance and business development functions. In February 2018, we implemented a restructuring plan that will reduce employee headcount by approximately 20% across several functional areas to approximately 70 employees by March 2018. None of our employees is represented by a labor union or covered by collective bargaining agreements. We believe our relations with our employees are good.

Information Available on the Internet

Our Internet address is www.achillion.com. We are not including the information contained in our website as part of, or incorporating it by reference into, this Annual Report on Form 10-K. We make available free of charge through our website our Annual Reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such materials with the Securities and Exchange Commission, or the SEC. We also make available on our website our corporate governance guidelines, the charters for our audit committee, nominating and corporate governance committee, compensation committee, compliance committee, and strategy committee, and our code of business conduct and ethics, which applies to our directors, officers and employees, and such information is available in print and free of charge to any of our stockholders who requests it. In addition, we intend to disclose on our website any amendments to, or waivers from, our code of business conduct and ethics that are required to be publicly disclosed pursuant to rules of the SEC.

Executive Officers of the Registrant

Name	Age	Position
Milind S. Deshpande, Ph.D.	61	Chief Executive Officer, Director
Mary Kay Fenton	53	Executive Vice President and Chief Financial Officer
Martha Manning, Esq.	63	Executive Vice President, General Counsel and Corporate Secretary
Joseph Truitt	53	President and Chief Operating Officer

Milind S. Deshpande, Ph.D., Chief Executive Officer. Dr. Deshpande has served as our Chief Executive Officer since May 2013, at which time he was also elected to our board of directors. Dr. Deshpande also served

as our President from May 2013 to February 2018. Previously, he was our President of Research and Development and Chief Scientific Officer from October 2010 to May 2013. Prior to joining Achillion in September 2001, Dr. Deshpande was Associate Director of Lead Discovery and Early Discovery Chemistry at the Pharmaceutical Research Institute at Bristol-Myers Squibb, a pharmaceutical company, from 1991 to 2001, where he managed the identification of new clinical candidates to treat infectious and neurological diseases. From 1988 to 1991, he held a faculty position at Boston University Medical School. Dr. Deshpande is on the board of directors of Spero Therapeutics, a biotechnology company. Dr. Deshpande received his Ph.D. in Organic Chemistry from Ohio University, following his undergraduate education in India.

Mary Kay Fenton, Executive Vice President and Chief Financial Officer. Ms. Fenton has served as our Executive Vice President and Chief Financial Officer since 2006. Prior to joining Achillion in October 2000, Ms. Fenton, a certified public accountant, held various positions within the Technology Industry Group at PricewaterhouseCoopers LLP, an independent registered public accounting firm, from 1991 to 2000, most recently as Senior Manager responsible for the life sciences practice in Connecticut. Prior to 1991, Ms. Fenton was an economic development associate in the nonprofit sector. Ms. Fenton is the chair of the board of directors of Connecticut Business and Industry Association, a representative business organization. Ms. Fenton holds an M.B.A. in Finance from the Graduate School of Business at the University of Connecticut and an A.B. in Economics from the College of the Holy Cross.

Martha Manning, Esq., Executive Vice President, General Counsel and Corporate Secretary. Ms. Manning has served as our Executive Vice President, General Counsel and Corporate Secretary since February 2016. Prior to joining Achillion in February 2016, Ms. Manning was General Counsel of iCeutica Inc., a drug development company from 2013 to 2016. She served as Chief Legal Officer of OraPharma, Inc., a pharmaceutical company, from 2011 to 2012 when the company was acquired by Valeant Pharmaceuticals, Inc. She joined OraPharma from Sandoz Inc., the generic pharmaceutical division of Novartis AG, where she served as Vice President and General Counsel from 2008 to 2011. Prior to Sandoz, she served as Senior Vice President, General Counsel and Secretary for Adolor Corporation, a publicly traded biopharmaceutical company from 2002 to 2008. Ms. Manning began her legal career with the law firm of Morgan, Lewis & Bockius. She received her J.D. from the University of Pennsylvania School of Law and her Bachelor of Business Administration from the University of Massachusetts.

Joseph Truitt, President and Chief Operating Officer. Mr. Truitt serves as our President and Chief Operating Officer. In September 2017, Mr. Truitt was promoted to Chief Operating Officer and in February 2018 he was promoted to President and Chief Operating Officer. Prior to his promotion to Chief Operating Officer in September 2017, Mr. Truitt had served as our Chief Commercial Officer since January 2009. Prior to joining Achillion in January 2009, Mr. Truitt was Vice President of Business Development and Product Strategy for Lev Pharmaceuticals, Inc., a biotechnology company, from October 2007 to December 2008. From July 2006 through September 2007, he served as Lev's Vice President of Sales and Marketing and led the build out of the commercial team and infrastructure in preparation for product launch. From February 2002 to July 2006, Mr. Truitt was Vice President of Sales and Operations at Johnson & Johnson, a pharmaceutical company, where he directed commercial operations at the company's OraPharma subsidiary. From 2000 to 2002, Mr. Truitt was Vice President of Sales and Operations of OraPharma, Inc., a pharmaceutical company, prior to its acquisition by Johnson & Johnson. Mr. Truitt holds an M.B.A. from St. Joseph's University, Philadelphia and a B.S. in Marketing from LaSalle University, Philadelphia.

ITEM 1A. RISK FACTORS

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 1 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

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 with other drug candidates in the preclinical phase. 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 recently 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;
- 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 disease 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 and Ra 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.

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.

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 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 achieve any further value from the HCV program.

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.

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 will reduce employee headcount by approximately 20% to approximately 70 employees in March 2018. 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 and ACH-5228, and late-stage preclinical compound, ACH-5548. We assessed the staffing levels required to accomplish our revised strategic goals and determined to reduce 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 and late-stage compounds through preclinical and clinical trials, 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;
- 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 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.

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 our factor D inhibitors ACH-4471 and ACH-5228, 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 patients for limited durations, the longest being approximately nine months, 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.

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.

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 candidate ACH-4471 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.

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 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 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 ®) is a marketed therapy for the treatment of PNH and atypical hemolytic uremic syndrome, or aHUS. 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.

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.

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.

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

$85.2 million, $61.7 million, and $5.0 million for the years ended December 31, 2017, 2016, and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $602.7 million. 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 preclinical and 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 preclinical testing, 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.

We will be required to expend significant funds in order to advance the development of our complement factor D inhibitor platform. 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 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 December 31, 2017, will enable us to fund our current projected operating requirements for at least the next 12 months. Our estimate as to how long we expect our existing cash and cash equivalents 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, 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 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. 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.

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.

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.

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 our exclusive collaboration and license agreement with them, 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
- 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.

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 any 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 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 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.

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:

- 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.

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. Our ability to attract and retain qualified personnel, consultants and advisors 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.

In the future, we may grow our organization, and as a result, we may encounter difficulties in managing our 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 European Medicines Agency 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 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.

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 enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act 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;
- fines, 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.

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 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.

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.

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 Securities and Exchange Commission, or 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.

Risks Related to Our Common Stock

Our executive officers, directors and principal stockholders have the ability to control 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 February 20, 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 40% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control 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 December 31, 2017, 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.

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 sovaprevir, our clinical-stage drug candidate for the treatment of chronic hepatitis C viral 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, as amended, and, in any event, we have filed a registration statement 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 controls 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 controls over financial reporting or, if our independent registered public accounting firm are unable to provide us with an attestation and an unqualified report as to the effectiveness of our internal controls 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.

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 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We currently lease approximately 41,509 square feet of laboratory and office space in New Haven, Connecticut, which we occupy under a lease expiring in March 2020. We believe our existing facilities are adequate for our current needs and that additional space will be available in the future on commercially reasonable terms as needed.

ITEM 3. LEGAL PROCEEDINGS

None.

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock trades on the NASDAQ Global Select Market under the symbol "ACHN". The following table sets forth the high and low sale prices per share for our common stock, as reported on the NASDAQ Global Select Market for the periods indicated:

	High	Low
2016		
First Quarter	$10.66	$5.57
Second Quarter	$10.06	$7.48
Third Quarter	$ 9.49	$7.36
Fourth Quarter	$ 8.25	$3.78
2017		
First Quarter	$ 4.74	$3.71
Second Quarter	$ 5.17	$3.15
Third Quarter	$ 5.66	$3.54
Fourth Quarter	$ 4.82	$2.69

Information regarding our equity compensation plans and the securities authorized for issuance thereunder is set forth in Item 12 below.

Holders of record

As of the close of business on February 15, 2018, there were approximately 64 holders of record of our common stock. The number of record holders may not be representative of the number of beneficial owners because many of the shares of our common stock are held by depositories, brokers or other nominees.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in our Proxy Statement for the 2017 Annual Meeting of Stockholders and is incorporated in this Annual Report on Form 10-K by reference.

Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain any earnings for future growth and, therefore, do not expect to pay cash dividends in the foreseeable future.

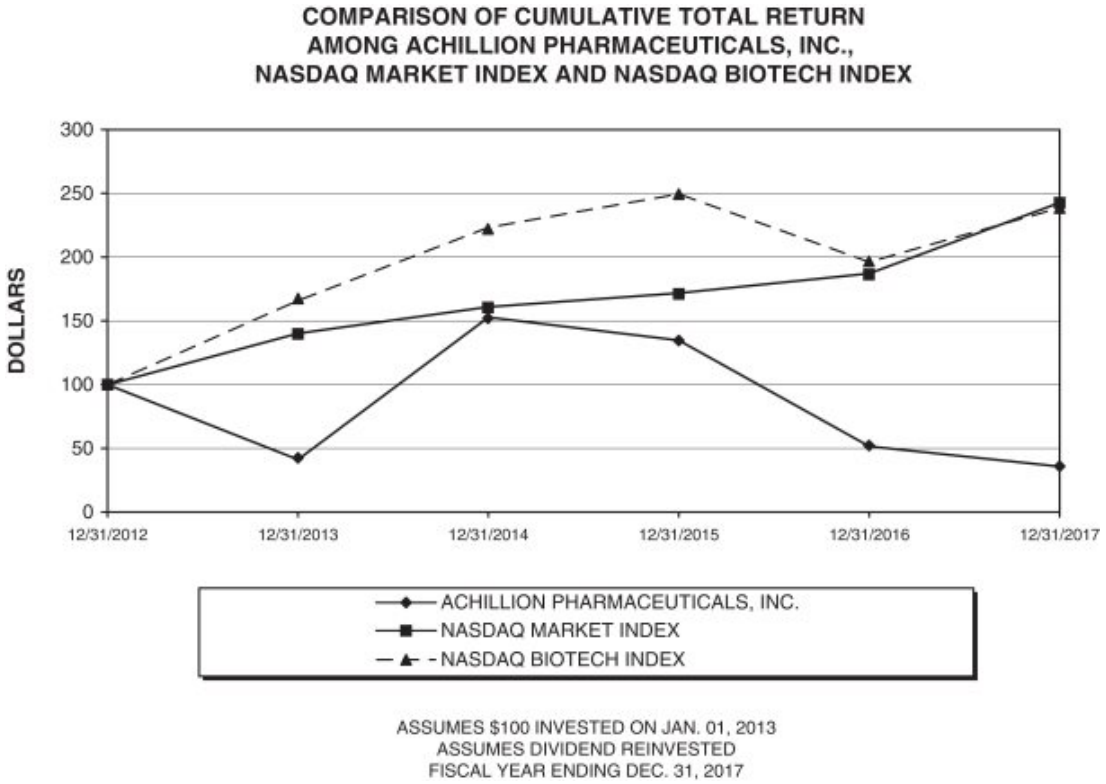
Issuer Purchases of Equity Securities

Neither we nor any affiliated purchaser or anyone acting on behalf of us or an affiliated purchaser made any purchases of shares of our common stock in the fourth quarter of 2017.

Comparative Stock Performance

The following graph and related information should not be deemed "soliciting material" or to be "filed" with the SEC for purposes of Section 18 of the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Securities Act or Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the cumulative total stockholder return on our common stock from December 31, 2012 to December 31, 2017 with the cumulative total return of (i) the NASDAQ Market Index and (ii) the NASDAQ Biotechnology Index. This graph assumes the investment of $100.00 after the market closed on December 31, 2012 in our common stock, and in the NASDAQ Market Index and the NASDAQ Biotechnology Index, and it assumes any dividends are reinvested. The stock price performance included in this graph is not necessarily indicative of future stock price performance.



ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data should be read together with the information under "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the notes to those financial statements included elsewhere in this Annual Report on Form 10-K. The selected statement of comprehensive loss data for the years ended December 31, 2017, 2016 and 2015 and balance sheet data as of December 31, 2017 and 2016 set forth below have been derived from our audited financial statements included elsewhere in this Annual Report on Form 10-K. The selected statement of comprehensive loss data for the years ended December 31, 2014 and 2013 and balance sheet data as of December 31, 2015, 2014 and 2013 set forth below have been derived from the audited financial statements for such years not included in this Annual Report on Form 10-K. The historical results presented here are not necessarily indicative of future results.

	Years Ended December 31,				
	2017	2016	2015	2014	2013
	(in thousands, except per share amounts)				
Statement of Comprehensive Loss Data:					
Total revenue (1)	$ —	$ 15,000	$ 66,122	$ —	$ —
Research and development	65,052	59,162	56,553	53,515	46,736
General and administrative	24,524	20,703	24,676	15,911	12,741
Total operating expenses	89,576	79,865	81,229	69,426	59,477
Loss from operations	(89,576)	(64,865)	(15,107)	(69,426)	(59,477)
Interest income (expense), net	4,340	3,159	1,188	418	530
Net loss	(85,236)	(61,706)	(5,030)	(69,008)	(58,947)
Net loss per share—basic and diluted	$ (0.62)	$ (0.45)	$ (0.04)	$ (0.70)	$ (0.63)
Weighted average number of shares outstanding—basic and diluted	137,180	136,667	125,592	98,367	93,983

	As of December 31,				
	2017	2016	2015	2014	2013
Balance Sheet Data:					
Cash and cash equivalents (1)(2)	$ 43,496	$ 77,261	$ 81,725	$ 73,664	$ 33,457
Short-term marketable securities (1)(2)	256,578	286,558	377,616	79,215	88,393
Long-term marketable securities	30,511	27,657	—	—	36,139
Working capital	291,054	368,564	447,930	141,816	115,379
Total assets	337,613	413,875	464,525	156,807	162,417
Long-term liabilities	214	450	231	279	56
Total liabilities	13,098	14,421	14,889	13,338	9,459
Total stockholders' equity	324,515	399,454	449,636	143,469	152,958

In addition to the following notes, see "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and the Consolidated Financial Statements and accompanying notes and previously filed Annual Reports on Form 10-K for further information regarding our results of operations and financial position for periods reported therein.

(1) In May 2015, we entered into an exclusive collaboration and license agreement with Janssen, and its affiliate, Johnson & Johnson Innovation-JJDC, Inc., or JJDC, which we refer to as the Janssen Agreement, for the further clinical advancement of a portfolio of antivirals we discovered and developed for the treatment of HCV. In addition, upon the closing of the transactions contemplated by the Janssen Agreement, we entered into a stock purchase agreement with JJDC. Pursuant to the JJDC Stock Purchase Agreement, on July 1, 2015, we issued 18,367,346 shares of common stock to JJDC at a price of $12.25 per share for an aggregate purchase price of $225 million. We recorded revenue of $66.1 million during the year ended December 31, 2015 associated with this transaction. We also recorded revenue of $15.0 million during the year ended December 31, 2016 related to

the achievement of a clinical enrollment milestone under the Janssen Agreement. On September 9, 2017, we received notice from Janssen of Janssen's termination of the Janssen Agreement effective November 8, 2017. As a result of the termination of the Janssen Agreement, we will not receive any future milestone-based or royalty payments under the agreement. Also refer to footnote 5 in our Notes to the Financial Statements.

(2) In February 2015, we entered into an underwriting agreement with Leerink Partners LLC and Deutsche Bank Securities Inc., as representatives of the several underwriters named therein (collectively, the "Underwriters"), relating to a public offering of shares of our common stock, par value $0.001 per share, at a price of $10.25 per share less underwriting discounts and commissions (the "Offering"). We issued and sold to the Underwriters an aggregate of 13,800,000 shares of common stock in connection with the Offering. The Offering resulted in net proceeds to us of $132.5 million. Also refer to footnote 3 in our Notes to the Financial Statements.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many important factors, such as those set forth in Part I, Item 1A. "Risk Factors" of this Annual Report on Form 10-K, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a science-driven, patient-focused biopharmaceutical company seeking to leverage our believed strengths across the continuum from discovery through commercialization by discovering and developing small molecule therapeutics to meet the needs of patients with complement-mediated diseases.

We have discovered and developed our complement inhibitor platform, directed at advancing 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 this 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 C3 glomerulopathy, or C3G, and immune complex membranoproliferative glomerulonephritis, or IC-MPGN, both kidney diseases, paroxysmal nocturnal hemoglobinuria, or PNH, a blood disorder, as well as several more prevalent indications.

Our lead drug candidate, ACH-4471, has demonstrated preliminary clinical proof-of-concept in patients with C3G and in patients with PNH.

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

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 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 also generated a platform of additional potent and specific orally-administered compounds that bind to factor D with high affinity, resulting in alternative pathway inhibition. One of these compounds, ACH-5228, is in phase I clinical testing in healthy volunteers, and additional compounds are in IND-enabling preclinical development. We may seek to advance certain of these factor D inhibitors for oral systemic administration to treat C3G, IC-MPGN, PNH, or other complement mediated diseases.

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 $588.8 million from inception through December 31, 2017 and

had an accumulated deficit of $602.7 million as of December 31, 2017, which includes preferred stock dividends recognized until our initial public offering in 2006. Our net losses were $85.2 million, $61.7 million, and $5.0 million for the years ended December 31, 2017, 2016, and 2015, respectively.

We have funded our operations primarily through proceeds from the sale of equity securities. Through December 31, 2017, 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 an early-stage 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.

Recent Development—Restructuring

In February 2018, we implemented a restructuring plan that will reduce employee headcount by approximately 20% to approximately 70 employees in March 2018. 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 and ACH-5228, and late-stage preclinical compound, ACH-5548. We assessed the staffing levels required to accomplish our revised strategic goals and determined to reduce our staff across several functional areas, while retaining the biology and chemistry core strengths necessary to advance our complement factor D portfolio.

Collaboration with Janssen Pharmaceuticals, Inc.

On September 9, 2017, we received notice from Janssen Pharmaceuticals, Inc., or Janssen, of Janssen's termination, effective as of November 8, 2017, of our exclusive collaboration and license agreement with them, which we refer to as the Janssen Agreement. Under the terms of the Janssen Agreement, we had granted Janssen exclusive worldwide rights to develop and commercialize products that contained one or more of our drug candidates for the treatment of chronic hepatitis C virus, or HCV, namely odalasvir, a second-generation NS5A inhibitor, ACH-3422, a NS5B HCV nucleoside polymerase inhibitor, and sovaprevir, a NS3/4A HCV protease inhibitor.

Janssen terminated the Janssen Agreement under section 14.6 of the Janssen Agreement, which allows for unilateral termination at Janssen's discretion upon 60 days' written notice to us at any time prior to the submission of the first application for marketing approval for a licensed product in any of the major market countries specified in the Janssen Agreement. Pursuant to its notice of termination, 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 that we licensed to Janssen under the Janssen Agreement. Following the termination, all licenses granted by either party to the other under the Janssen Agreement terminated, except to the extent necessary to allow either party to perform any obligations or exercise rights that survive the termination.

As a result of the termination of the Janssen Agreement, we will not receive any future milestone-based or royalty payments under that agreement, and Janssen will not bear the future costs of developing and commercializing our HCV portfolio. We currently have no plans to advance the HCV program on our own.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from the commercial sale of any drugs. During the year ended December 31, 2017 we did not recognize any revenue. During the years ended December 31, 2016 and 2015, we recognized revenue of $15.0 million and $66.1 million, respectively, under the Janssen Agreement which was terminated effective November 8, 2017.

Pursuant to the terms of the Janssen Agreement, we were required to provide technology transfer services related to the chemistry, manufacturing and know-how to Janssen for up to 180 days after the effective date of the Janssen Agreement. We completed this transfer in December 2015. We determined that the amount received in excess of the fair value of our common stock upon issuance to JJDC of $66.1 million of our common stock was attributed to the license and technology services and straight-line attribution of the license and technology services revenues would be used to recognize revenue. As such, revenue of $66.1 million was recorded during the year ended December 31, 2015 associated with this transaction.

During the year ended December 31, 2016, we recognized revenue of $15.0 million under the Janssen Agreement due to the achievement of a clinical enrollment milestone.

As a result of the termination of the Janssen Agreement, we will not receive any future milestone-based or royalty payments under that agreement, and Janssen will not bear the future costs of developing and commercializing our HCV portfolio.

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 focus is on our complement inhibitor platform, directed at advancing 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 comprise three pathways: the alternative pathway, the lectin pathway and the classical pathway. We are advancing novel small molecules from this platform which target complement factor D, an essential protein within the amplification loop of the alternative pathway. The alternative pathway is thought to play a critical role in a number of disease conditions including rare orphan conditions such as PNH, a blood disorder, C3G and IC-MPGN, both kidney diseases, as well as several more prevalent indications.

In addition to ACH-4471, our lead drug candidate, we have also generated a platform of additional potent and specific orally-administered compounds that bind to factor D with high affinity, resulting in alternative

pathway inhibition. One of these compounds, ACH-5228, is in phase I clinical testing in healthy volunteers, and an additional compound, ACH-5548, is in late-stage preclinical development. We may seek to advance certain of these additional factor D inhibitors for oral systemic administration to treat PNH, C3G, IC-MPGN, or other diseases.

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 drug candidates are expensed as incurred as indirect costs. Our research and development expenses for the years ended December 31, 2017, 2016 and 2015 were as follows:

	For the Years Ended December 31,		
	2017	2016	2015
	(in thousands)		
Direct external costs:			
ACH-4471	$17,073	$26,347	$13,320
ACH-5228	10,844	—	—
ACH-5548	474	—	—
Other next generation factor D inhibitors (oral and intravitreal)	8,053	6,276	—
HCV compounds and combination trials	87	326	20,956
Other	10	—	47
	36,541	32,949	34,323
Direct internal personnel costs	19,746	19,514	17,605
Sub-total direct costs	56,287	52,463	51,928
Indirect costs and overhead	8,600	7,110	5,265
Connecticut research and development tax credit	165	(411)	(640)
Total research and development	$65,052	$59,162	$56,553

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.

Following the termination of the Janssen Agreement on November 8, 2017, we are responsible for all expenses associated with our HCV program. Since we have no plans to advance the HCV program on our own, we expect these expenses will be limited to the intellectual property costs related to our HCV compounds.

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 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

The discussion and analysis of our financial condition and results of operations set forth below are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, we evaluate our estimates and assumptions, including those described below. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management makes estimates and exercises judgment in revenue recognition, research and development costs, stock-based compensation and accrued expenses. Actual results may differ from these estimates under different assumptions or conditions.

We believe the following critical accounting policies affect management's more significant judgments and estimates used in the preparation of our financial statements:

Revenue Recognition

We recognize revenue from contract research and development and research progress payments in accordance with Accounting Standards Codification 605, or ASC 605, *Revenue Recognition* . Revenue-generating research and development collaborations are often multiple element arrangements, providing for a license as well as research and development services. In order to account for these arrangements, we must identify the deliverable included within the arrangement and evaluate which deliverables represent separate units of accounting based on whether certain criteria are met, including whether the delivered element has stand-alone value to the collaborator. The consideration received is allocated among the separate units of accounting and the applicable revenue recognition criteria are applied to each of the separate units.

When we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be performed and revenue related to upfront license payments will be recognized. Revenue will be recognized using either a proportionate performance or straight-line method. We recognize revenue using the proportionate performance method provided that we can reasonably estimate the level of effort required to complete our performance obligations under an arrangement and such performance obligations are provided on a best-efforts basis. Under the proportionate performance method, periodic revenue related to up-front license payments is recognized as the percentage of actual effort expended in that period to total effort expected for all of our performance obligations under the arrangement. Actual effort is generally determined based upon actual direct labor hours, or FTEs, incurred and include research and development activities performed by internal scientists. Total expected effort is generally based upon the total projected direct labor hours. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we expect to complete the related performance obligations. In the event that a change in estimate occurs, the change will be accounted for using the cumulative catch-up method which provides for an adjustment to revenue in the current period. Estimates of our level of effort may change in the future, resulting in a material change in the amount of revenue recognized in future periods, including negative revenue in some periods. Generally, under collaboration arrangements, payments received during the period of performance may include up-front payments, time-or performance-based milestones and reimbursement of internal and external costs. The proportion of actual performance to total expected performance is applied to these payments in determining periodic revenue but will be limited by the aggregate cash received or receivable to date.

Substantive milestone payments are recognized upon achievement of the milestone. Determining whether a milestone is substantive requires judgment that should be made at the inception of the arrangement. To meet the definition of a substantive milestone, the consideration earned by achieving the milestone (1) would have to be commensurate with either the level of effort required to achieve the milestone or the enhancement in the value of the item delivered, (2) would have to relate solely to past performance, and (3) should be reasonable relative to all deliverables and payment terms in the arrangement. No bifurcation of an individual milestone is allowed and there can be more than one milestone in an arrangement.

Under the terms of the Janssen Agreement, we granted Janssen exclusive worldwide rights to develop and commercialize products that contained one or more of our drug candidates for the treatment of HCV, namely odalasvir, a second-generation NS5A inhibitor, ACH-3422, a NS5B HCV polymerase inhibitor, and sovaprevir, a NS3/4A HCV protease inhibitor. In May 2015, we also entered into a parallel transaction with Janssen's affiliate, JJDC, Inc., or JJDC, pursuant to which JJDC purchased 18,367,346 shares of our common stock at a price of $12.25 per share, for an aggregate purchase price of $225.0 million pursuant to a stock purchase agreement, or the JJDC Stock Purchase Agreement. In connection with the purchase of the shares, we and JJDC also entered into an investor agreement, or the Investor Agreement, on July 1, 2015 governing specified rights and obligations of JJDC with respect to its ownership of such shares.

Pursuant to the terms of the Janssen Agreement, we were required to provide technology transfer services related to the chemistry, manufacturing and know-how to Janssen for up to 180 days after the effective date of the agreement. In accordance with ASC 605-25, which provides guidance on accounting for multiple-element arrangements, including the determination of the units of accounting and allocation of total arrangement consideration, we identified all of the obligations at the inception of the Janssen Agreement. The significant obligations were determined to be the license and the technology transfer services. We determined that license and technology transfer services represented a single unit of accounting because they were not viewed to have standalone value. The Janssen Agreement entered into by us and Janssen, and the JJDC Stock Purchase Agreement and the Investor Agreement, which were entered into by us and Janssen's affiliate, were entered into in contemplation of each other. The only upfront amount received by us in exchange for the license and technology transfer services and the issuance of the shares was the $225.0 million. We determined that the amount received in excess of the fair value of the shares upon issuance of $66.1 million was attributed to the license and technology services. We also determined that there was no discernable pattern in which the

technology services would be provided during the 180 day period after the effective date. In accordance with ASC 605-10, we determined that straight-line attribution of the license and technology services revenues would be used to recognize revenue. As such, revenue of $66.1 million was recorded during the year ended December 31, 2015 associated with this transaction.

Under the terms of the Janssen Agreement, we earned a $15.0 million clinical milestone payment in December 2016 and would have been eligible to receive additional milestones in the future. We elected to apply the guidance in ASC 605-28 to the milestones. These milestones, if achieved, were substantive as they would relate solely to past performance and were commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of our performance.

On September 9, 2017, we received notice from Janssen of Janssen's termination, effective as of November 8, 2017, of the Janssen Agreement. As a result of the termination of the Janssen Agreement, we will not receive any future milestone-based or royalty payments under that agreement, and Janssen will not bear the future costs of developing and commercializing our HCV portfolio.

Stock-Based Compensation—Employee Stock-Based Awards

We apply ASC 718, *Stock Compensation,* which requires measurement and recognition of compensation expense for all stock-based awards made to employees and directors, including employee stock options under our stock incentive plans and employee stock purchases under our 2006 ESPP Plan, based on estimated fair values.

We primarily grant stock options for a fixed number of shares to employees with an exercise price equal to the market value of the shares at the date of grant. Under the fair value recognition provisions, stock-based compensation cost is based on the value of the portion of stock-based awards that is ultimately expected to vest.

We utilize 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. Determining the fair value of stock-based awards at the grant date requires judgment, including estimating the expected term of stock options, the expected volatility of our stock and expected dividends.

We base our estimate of the expected term on historical data for similar stock option grants and we calculate volatility based on actual volatility for the expected term of the option. We estimate forfeitures at the grant date and recognize compensation costs for only those awards that are expected to vest.

If factors change and we employ different assumptions in future periods, or if we experience significant fluctuations in our stock price, the compensation expense that we record may differ significantly from what we have recorded in the current period. Therefore, we believe it is important for investors to be aware of the degree of subjectivity involved when using option pricing models to estimate stock-based compensation. There is risk that our estimates of the fair values of our stock-based compensation awards on the grant dates may differ from the actual values realized upon the exercise, expiration, early termination or forfeiture of those share-based payments in the future. Certain stock-based payments, such as employee stock options, may expire worthless or otherwise result in zero intrinsic value as compared to the fair values originally estimated on the grant date and reported in our financial statements. Alternatively, value may be realized from these instruments that is significantly in excess of the fair values originally estimated on the grant date and reported in our financial statements. Although the fair value of employee share-based awards is determined using an option pricing model, that value may not be indicative of the fair value observed in a willing buyer/willing seller market transaction.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our financial statements.

In accruing service fees, we estimate the time period over which services will be provided and the level of effort in each period. If the actual timing of the provision of services or the level of effort varies from the estimate, we will adjust the accrual accordingly. The majority of our service providers invoice us monthly in arrears for services performed. Some of our service providers require upfront or milestone payments. If our estimate of services performed is less than the upfront or milestone payments, the difference is accounted for as a prepaid expense. In the event that we do not identify costs that have been incurred or we underestimate or overestimate the level of services performed or the costs of such services, our actual expenses could differ from such estimates. The date on which some services commence, the level of services performed on or before a given date and the cost of such services are often subjective determinations.

Income Taxes

We use an asset and liability approach for financial accounting and reporting of income taxes. Deferred tax assets and liabilities are determined based on temporary differences between financial reporting and tax basis assets and liabilities and are measured by applying enacted rates and laws to taxable years in which differences are expected to be recovered or settled. Further, the effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that the rate changes. A valuation allowance is required when it is "more likely than not" that all or a portion of deferred tax assets will not be realized.

We apply the provisions of ASC 740, *Income Taxes,* which prescribes a comprehensive model for how a company should recognize, measure, present and disclose in its financial statements uncertain tax positions that the company has taken or expects to take on a tax return, including a decision whether to file or not file a return in a particular jurisdiction. Our financial statements reflect expected future tax consequences of such positions presuming the taxing authorities' full knowledge of the position and all relevant facts.

We do not have any unrecognized tax benefits as of December 31, 2017. We review all tax positions to ensure the tax treatment selected is sustainable based on its technical merits and that the position would be sustained if challenged.

Results of Operations

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

Revenues:

During the year ended December 31, 2017, we did not recognize any revenue. During the years ended December 31, 2016 and 2015, we recognized revenue of $15.0 million and $66.1 million, respectively, under the Janssen Agreement which was terminated effective November 8, 2017.

Comparison of the Years Ended December 31, 2017 and 2016

The decrease in collaboration revenue in 2017 is related to the recognition of revenue under the Janssen Agreement. During the year ended December 31, 2016, we recognized $15.0 million of revenue due to the achievement of a clinical enrollment milestone. The Janssen Agreement was terminated effective November 8, 2017 and there were no amounts recognized as revenue in 2017.

Comparison of the Years Ended December 31, 2016 and 2015

The decrease in collaboration revenue in 2016 is related to the recognition of revenue under the Janssen Agreement. During the year ended December 31, 2016, we recognized $15.0 million of revenue under the

Janssen Agreement due to the achievement of a clinical enrollment milestone. During the year ended December 31, 2015, we recognized $66.1 million of revenue under the Janssen Agreement related to the upfront payment received by us in exchange for the license and technology transfer services and the issuance of our common stock to an affiliate of Janssen's.

Research and Development Expenses:

Our research and development expenses 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 laboratories and clinical development space, operating supplies and other costs associated with our research and development activities. Research and development expenses consisted of the following:

	For the Years Ended			Change			
	2017	2016	2015	2017 vs. 2016		2016 vs. 2015	
	(in thousands)						
Personnel costs	$15,256	$14,824	$13,130	$ 432	3%	$ 1,694	13%
Stock based compensation	4,490	4,695	4,500	(205)	(4)%	195	4%
Outsourced research and supplies	34,262	30,062	31,214	4,200	14%	(1,152)	(4)%
Professional and consulting fees	5,847	5,501	5,287	346	6%	214	4%
Facilities costs	3,261	3,320	2,505	(59)	(2)%	815	33%
Travel and other costs	1,801	1,171	557	630	54%	614	110%
Research and development tax credit	135	(411)	(640)	546	133%	229	(36)%
Total	$65,052	$59,162	$56,553	$5,890	10%	$ 2,609	5%

Comparison of the Years Ended December 31, 2017 and 2016

The increase for year ended December 31, 2017 was primarily due to increased clinical trial costs related to ACH-4471 combined with increased preclinical and manufacturing costs for ACH-5228. Discovery research costs related to our next generation factor D inhibitors also increased. These amounts were partially offset by decreased preclinical and manufacturing costs related to ACH-4471.

We expect research and development expenses over the next year will decrease somewhat as compared to 2017 as we focus primarily on the development of our existing clinical candidates and late preclinical compounds and implement our restructuring plan.

Comparison of the Years Ended December 31, 2016 and 2015

The increase in research and development costs from 2015 to 2016 was primarily due to increased manufacturing, clinical trial and consulting costs related to the advancement of ACH-4471, partially offset by decreased manufacturing, clinical trial and consulting costs related to our HCV compounds, which were licensed to Janssen in 2015. Personnel costs also increased in 2016 due to the addition of personnel in our discovery and development groups.

General and Administrative Expenses:

General and administrative expenses consist primarily of salaries and benefits for management and administrative personnel, professional and consulting fees for legal, business development, accounting and other services, travel costs and facility-related costs such as rent, utilities and other general office expenses. General and administrative expenses consisted of the following:

	For the Years Ended			Change			
	2017	2016	2015	2017 vs. 2016		2016 vs. 2015	
	(in thousands)						
Personnel costs	$ 6,317	$ 6,136	$ 5,099	$ 181	3%	$ 1,037	20%
Stock based compensation	6,083	6,311	5,572	(228)	(4)%	739	13%
Professional and consulting fees	5,929	4,771	11,038	1,158	24%	(6,267)	(57)%
Facilities costs	1,363	1,114	875	249	22%	239	207%
Travel and other costs	4,832	2,371	2,092	2,461	104%	279	13%
Total	$24,524	$20,703	$24,676	$3,821	18%	$(3,973)	(16)%

Comparison of the Years Ended December 31, 2017 and 2016

The increase in general and administrative costs from 2016 to 2017 was primarily due to increased corporate legal fees and market related consulting fees combined with our payment of $2.9 million in underwriting fees in connection with the sale by JJDC in November 2017 of all of the shares of our common stock it acquired pursuant to the JJDC Stock Purchase Agreement. These amounts were partially offset by a decrease in corporate taxes.

We expect that general and administrative costs during the next year will decrease somewhat from 2017 as we implement our restructuring plan.

Comparison of the Years Ended December 31, 2016 and 2015

The decrease in general and administrative costs from 2015 to 2016 was primarily due to decreased business development consulting fees and corporate legal fees that were incurred in 2015 related to the Janssen Agreement, partially offset by increased personnel and non-cash stock compensation largely related to the addition of personnel.

Other Income and Expense:

Comparison of the Years Ended December 31, 2017 and 2016

Interest income was $4.4 million and $3.2 million for the years ended December 31, 2017 and 2016, respectively. The $1.2 million, or 38%, increase from 2016 to 2017 was primarily due to a greater return on investments during the period.

Interest expense was $50,000 and $68,000 for the years ended December 31, 2017 and 2016, respectively. The decrease of $18,000, or 26%, was primarily due to lower average debt balances outstanding in 2017.

Comparison of the Years Ended December 31, 2016 and 2015

Other income was $0 and $8.9 million for the years ended December 31, 2016 and 2015, respectively. The $8.9 million decrease was due to the nonrecurring receipt of an $8.9 million payment by a stockholder representing the disgorgement of short swing profits under Section 16(b) of the Securities Exchange Act in 2015.

Interest income was $3.2 million and $1.2 million for the years ended December 31, 2016 and 2015, respectively. The $2.0 million, or 172%, increase from 2015 to 2016 was primarily due to increased average cash balances.

Interest expense was $68,000 and $55,000 for the years ended December 31, 2016 and 2015, respectively. The increase of $13,000, or 24%, was primarily due to higher average debt balances outstanding in 2016.

Liquidity and Capital Resources

Since our inception, we have financed our operations primarily through proceeds from the sale of equity securities. Through December 31, 2017, 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. Under the 2014 Credit Facility, we were entitled to draw down equipment loan advances for the purchase of new laboratory equipment through October 3, 2015. Each advance under the 2014 Credit Facility is payable over a three-year term and bears interest at a fixed rate, determined at the time of each advance, equal to the three-year Federal Home Loan Bank of Boston Classic Advance rate plus 4.75%. In October 2014 and March 2015, Webster advanced $440,000 and $229,000, respectively, to us under the 2014 Credit Facility.

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 December 31, 2017, our debt balance due to borrowings was $301,000 with a weighted average interest rate of 6.02%. As of December 31, 2017, the following amounts remained outstanding under the 2014 Credit Facility and the 2016 Credit Facility:

Lender	Date	Interest Rate (per annum)	Principal Amount	Outstanding Balance	Maturity Date
Webster Bank	March 2015	6.20%	$228,962	$ 20,774	March 2018
Webster Bank	October 2016	6.01%	$443,000	$ 279,935	October 2019

In February 2017, we filed a universal shelf registration on Form S-3 with the U.S. Securities and Exchange Commission, or SEC, 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 offerings. Further, in February 2017, we entered into a sales agreement with Cantor Fitzgerald & Co., or Cantor, 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 $330.6 million and $391.5 million in cash, cash equivalents and marketable securities as of December 31, 2017 and 2016, respectively. We regularly review our investments and monitor the financial markets. As of December 31, 2017, 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.

Operating Activities

Cash used in operating activities was $59.5 million for the year ended December 31, 2017 and was primarily attributable to our net loss during the period of $85.2 million, partially offset by a $15.2 million decrease in accounts receivable, primarily related to the receipt of a $15.0 million Janssen milestone payment in January 2017, combined with $11.7 million in non-cash stock-based compensation. Cash used in operating activities was $65.7 million for the year ended December 31, 2016 and was primarily attributable to our net loss during the period of $61.7 million, combined with an increase in other receivables of $14.8 million and a decrease in accrued expenses of $3.7 million. This amount was partially offset by $12.9 million in non-cash charges related to depreciation, amortization of premiums on marketable securities and stock-based compensation combined with a $2.7 million increase in accounts payable. Cash provided by operating activities was $5.6 million for the year ended December 31, 2015 and was primarily attributable to our net loss during the period of $5.0 million, adjusted for $12.8 million in non-cash charges related to depreciation, amortization of premiums on marketable securities and stock-based compensation combined with a $3.9 million increase in accrued expenses. This amount was partially offset by our $5.0 million net loss combined with $2.5 million in premiums paid on the purchase of investments and a $2.3 million decrease in accounts payable.

Investing Activities

Cash provided by investing activities was $26.0 million for the year ended December 31, 2017 and was primarily attributable to maturities of marketable securities and was partially offset by purchases of marketable securities. Cash provided by investing activities was $60.7 million for the year ended December 31, 2016 and was primarily attributable to maturities of marketable securities and was partially offset by purchases of marketable securities. Cash used in investing activities was $298.7 million for the year ended December 31, 2015 and was primarily attributable to the purchase of marketable securities and partially offset by maturities of marketable securities.

Financing Activities

Cash used in financing activities was $0.3 million for the year ended December 31, 2017 and was primarily attributable to repayments of debt combined with $175,000 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. Cash provided by financing activities was $0.5 million for the year ended December 31, 2016 and was primarily attributable to borrowings of debt under the 2016 Credit Facility combined with proceeds from our employee stock purchase plan and the exercise of stock options, partially offset by repayments of debt. Cash provided by financing activities was $301.1 million for the year ended December 31, 2015 and was primarily attributable to $158.9 million in proceeds related to the JJDC Stock Purchase Agreement, $132.6 million in net proceeds from our February 2015 public offering of common stock combined with $5.6 million in net proceeds from the issuance of stock under an at-the-market sales agreement with Cantor.

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

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 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 market 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.

Furthermore, in February 2018, we implemented a restructuring plan that will reduce 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.

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 or acceptable 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.

Contractual Obligations and Commitments

The following table sets forth a summary of our commitments as of December 31, 2017:

	Payment Due by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More than 5 Years
	(in thousands)				
Debt, including interest	$ 318	$ 183	$ 135	$ —	$ —
Operating lease obligations	2,047	925	1,122	—	—
Clinical research obligations	29,517	25,699	3,801	17	—
Other professional obligations	1,941	1,849	92	—	—
Total	$33,823	$ 28,656	$ 5,150	$ 17	$ —

Clinical research obligations consist of costs of services by clinical organizations, other outsourced research and materials used in research and development activities. Other professional obligations consist mainly of general and administrative consulting obligations.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements as of December 31, 2017.

Recently Issued Accounting Standards

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or 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. In August 2015, the FASB issued ASU No. 2015-14, "Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date," which delays the effective date of ASU No. 2014-09 by one year. The new standard is effective for reporting periods beginning after December 15, 2017. In March 2016, FASB also issued 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. Further, in April 2016, FASB issued 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. ASU No. 2014-09 or Topic 606 will not have an impact on our financial position and results of operations, as we do not have any material revenue-generating contracts.

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 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. We are currently evaluating the impact ASU No. 2016-02 will have on our financial position and results of operations.

In March 2016, FASB issued ASU No. 2016-09, "Compensation—Stock Compensation (Topic 718)." The new guidance simplifies certain aspects related to income taxes, statement of cash flows, and forfeitures when accounting for share-based payment transactions. ASU No. 2016-09 is effective for annual periods beginning after December 15, 2017, and interim periods within annual periods beginning after December 15, 2018. Early adoption is permitted. We adopted ASU No 2016-09 as of January 1, 2017. The adoption of this guidance did not have a material effect on our financial position and results of operations.

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. We do not believe ASU No. 2016-15 will have a material effect on our 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. Early adoption is permitted, and the new guidance is to be applied retrospectively. We do not believe ASU 2016-18 will have a material effect on our 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. We do not believe ASU 2017-01 will have a material effect on our 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. We do not believe ASU No. 2017-09 will have a material effect on our financial position and results of operations.

ITEM 7A. 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 specifically and on the capital markets generally.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item is included in our Financial Statements and Supplementary Data listed in Item 15 of Part IV of this Annual Report on Form 10-K.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure 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 December 31, 2017. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under 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 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 December 31, 2017, 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.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) promulgated under the Securities Exchange Act of 1934 as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by its board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2017. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in *Internal Control Integrated Framework* (2013).

Based on its assessment, management concluded that, as of December 31, 2017 , our internal control over financial reporting is effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2017 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which is included herein.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting occurred during the fiscal quarter ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Achillion Pharmaceuticals, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying balance sheets of Achillion Pharmaceuticals, Inc. as of December 31, 2017 and 2016, and the related statements of comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, including the related notes (collectively referred to as the "financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in *Management's Annual Report on Internal Control Over Financial Reporting* appearing under Item 9A. Our responsibility is to express opinions on the Company's financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail,

accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PricewaterhouseCoopers LLP

Hartford, Connecticut
February 22, 2018
We have served as the Company's auditor since 2002.

ITEM 9B. OTHER INFORMATION

Restructuring

On February 18, 2018, our board of directors committed to the implementation of a restructuring plan that will reduce employee headcount by approximately 20% to approximately 70 employees. We expect this reduction in employee headcount to be completed by March 2018. 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 and late-stage preclinical compounds. We assessed the staffing levels required to accomplish our revised strategic goals and determined to reduce our staff across several functional areas, while retaining the biology and chemistry core strengths necessary to advance our complement factor D portfolio.

In connection with the restructuring, we estimate that we will incur approximately $1.5 million of charges during the first quarter of 2018 related to expected severance and other employee costs. We expect to realize estimated cost savings of approximately $10 million in 2018 compared to our 2017 expense level.

Changes in Executive Officer Roles

On February 18, 2018, our board of directors appointed Joseph Truitt to the position of President and Chief Operating Officer, effective immediately. Mr. Truitt, age 53, has served as our Executive Vice President and Chief Operating Officer since September 2017 and, prior to that, as our Executive Vice President and Chief Commercial Officer since joining Achillion in January 2009.

Prior to joining Achillion in January 2009, Mr. Truitt was Vice President of Business Development and Product Strategy for Lev Pharmaceuticals, Inc., a biotechnology company, from October 2007 to December 2008. From July 2006 through September 2007, he served as Lev's Vice President of Sales and Marketing and led the build out of the commercial team and infrastructure in preparation for product launch. From February 2002 to July 2006, Mr. Truitt was Vice President of Sales and Operations at Johnson & Johnson, a pharmaceutical company, where he directed commercial operations at the company's OraPharma subsidiary. From 2000 to 2002, Mr. Truitt was Vice President of Sales and Operations of OraPharma, Inc., a pharmaceutical company, prior to its acquisition by Johnson & Johnson. Mr. Truitt holds an M.B.A. from St. Joseph's University, Philadelphia and a B.S. in Marketing from LaSalle University, Philadelphia.

There are no family relationships between Mr. Truitt and any director or executive officer of Achillion. Mr. Truitt has not has engaged in any related person transaction (as defined in Item 404(a) of Regulation S-K) with Achillion.

In connection with Mr. Truitt's promotion to President and Chief Operating Officer, effective on February 18, 2018, Dr. Deshpande's title and role were changed from "President and Chief Executive Officer" to "Chief Executive Officer." Mr. Truitt will continue to report to Dr. Deshpande.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We intend to file with the Securities and Exchange Commission a definitive Proxy Statement, which we refer to herein as the Proxy Statement, not later than 120 days after the close of the fiscal year ended December 31, 2017. The information required by this item is incorporated herein by reference to the information contained under the sections captioned "Election of Directors," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Corporate Governance" of the Proxy Statement. The information required by this item relating to executive officers is included in "Part I, Item 1—Business—Executive Officers of the Registrant" of this Annual Report on Form 10-K on page 31 and is incorporated by reference.

We have adopted a written code of business conduct and ethics, which applies to our principal executive officer, principal financial or accounting officer or person serving similar functions and all of our other employees and members of our board of directors. The text of our code of ethics is available on our website at www.achillion.com. We did not waive any provisions of the code of business ethics during the year ended December 31, 2017. If we amend, or grant a waiver under, our code of business ethics that applies to our principal executive officer, principal financial or accounting officer, or persons performing similar functions, we intend to post information about such amendment or waiver on our website at www.achillion.com.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated herein by reference to the information contained under the sections captioned "Information About Executive and Director Compensation" of the Proxy Statement.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated herein by reference to the information contained under the sections captioned "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" of the Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated herein by reference to the information contained under the sections captioned "Certain Relationships and Related Transactions" of the Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this item is incorporated herein by reference to the information contained under the sections captioned "Auditor's Fees" and "Pre-Approval Policies and Procedures" of the Proxy Statement.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a)(1) Financial Statements

The following documents are included on pages F-1 through F-29 attached hereto and are filed as part of this Annual Report on Form 10-K.

(a)(2) Financial Statement Schedules

Not applicable

(a)(3) List of Exhibits

EXHIBIT INDEX

		Incorporated by Reference			
Exhibit No.	Description	Form	SEC Filing date	Exhibit Number	Filed with this 10-K
3.1	Amended and Restated Certificate of Incorporation of the Registrant, as amended.	10-K	03/08/12	3.1	
3.2	Amended and Restated Bylaws of the Registrant.	10-K	03/29/07	3.2	
4.1	Specimen Certificate evidencing shares of common stock.	S-1/A	09/22/06	4.1	
10.1	Form of Common Stock Warrant issued by the Registrant pursuant to the Loan and Security Agreement of GE Capital Corporation and Oxford Finance Corporation.	10-K	03/05/08	10.14	
10.2	Master Security Agreement between the Registrant and Webster Bank, National Association, dated as of October 3, 2014.	8-K	10/06/14	10.1	
10.3	First Amendment to Master Security Agreement between the Registrant and Webster Bank, National Association, dated as of May 26, 2016, as further amended on July 11, 2017.	10-Q	08/08/17	10.6	
10.4	Lease Agreement by and between the Registrant and WE George Street LLC for Suite 202, dated as of March 6, 2002.	S-1	03/31/06	10.14	
10.5	Amendment No. 2 to Lease, dated as of March 31, 2010, by and between the Registrant and WE George Street, LLC.	8-K	04/06/10	10.1	

	Exhibit No.	Description	Incorporated by Reference			Filed with this 10-K
			Form	SEC Filing date	Exhibit Number	
	10.6	Amendment No. 3 to Lease, dated as of August 20, 2015, by and between the Registrant and WE George Street, LLC.	8-K	08/24/15	10.1	
	10.7	Amendment No. 4 to Lease, dated as of April 7, 2016, by and between the Registrant and WE George Street, LLC.	8-K	04/08/16	10.1	
	10.8	Amendment No. 5 to Lease, dated as of October 3, 2017, by and between the Registrant and WE George Street, LLC.	10-Q	11/01/17	10.2	
#	10.9	2006 Stock Incentive Plan as amended September 18, 2006, March 9, 2010, June 10, 2010, April 11, 2012 and June 5, 2012.	8-K	06/11/12	99.3	
#	10.10	Form of Nonstatutory Stock Option Agreement under the 2006 Stock Incentive Plan.	8-K	12/22/10	99.1	
#	10.11	Form of Incentive Stock Option Agreement under the 2006 Stock Incentive Plan.	8-K	12/22/10	99.2	
#	10.12	2015 Stock Incentive Plan, dated June 2, 2015.	8-K	06/08/15	10.1	
#	10.13	Form of Incentive Stock Option Agreement under the 2015 Stock Incentive Plan.	10-K	02/25/16	10.16	
#	10.14	Form of Nonstatutory Stock Option Agreement under the 2015 Stock Incentive Plan.	10-K	02/25/16	10.17	
#	10.15	Amended and Restated Employment Agreement, dated August 4, 2017, by and between the Registrant and Milind S. Deshpande.	10-Q	08/08/17	10.1	
#	10.16	Amended and Restated Employment Agreement, dated August 4, 2017, by and between the Registrant and Mary Kay Fenton.	10-Q	08/08/17	10.2	
#	10.17	Amended and Restated Employment Agreement, dated August 4, 2017, by and between the Registrant and Joseph Truitt.	10-Q	08/08/17	10.4	
#	10.18	Amended and Restated Employment Agreement, dated August 4, 2017, by and between the Registrant and Martha Manning.	10-Q	08/08/17	10.5	
#	10.19	Non-Executive Directors Compensation Policy, dated March 28, 2017.	10-Q	05/04/17	10.1	
	10.20	Controlled Equity Offering SM Sales Agreement, dated as of February 23, 2017, by and between the Registrant and Cantor Fitzgerald & Co.	10-K	02/23/17	10.27	
	10.21	Letter Agreement, dated February 23, 2017, by and between the Registrant and Johnson & Johnson Innovation-JJDC, Inc.	10-K	02/23/17	10.28	
	10.22	Letter Agreement, dated November 14, 2017, by and between the Registrant and Johnson & Johnson Innovation-JJDC, Inc.	8-K	11/16/17	10.1	

	Exhibit No.	Description	Incorporated by Reference			Filed with this 10-K
			Form	SEC Filing date	Exhibit Number	
#	10.23	Form of Inducement Grant Nonstatutory Stock Option Agreement	10-Q	11/01/17	10.1	
	23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.				X
	31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934				X
	31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a)/Rule 15d-14(a) of the Securities Exchange Act of 1934				X
	32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
	32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
	101.CAL	XBRL Taxonomy Calculation Linkbase Document				X
	101.INS	XBRL Instance Document				X
	101.SCH	XBRL Taxonomy Extension Schema Document				X
	101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X
	101.LAB	XBRL Taxonomy Label Linkbase Document				X
	101.PRE	XBRL Taxonomy Presentation Linkbase Document				X

Management contracts or compensatory plans or arrangement

† Indicates confidential treatment requested as to certain portions, which portions were omitted and filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Request.

Attached as Exhibit 101 to this report are the following formatted in XBRL (Extensible Business Reporting Language): (i) Balance Sheets at December 31, 2017 and December 31, 2016, (ii) Statements of Comprehensive Loss for the years ended December 31, 2017, 2016 and 2015, (iii) Statements of Stockholders' Equity and Comprehensive Loss for the years ended December 31, 2017, 2016 and 2015, (iv) Statements of Cash Flows for the years ended December 31, 2017, 2016 and 2015 and (v) Notes to Financial Statements.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) 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, on February 22, 2018.

ACHILLION PHARMACEUTICALS, INC.

By: /S/ MILIND S. DESHPANDE
Milind S. Deshpande
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, the Report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/S/ MILIND S. DESHPANDE **Milind S. Deshpande**	Chief Executive Officer and Director (Principal executive officer)	February 22, 2018
/S/ MARY KAY FENTON **Mary Kay Fenton**	Executive Vice President and Chief Financial Officer (Principal financial and accounting officer)	February 22, 2018
/S/ DAVID SCHEER **David Scheer**	Chairman of the Board	February 22, 2018
/S/ JASON FISHERMAN, M.D. **Jason Fisherman, M.D.**	Director	February 22, 2018
/S/ GARY E. FRASHIER **Gary E. Frashier**	Director	February 22, 2018
/S/ KURT GRAVES **Kurt Graves**	Director	February 22, 2018
/S/ MICHAEL D. KISHBAUCH **Michael D. Kishbauch**	Director	February 22, 2018
/S/ ROBERT VAN NOSTRAND **Robert Van Nostrand**	Director	February 22, 2018
/S/ FRANK VERWIEL **Frank Verwiel**	Director	February 22, 2018
/S/ NICOLE VITULLO **Nicole Vitullo**	Director	February 22, 2018

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of
Achillion Pharmaceuticals, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying balance sheets of Achillion Pharmaceuticals, Inc. as of December 31, 2017 and 2016, and the related statements of comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2017, including the related notes (collectively referred to as the "financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework* (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in *Management's Annual Report on Internal Control Over Financial Reporting* appearing under Item 9A. Our responsibility is to express opinions on the Company's financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in

accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ PricewaterhouseCoopers LLP

Hartford, Connecticut
February 22, 2018
We have served as the Company's auditor since 2002.

Achillion Pharmaceuticals, Inc.

Balance Sheets
(in thousands, except per share amounts)

	As of December 31,	
	2017	2016
Assets		
Current assets:		
Cash and cash equivalents	43,496	$ 77,261
Marketable securities	256,578	286,558
Accounts and other receivables	60	15,256
Prepaid expenses and other current assets	3,804	3,460
Total current assets	303,938	382,535
Marketable securities	30,511	27,657
Fixed assets, net	2,816	3,479
Other assets	196	52
Restricted cash	152	152
Total assets	$ 337,613	$ 413,875
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 5,253	$ 7,002
Accrued expenses	7,461	6,618
Current portion of long-term debt	170	351
Total current liabilities	12,884	13,971
Other long-term liabilities	83	149
Long-term debt	131	301
Total liabilities	13,098	14,421
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Common Stock, $0.001 par value; 200,000 shares authorized at December 31, 2017 and 2016; 137,894 and 136,722 shares issued and outstanding at December 31, 2017 and 2016, respectively	138	137
Additional paid-in capital	927,420	916,584
Accumulated deficit	(602,654)	(517,418)
Accumulated other comprehensive income (loss)	(389)	151
Total stockholders' equity	324,515	399,454
Total liabilities and stockholders' equity	$ 337,613	$ 413,875

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

Achillion Pharmaceuticals, Inc.

Statements of Comprehensive Loss
(in thousands, except per share amounts)

	Years Ended December 31,		
	2017	2016	2015
Revenue	$ —	$ 15,000	$ 66,122
Operating expenses			
Research and development	65,052	59,162	56,553
General and administrative	24,524	20,703	24,676
Total operating expenses	89,576	79,865	81,229
Loss from operations	(89,576)	(64,865)	(15,107)
Other income (expense)			
Interest income	4,390	3,227	1,188
Interest expense	(50)	(68)	(55)
Other income	—	—	8,944
Net loss	$ (85,236)	$ (61,706)	$ (5,030)
Unrealized income (loss) on marketable securities	(540)	196	(33)
Total other comprehensive income (loss)	(540)	196	(33)
Total comprehensive income (loss)	$ (85,776)	$ (61,510)	$ (5,063)
Basic and diluted net loss per share attributable to common stockholders (Note 4)	$ (0.62)	$ (0.45)	$ (0.04)
Weighted average shares used in computing basic and diluted net loss per share attributable to common stockholders	137,180	136,667	125,592

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

Achillion Pharmaceuticals, Inc.

Statements of Stockholders' Equity for the Years Ended December 31, 2015, 2016 and 2017
(in thousands)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Stock Subscription Receivable	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount					
Balances at December 31, 2014	103,594	$ 104	$599,796	$ (450,682)	$ (5,737)	$ (12)	$ 143,469
Net loss	—	—	—	(5,030)	—	—	(5,030)
Other comprehensive income (loss)	—	—	—	—	—	(33)	(33)
Stock compensation	—	—	10,072	—	—	—	10,072
Issuance of common stock upon exercise of warrants	8	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	835	1	3,730	—	126	—	3,857
Issuance of common stock under the employee stock purchase plan	36	—	290	—	—	—	290
Issuance of common stock in connection with public offerings, net of issuance costs	13,800	14	132,509	—	5,611	—	138,134
Issuance of common stock in connection with the JJDC Stock Purchase Agreement	18,367	18	158,859	—	—	—	158,877
Balances at December 31, 2015	136,640	$ 137	$905,256	$ (455,712)	$ —	$ (45)	$ 449,636
Net loss	—	—	—	(61,706)	—	—	(61,706)
Other comprehensive income (loss)	—	—	—	—	—	196	196
Stock compensation	—	—	11,006	—	—	—	11,006
Issuance of common stock upon exercise of stock options	41	—	108	—	—	—	108
Issuance of common stock under the employee stock purchase plan	41	—	214	—	—	—	214
Balances at December 31, 2016	136,722	$ 137	$916,584	$ (517,418)	$ —	$ 151	$ 399,454
Net loss	—	—	—	(85,236)	—	—	(85,236)
Other comprehensive income (loss)	—	—	—	—	—	(540)	(540)
Stock compensation	—	—	10,573	—	—	—	10,573
Issuance of common stock upon exercise of warrants	1,084	1	(1)	—	—	—	—
Issuance of common stock upon exercise of stock options	14	—	39	—	—	—	39
Issuance of common stock under the employee stock purchase plan	74	—	225	—	—	—	225
Balances at December 31, 2017	137,894	$ 138	$927,420	$ (602,654)	$ —	$ (389)	$ 324,515

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

Achillion Pharmaceuticals, Inc.

Statements of Cash Flows
(in thousands)

	Years Ended December 31,		
	2017	2016	2015
Cash flows from operating activities			
Net loss	$ (85,236)	$ (61,706)	$ (5,030)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation and amortization	1,126	955	694
Noncash stock-based compensation	10,573	11,006	10,072
Loss on disposal of equipment	—	8	2
Premium on purchases of marketable securities	(1,094)	(565)	(2,486)
Amortization of premium on marketable securities	1,079	985	2,002
Changes in operating assets and liabilities:			
Accounts and other receivables	15,196	(14,750)	(411)
Prepaid expenses and other current assets	(313)	(721)	(837)
Accounts payable	(1,577)	2,693	(2,285)
Accrued expenses	834	(3,707)	3,856
Other long-term liabilities	(66)	149	—
Net cash provided by (used in) operating activities	(59,478)	(65,653)	5,577
Cash flows from investing activities			
Purchase of fixed assets	(626)	(2,508)	(704)
Purchase of marketable securities	(345,490)	(499,115)	(692,525)
Maturities of marketable securities	372,091	562,292	394,575
Net cash provided by (used in) investing activities	25,975	60,669	(298,654)
Cash flows from financing activities			
Proceeds from issuance of common stock in connection with public offerings, net of issuance costs	—	—	138,260
Proceeds from issuance of common stock in connection with the JJDC Stock Purchase Agreement	—	—	158,877
Proceeds from exercise of stock options	39	108	3,730
Proceeds from sale of stock under the employee stock purchase plan	225	214	290
Payment of deferred financing costs	(175)	—	—
Borrowings of debt	—	444	229
Repayments of debt	(351)	(246)	(248)
Net cash provided by (used in) financing activities	(262)	520	301,138
Net increase (decrease) in cash and cash equivalents	(33,765)	(4,464)	8,061
Cash and cash equivalents, beginning of period	77,261	81,725	73,664
Cash and cash equivalents, end of period	$ 43,496	$ 77,261	$ 81,725
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 52	$ 46	$ 50
Supplemental disclosure of noncash investing and financing activities			
Cashless exercise of warrants	$ 8,750	$ —	$ 53
Purchases of equipment in accounts payable or accrued expenses	$ 36	$ 199	—

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

Achillion Pharmaceuticals, Inc.

Notes to Financial Statements
(in thousands, except per share amounts)

1. Nature of the Business

Achillion Pharmaceuticals, Inc. (the "Company") was incorporated on August 17, 1998 in Delaware. The Company is a science-driven, patient-focused biopharmaceutical company seeking to leverage its believed strengths across the continuum from discovery through commercialization by discovering and developing small molecule therapeutics to meet the needs of patients with complement-mediated diseases. The Company is devoting substantially all of its efforts towards product research and development.

The Company incurred losses of $588,793 from inception through December 31, 2017 and had an accumulated deficit of $602,654 at December 31, 2017, which includes preferred stock dividends recognized until the Company's initial public offering in 2006. 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. 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 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.

Achillion Pharmaceuticals, Inc.

Notes to Financial Statements—(Continued)
(in thousands, except per share amounts)

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States ("GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Revenue Recognition

The Company recognizes revenue from contract research and development and research progress payments in accordance with Accounting Standards Codification ("ASC") 605, *Revenue Recognition* . Revenue-generating research and development collaborations are often multiple element arrangements, providing for a license as well as research and development services. In order to account for these arrangements, the Company must identify the deliverables included within the arrangement and evaluate which deliverables represent separate units of accounting based on if certain criteria are met, including whether the delivered element has stand-alone value to the collaborator. The consideration received is allocated among the separate units of accounting and the applicable revenue recognition criteria are applied to each of the separate units.

When the Company determines that an arrangement should be accounted for as a single unit of accounting, it must determine the period over which the performance obligations will be performed and revenue related to upfront license payments will be recognized. Revenue will be recognized using either a proportionate performance or straight-line method. The Company recognizes revenue using the proportionate performance method provided that it can reasonably estimate the level of effort required to complete its performance obligations under an arrangement and such performance obligations are provided on a best-efforts basis. Under the proportionate performance method, periodic revenue related to up-front license payments is recognized as the percentage of actual effort expended in that period to total effort expected for all of its performance obligations under the arrangement. Actual effort is generally determined based upon actual direct labor hours or full-time equivalents ("FTE") incurred and include research and development activities performed by internal scientists. Total expected effort is generally based upon the total direct labor hours of FTEs incorporated into the detailed budget and project plan that is agreed to by both parties to the collaboration. Significant management judgment is required in determining the level of effort required under an arrangement and the period over which the Company expects to complete the related performance obligations. In the event that a change in estimate occurs, the change will be accounted for using the cumulative catch-up method which provides for an adjustment to revenue in the current period. Estimates of the Company's level of effort may change in the future, resulting in a material change in the amount of revenue recognized in future periods, including negative revenue in some periods. Generally, under collaboration arrangements, payments received during the period of performance may include up-front payments, time-or performance-based milestones and reimbursement of internal and external costs. The proportion of actual performance to total expected performance is applied to these payments in determining periodic revenue but will be limited by the aggregate cash received or receivable to date.

Substantive milestone payments are recognized upon achievement of the milestone. Determining whether a milestone is substantive requires judgment that should be made at the inception of the arrangement. To meet the definition of a substantive milestone, the consideration earned by achieving the milestone (1) would have to be commensurate with either the level of effort required to achieve the milestone or the enhancement in the value of the item delivered, (2) would have to relate solely to past performance, and (3) should be reasonable relative to

all deliverables and payment terms in the arrangement. No bifurcation of an individual milestone is allowed and there can be more than one milestone in an arrangement.

Under the terms of the Collaboration and License Agreement between the Company and Janssen Pharmaceuticals, Inc. ("Janssen") dated May 19, 2015, as amended (the "Janssen Agreement"), the Company had granted Janssen exclusive worldwide rights to develop and commercialize products that contained one or more of the Company's drug candidates for the treatment of chronic hepatitis C virus, ("HCV"), namely odalasvir, a second-generation NS5A inhibitor, ACH-3422, a NS5B HCV polymerase inhibitor, and sovaprevir, a NS3/4A HCV protease inhibitor. In May 2015, the Company also entered into a parallel transaction with Janssen's affiliate, JJDC, Inc. ("JJDC") pursuant to which JJDC purchased 18,367 shares (the "Shares") of the Company's common stock at a price of $12.25 per share, for an aggregate purchase price of $225,000 pursuant to a stock purchase agreement (the "JJDC Stock Purchase Agreement"). In connection with the purchase of the Shares, the Company and JJDC also entered into an investor agreement (the "Investor Agreement") on July 1, 2015 governing specified rights and obligations of JJDC with respect to its ownership of the Shares.

Pursuant to the terms of the Janssen Agreement, the Company was required to provide technology transfer services related to the chemistry, manufacturing and know-how to Janssen for up to 180 days after the effective date of the agreement. In accordance with ASC 605-25, which provides guidance on accounting for multiple-element arrangements, including the determination of the units of accounting and allocation of total arrangement consideration, the Company identified all of the obligations at the inception of the Janssen Agreement. The significant obligations were determined to be the license and the technology transfer services. The Company determined that license and technology transfer services represented a single unit of accounting because they were not viewed to have standalone value. The Janssen Agreement entered into by the Company and Janssen, and the JJDC Stock Purchase Agreement and the Investor Agreement, which were entered into by the Company and Janssen's affiliate, were entered into in contemplation of each other. The only upfront amount received by the Company in exchange for the license and technology transfer services and the issuance of the Shares was the $225,000. The Company determined that the amount received in excess of the fair value of the Shares upon issuance of $66,122 was attributed to the license and technology services. The Company also determined that there was no discernable pattern in which the technology services would be provided during the 180 day period after the effective date. In accordance with ASC 605-10, the Company determined that straight-line attribution of the license and technology services revenues would be used to recognize revenue. As such, revenue of $66,122 was recorded during the year ended December 31, 2015 associated with this transaction.

Under the terms of the Janssen Agreement, the Company earned a $15,000 clinical milestone payment in December 2016 and would have been eligible to receive additional milestones in the future. The Company elected to apply the guidance in ASC 605-28 to the milestones. These milestones, if achieved, were substantive as they would relate solely to past performance and were commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of the Company's performance.

On September 9, 2017, the Company received notice from Janssen of Janssen's termination, effective as of November 8, 2017, of the Janssen Agreement. In November 2017, JJDC sold all of the Shares of the Company's common stock it acquired under the JJDC Stock Purchase Agreement.

Stock-Based Compensation—Employee Stock-Based Awards

The Company applies the provisions of ASC 718, *Stock Compensation,* which requires measurement and recognition of compensation expense for all stock-based awards made to employees and directors, including

employee stock options and employee stock purchases under the Company's 2006 ESPP Plan based on estimated fair values.

The Company primarily grants nonqualified stock options for a fixed number of shares to employees with an exercise price equal to the market value of the shares at the date of grant. Under the fair value recognition provisions, stock-based compensation cost is based on the fair value of the portion of stock-based awards that is ultimately expected to vest.

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. Determining the fair value of stock-based awards at the grant date requires judgment, including estimating the expected term of stock options, the expected volatility of our stock and expected dividends.

The Company bases its estimate of the expected term on historical data for similar stock option grants and calculates volatility based on actual volatility for the expected term of the option. The Company estimates forfeitures at the grant date and recognizes compensation costs for only those awards that are expected to vest.

Accrued Expenses

As part of the process of preparing financial statements, the Company is required to estimate accrued expenses. This process involves identifying services which have been performed on its behalf and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in its financial statements.

In accruing service fees, the Company estimates the time period over which services will be provided and the level of effort in each period. If the actual timing of the provision of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. The majority of service providers invoice the Company monthly in arrears for services performed. Some service providers require upfront or milestone payments. If the estimate of services performed is less than the upfront or milestone payments, the difference is accounted for as a prepaid expense. In the event that the Company does not identify costs that have begun to be incurred or the Company underestimates or overestimates the level of services performed or the costs of such services, actual expenses could differ from such estimates. The date on which some services commence, the level of services performed on or before a given date and the cost of such services are often subjective determinations. The Company makes judgments based upon facts and circumstances known to it in accordance with GAAP.

Cash, Cash Equivalents and Restricted Cash

Cash and cash equivalents are stated at cost, which approximates fair value, and include short-term, highly-liquid investments with original maturities of less than three months. The Company also holds certificates of deposit, which collateralize the Company's facility lease which are classified as restricted cash in the accompanying balance sheets. The restricted cash will be released from restriction in 2020. At December 31, 2017 and 2016, the Company had $43,496 and $77,261, respectively, of cash and cash equivalents.

Marketable Securities and Equity Investments

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. The guidance requires that fair value measurements be classified and disclosed in one of 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 in active markets, that are observable either directly or indirectly, such as quoted prices for similar assets or liabilities, quoted in markets that are not active, or other inputs that are observable; or

Level 3: Unobservable inputs.

The fair value of the Company's marketable securities of $287,089 and $314,215 as of December 31, 2017 and 2016, respectively, was 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.

Fair Value of Financial Instruments

The Company's financial instruments, including cash, cash equivalents, accounts receivable, and accounts payable are carried at cost, which approximates their fair value because of the short-term maturity of these instruments.

The Company believes that the carrying value of its debt balance outstanding approximates fair value. Fair value is determined using a discounted cash flow model based on current interest rates.

Concentration of Risk

Concentration of credit risk exists with respect to cash and cash equivalents and investments. The Company maintains its cash and cash equivalents and investments with high quality financial institutions. At times, amounts may exceed federally insured deposit limits.

For the years ended December 31, 2017, 2016, and 2015, 0%, 100% and 100%, respectively, of the Company's revenue was generated from the Janssen Agreement. At December 31, 2017 and 2016, 53% and 99%, respectively, of the Company's accounts receivable was from Janssen.

Achillion Pharmaceuticals, Inc.

Notes to Financial Statements—(Continued)
(in thousands, except per share amounts)

Fixed Assets

Property and equipment are recorded at cost and are depreciated and amortized over the shorter of their remaining lease term or their estimated useful lives on a straight-line basis as follows:

Laboratory equipment	4-7 years
Office equipment	3-5 years
Leasehold improvements	Lesser of life of improvement or lease term

Expenditures for maintenance and repairs, which do not improve or extend the useful lives of the respective assets, are expensed as incurred. When assets are sold or retired, the related cost and accumulated depreciation are removed from their respective accounts and any resulting gain or loss is included in income (loss) from operations.

Long-lived Assets

ASC 360, *Property, Plant and Equipment,* addresses the financial accounting and reporting for impairment or disposal of long-lived assets. The Company reviews the recorded values of long-lived assets for impairment whenever events or changes in business circumstance indicate that the carrying amount of an asset or group of assets may not be fully recoverable.

Research and Development Expenses

All costs associated with internal research and development, research and development services for which the Company has externally contracted and licensed technology are expensed as incurred. Research and development expense includes direct and indirect costs for salaries, employee benefits, subcontractors, including clinical research organizations (“CROs”), operating supplies, facility-related expenses and depreciation.

Patent Costs

The Company expenses the costs of obtaining and maintaining patents.

Income Taxes

The Company uses an asset and liability approach for financial accounting and reporting of income taxes. Deferred tax assets and liabilities are determined based on temporary differences between financial reporting and tax basis of assets and liabilities and are measured by applying enacted rates and laws to taxable years in which differences are expected to be recovered or settled. Further, the effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that the rate change is enacted. A valuation allowance is required when it is “more likely than not” that all or a portion of deferred tax assets will not be realized.

The Company applies the provisions of ASC 740, *Income Taxe* s, which prescribes a comprehensive model for how a company should recognize, measure, present, and disclose in its financial statements uncertain tax positions that the company has taken or expects to take on a tax return (including a decision whether to file or not file a return in a particular jurisdiction). The financial statements reflect expected future tax consequences of such positions presuming the taxing authorities’ full knowledge of the position and all relevant facts.

Achillion Pharmaceuticals, Inc.

Notes to Financial Statements—(Continued)
(in thousands, except per share amounts)

The Company did not have any unrecognized tax benefits as of December 31, 2017. The Company reviews all tax positions to ensure the tax treatment selected is sustainable based on its technical merits and that the position would be sustained if challenged.

Segment Information

The Company is engaged solely in the discovery and development of innovative small molecule drug therapies. Accordingly, the Company has determined that it operates in one operating segment.

Accounting Standards Updates

In May 2014, the Financial Accounting Standards Board ("FASB") issued 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. In August 2015, the FASB issued ASU No. 2015-14, "Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date," which delays the effective date of ASU No. 2014-09 by one year. The new standard is effective for reporting periods beginning after December 15, 2017. In March 2016, FASB also issued 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. Further, in April 2016, FASB issued 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. ASU No. 2014-09 or Topic 606 will not have a material impact on its financial position and results of operations, as it does not have any material revenue-generating contracts.

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 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.

In March 2016, FASB issued ASU No. 2016-09, "Compensation—Stock Compensation (Topic 718)." The new guidance simplifies certain aspects related to income taxes, statement of cash flows, and forfeitures when accounting for share-based payment transactions. ASU No. 2016-09 is effective for annual periods beginning after December 15, 2017, and interim periods within annual periods beginning after December 15, 2018. Early adoption is permitted. The Company adopted ASU No 2016-09 as of January 1, 2017. The adoption of this guidance did not have a material effect on the Company's financial position and results of operations.

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 Company does not believe ASU No. 2016-15 will have a material effect on its 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. Early adoption is permitted, and the new guidance is to be applied retrospectively. The Company does not believe ASU 2016-18 will have a material effect on its 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 Company does not believe ASU 2017-01 will have a material effect on its 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 Company does not believe ASU No. 2017-09 will have a material effect on its financial position and results of operations.

3. Financing Activities

Public Offerings

In February 2015, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Leerink Partners LLC and Deutsche Bank Securities Inc., as representatives of the several underwriters named therein (collectively, the "Underwriters"), relating to a public offering of shares of the Company's common stock, par value $0.001 per share, at a price of $10.25 per share less underwriting discounts and commissions (the "Offering"). The Company issued and sold to the Underwriters an aggregate of 13,800 shares of common stock in connection with the Offering. The Offering resulted in net proceeds to the Company of $132,558.

4. Earnings (Loss) Per Share

Basic earnings (loss) per share ("EPS") is calculated in accordance with Accounting Standards Codification ("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:

	Years Ended December 31,		
	2017	2016	2015
		(in thousands)	
Net loss (numerator)	$ (85,236)	$ (61,706)	$ (5,030)
Weighted-average shares, in thousands (denominator)	137,180	136,667	125,592
Basic and diluted net loss per share	$ (0.62)	$ (0.45)	$ (0.04)

Achillion Pharmaceuticals, Inc.

Notes to Financial Statements—(Continued)
(in thousands, except per share amounts)

Potentially dilutive securities outstanding as of December 31, 2017, 2016 and 2015 are as follows:

	Years Ended December 31,		
	2017	2016	2015
	(in thousands)		
Stock Options	12,160	10,394	8,501
Warrants	21	2,833	2,833

5. Collaboration Arrangements

Janssen Pharmaceuticals, Inc.

On September 9, 2017, the Company received notice from Janssen of its termination, effective as of November 8, 2017, of the Collaboration and License Agreement between the Company and Janssen dated May 19, 2015, as amended (the "Janssen Agreement").

Under the terms of the Janssen Agreement, the Company granted Janssen exclusive worldwide rights to develop and commercialize products that contained one or more of the Company's drug candidates for the treatment of chronic hepatitis C virus, ("HCV"), namely odalasvir, a second-generation NS5A inhibitor, ACH-3422, a NS5B HCV polymerase inhibitor, and sovaprevir, a NS3/4A HCV protease inhibitor. In May 2015, the Company also entered into a parallel transaction with Janssen's affiliate, JJDC, Inc. ("JJDC") pursuant to which JJDC purchased 18,367 shares (the "Shares") of the Company's common stock at a price of $12.25 per share, for an aggregate purchase price of $225,000. In connection with the purchase of the Shares, the Company and JJDC also entered into an investor agreement (the "Investor Agreement") on July 1, 2015 governing specified rights and obligations of JJDC with respect to its ownership of the Shares.

Janssen terminated the Janssen Agreement under section 14.6 of the Janssen Agreement, which allows for unilateral termination at Janssen's discretion upon 60 days' written notice to the Company at any time prior to the submission of the first application for marketing approval for a licensed product in any of the major market countries specified in the Janssen Agreement. Pursuant to its notice of termination, Janssen informed the Company 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 the Company's HCV product candidates that it licensed to Janssen under the Janssen Agreement. Following the termination, all licenses granted by either party to the other under the Janssen Agreement terminated, except to the extent necessary to allow either party to perform any obligations or exercise rights that survive the termination.

Under the terms of the Janssen Agreement, the Company earned a $15,000 clinical milestone payment in December 2016 and would have been eligible to receive (1) up to an additional $100,000 of clinical milestone payments based upon the achievement of clinical enrollment and dosing in a phase III study, (2) up to an additional $290,000 of milestone payments based upon regulatory approvals and first commercial sale in specified territories, the majority of which related to regulatory approval and the first commercial sale in the United States, and (3) up to an additional $500,000 of milestone payments based upon achieving worldwide sales targets. The Company would also have been eligible to receive royalties on worldwide annual net sales of licensed products, if any, at tiered royalty rate percentages beginning in the mid-teens and rising to the low-twenties, subject to customary reductions. Janssen was to bear the future costs of worldwide development and commercialization of licensed products.

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Pursuant to the terms of the Janssen Agreement, the Company was required to provide technology transfer services related to the chemistry, manufacturing and know-how to Janssen for up to 180 days after the effective date. In accordance with ASC 605-25, "Revenue Recognition—Multiple-element arrangements," which provides guidance on accounting for multiple-element arrangements, including the determination of the units of accounting and allocation of total arrangement consideration, the Company identified all of the obligations at the inception of the Janssen Agreement. The significant obligations were determined to be the license and the technology transfer services. The Company determined that license and technology transfer services represented a single unit of accounting because they were not viewed to have standalone value. The only upfront amount received by the Company in exchange for the license and technology transfer services and the issuance of the Company's common stock was the $225,000. The Company determined that the amount received in excess of the fair value of the Company's common stock upon issuance of $66,122 was attributed to the license and technology services. The Company also determined that there was no discernable pattern in which the technology services would be provided during the 180 day period after the effective date. In accordance with ASC 605-10, "Revenue Recognition—Overall," the Company determined that straight-line attribution of the license and technology services revenues would be used to recognize revenue. As such, revenue of $66,122 was recorded during the year ended December 31, 2015 associated with this transaction.

Pursuant to the terms of the Investor Agreement, which remained in effect following the termination of the Janssen Agreement, the Shares were subject to a lock-up restriction, voting covenants and a standstill agreement, each of which expired on July 1, 2016. In February 2017, the Company entered into an agreement with JJDC (the "Lock-Up Agreement") pursuant to which the Shares became subject to a new lock-up restriction, which expired on the earlier of January 31, 2018, or the date that was sixty days after the first public announcement of top-line clinical results from Janssen's phase IIb OMEGA-1 clinical trial of JNJ-4178, a three drug combination for the treatment of HCV which contained odalasvir, one of the HCV drug candidates the Company had licensed to Janssen under the Janssen Agreement. On November 15, 2017, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Goldman Sachs & Co. LLC and Leerink Partners LLC, acting as representatives of the underwriters named therein, and JJDC, as selling stockholder, relating to an underwritten public offering (the "Offering") of the Shares of the Company's common stock, held by JJDC. The Shares were offered pursuant to a shelf registration that was declared effective on April 28, 2017. In connection with the Offering, the Company entered into a letter agreement (the "Letter Agreement"), dated November 14, 2017, with JJDC pursuant to which the Company and JJDC agreed, that effective upon execution and delivery of the Underwriting Agreement: (1) the Company agreed to release the restrictions on the disposition of the Shares by JJDC, which JJDC previously agreed to in the Lock-Up Agreement in connection with the filing of the shelf registration statement referred to above; (2) the Company and JJDC agreed to amend the investor agreement (the "Investor Agreement") that the Company and JJDC entered into on July 1, 2015 in connection with JJDC's acquisition of the Shares to provide that the Company would pay $2,900 of the aggregate underwriting discounts and commissions of the Offering, which was determined based on a calculation set forth in the Letter Agreement; and (3) the Company and JJDC agreed that, following the closing of the Offering, the Investor Agreement would terminate and be of no further force or effect.

Other Arrangements.

The Company also has license agreements with GCA Therapeutics, Ltd ("GCAT"), for elvucitabine, its nucleoside reverse transcriptase inhibitor for the treatment of both hepatitis B infection and human immunodeficiency virus infection and with Ora, Inc. ("ORA"), for the development and commercialization of ACH-702 delivered topically or locally. The Company does not believe that the milestones specified under these agreements are substantive as achievement of the milestones is based solely on the performance of GCAT and

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ORA and does not relate to any past or future performance by the Company. Because the Company has no performance obligations under these agreements, it intends to recognize revenue related to any milestone payment upon achievement of a milestone by GCAT or Ora.

6. Marketable Securities

The fair value of the Company's marketable securities of $287,089 and $314,215 as of December 31, 2017 and 2016, 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. There were no transfers between levels within the hierarchy during the years ended December 31, 2017 and 2016. 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 in other comprehensive income.

The unrealized (loss) gain from marketable securities was $(389), $151 and $(45) at December 31, 2017, 2016 and 2015, respectively.

As of 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:

	December 31, 2017				December 31, 2016			
	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value	Amortized Cost	Unrealized Gain	Unrealized (Loss)	Estimated Fair Value
Commercial Paper	$ 29,079	$ 9	(2)	$ 29,086	$ 96,891	$ 267	—	$ 97,158
Corporate Debt Securities	216,297	—	(324)	215,973	163,286	4	(129)	163,161
Government and Agency Securities	42,102	—	(72)	42,030	53,887	19	(10)	53,896
Total	$287,478	$ 9	(398)	$287,089	$314,064	$ 290	(139)	$314,215

The following additional table summarizes, by industry, the fair value of investments:

	As of December 31,	
	2017	2016
Government	42,030	53,896
Banking	74,884	86,844
Industrial	170,175	173,475
Total	$287,089	$314,215

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The following table summarizes the contractual maturities of the Company's investments:

	December 31, 2017	December 31, 2016
Mature in less than one year	$ 256,578	$ 286,558
Mature in one to five years	30,511	27,657
Total	$ 287,089	$ 314,215

7. Prepaid Expenses and Other Current Assets

A summary of prepaid expenses and other current assets is as follows:

	As of December 31,	
	2017	2016
Prepaid research and development costs	$1,599	$1,228
Tax credit receivable	275	410
Software and maintenance agreements	465	416
Interest receivable	1,260	1,010
Other prepaid expenses	205	396
Total	$3,804	$3,460

8. Fixed Assets, net

A summary of property and equipment is as follows:

	As of December 31,	
	2017	2016
Laboratory equipment	$ 4,277	$ 4,252
Office equipment	1,885	1,729
Leasehold improvements	4,706	4,598
Construction in process	8	33
	10,876	10,612
Less—accumulated depreciation and amortization	(8,060)	(7,133)
Total	$ 2,816	$ 3,479

Depreciation expense was $1,126, $955 and $693 for the years ended December 31, 2017, 2016 and 2015, respectively.

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9. Accrued Expenses and Other Long-Term Liabilities

Accrued expenses consist of the following:

	As of December 31,	
	2017	2016
Accrued compensation	$4,014	$3,810
Accrued research and development expenses	2,384	1,441
Accrued professional expenses	735	972
Other accrued expenses	328	544
Total	$7,461	$6,767

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

10. Capital Structure

Preferred Stock

At December 31, 2017, the Company had 5,000 authorized shares of undesignated preferred stock of which no shares were issued and outstanding.

Common Stock

At December 31, 2017, the Company had 200,000 authorized shares of $0.001 par value common stock of which 137,894 shares were issued and outstanding and 18,961 shares were reserved for future issuance.

Warrants

At December 31, 2017, there were 21 warrants outstanding with an exercise price of $4.68 and a remaining contractual life of 0.2 years.

11. Stock-Based Compensation

2006 Stock Incentive Plan

The Company's 2006 Stock Incentive Plan ("the 2006 Plan") was adopted by the Company's board of directors in May 2006, amended by its board of directors in September 2006, approved by its stockholders in September 2006 and became effective in October 2006, upon the closing of the Company's initial public offering. The Company originally reserved for issuance 750 shares of common stock under the 2006 Plan. In addition, the Plan contained an "evergreen" provision, which allowed for an annual increase in the number of shares available for issuance under the Plan on the first day of each fiscal year during the period beginning on the first day of fiscal year 2007 and ending on the second day of fiscal year 2010. Under the evergreen provision, the Company registered an additional 2,673 shares of common stock to be issued under the 2006 Plan.

On June 10, 2010, stockholders of the Company approved an amendment to the 2006 Plan to increase by 3,000 shares the number of shares of common stock reserved for issuance under the 2006 Plan from 3,423 shares to 6,423 shares.

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On June 5, 2012, stockholders of the Company approved an amendment to the 2006 Plan to increase by 7,000 shares the number of shares of common stock reserved for issuance under the 2006 Plan from 6,423 shares to 13,423 shares.

The 2006 Plan provided 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, and those of any subsidiaries, were eligible to receive awards under the 2006 Plan. The Company's board of directors administered the 2006 Plan.

Following the adoption of the 2015 Stock Incentive Plan, the Company no longer grants stock options or other awards under the 2006 Plan.

2015 Stock Incentive Plan

The Company's 2015 Stock Incentive Plan ("the 2015 Plan") was approved by the Company's stockholders in June 2015. The 2015 Plan replaced the Company's 2006 Plan. Upon the approval of the 2015 Plan by stockholders, the 2006 Plan terminated, and all then outstanding awards under the 2006 Plan remained in effect, but no additional awards will be made under the 2006 Plan. However, the terms of the 2006 Plan will continue to apply to awards previously granted under the 2006 Plan.

The 2015 Plan allows for the issuance of 6,900 new shares of common stock plus up to 1,894 shares of common stock that remained available for issuance under the previously approved 2006 Plan immediately prior to the effectiveness of the 2015 Plan, all of which shares rolled over and became available for issuance under the 2015 Plan upon its effectiveness. Solely to the extent that any of the 8,727 shares of common stock subject to awards that were issued and outstanding under the 2006 Plan immediately prior to the effectiveness of the 2015 Plan expire, terminate, are surrendered, cancelled or forfeited, such shares also will become available for the future grant of awards under the 2015 Plan. All of the foregoing share numbers are subject, in the case of incentive stock options, to any limitations under the Internal Revenue Code of 1986, as amended (the "Code"), and are also subject to adjustment upon stock splits, stock dividends, and other specified events. Certain sub-limitations apply to the shares available for issuance under the 2015 Plan. The 2015 Plan allows for the issuance of incentive stock options intended to qualify under Section 422 of the Code, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The maximum number of shares with respect to which awards may be granted to any participant under the 2015 Plan may not exceed 1,500 shares per fiscal year (subject to adjustment upon stock splits, stock dividends, and other specified events). The maximum aggregate number of shares with respect to which awards may be granted to directors who are not employees of the Company at the time of grant will be 10% of the maximum number of shares authorized for issuance under the 2015 Plan.

The 2015 Plan is administered by the Company's Board of Directors. 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.

Options granted under the Company's 2006 Stock Incentive Plan and the 2015 Stock Incentive Plan (the "Plans"), are exercisable for a period determined by the Company, but in no event longer than ten years from the date of the grant. Options generally vest over four years.

As of December 31, 2017, there were 5,189 shares available to be granted under the 2015 Plan.

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A summary of the status of the Company's stock option activity for the year ended December 31, 2017 is presented in the table and narrative below:

	2017	
	Options	Weighted Average Exercise Price
Outstanding at January 1, 2017	10,394	$ 7.04
Granted	3,055	4.10
Exercised	(14)	2.70
Forfeited	(801)	6.37
Cancelled	(474)	6.64
Outstanding at December 31, 2017	12,160	$ 6.37
Options exercisable at December 31, 2017	8,321	$ 6.63
Options vested and expected to vest at December 31, 2017	11,758	$ 6.37

The following table summarizes information about stock options outstanding at December 31, 2017:

	Options Outstanding			Options Vested	
Range of Exercise Prices	Number Outstanding	Weighted Average Remaining Contractual Life (Years)	Weighted Average Exercise Price	Number Vested	Weighted Average Exercise Price
$0.00 – $2.00	128	1.0	$ 1.05	128	$ 1.05
$2.01 – $4.00	3,360	4.3	3.08	3,195	3.07
$4.01 – $6.00	2,487	9.0	4.19	166	4.50
$6.01 – $8.00	3,526	6.1	7.49	2,581	7.48
$8.01 – $10.00	1,113	5.4	8.71	1,022	8.71
$10.01 – $12.00	134	6.7	10.50	93	10.55
$12.01 – $14.00	1,412	6.3	13.44	1,136	13.43
	12,160	6.1	$ 6.37	8,321	$ 6.63

As of December 31, 2017, the intrinsic value of the options outstanding was $258, of which $257 related to vested stock options and $1 related to unvested stock options. The intrinsic value for stock options is calculated based on the difference between the exercise prices of the underlying awards and the quoted stock price of the Company's common stock as of the reporting date.

The total intrinsic value of stock options exercised for the years ended December 31, 2017, 2016 and 2015 was $261, $193 and $5,302, respectively.

The weighted-average, grant-date fair value of options granted during the years ended December 31, 2017, 2016 and 2015 was $2.91, $5.56 and $6.66, respectively. The weighted-average, grant-date fair value of options vested at December 31, 2017, 2016 and 2015 was $4.92, $4.67 and $4.64, respectively.

The weighted average remaining contractual life is 4.9 years for options exercisable and 4.7 years for options vested and expected to vest.

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Stock-Based Compensation

Under the provisions of ASC 718, stock-based compensation cost is based on the fair value of the portion of stock-based awards that is ultimately expected to vest during the period. 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. Determining the fair value of stock-based awards at the grant date requires judgment, including estimating the expected term of stock options, the expected volatility of our stock and expected dividends. The Company also estimates forfeitures at the grant date and recognizes compensation costs for only those awards that are expected to vest. Judgment is required in estimating the number of stock-based awards that are expected to be forfeited. The Company bases its estimate of the expected term on historical data for similar stock option grants, and calculates volatility based on actual volatility for the expected term of the option.

The assumptions used to value options granted are as follows:

	For the Years Ended December 31,		
	2017	2016	2015
Expected term of option	6.0 years	6.0 – 6.25 years	6.25 years
Expected volatility	82% – 83%	81% – 84%	84% – 91%
Risk free interest rate	2.04 – 2.27%	1.15 – 2.09%	1.54 – 1.93%
Expected dividend yield	0%	0%	0%

Total compensation expense recorded in the accompanying statements of comprehensive loss associated with option grants made to employees for the years ended December 31, 2017, 2016 and 2015 was $10,479, $10,900 and $9,887, respectively. Total compensation expense recorded in the accompanying statements of comprehensive loss associated with option grants made to consultants for the years ended December 31, 2017, 2016 and 2015 was $0, $5 and $25, respectively.

The Company recorded no tax benefit related to these options as the Company is currently in a net operating loss position and maintains a full valuation allowance.

As of December 31, 2017, the total compensation cost related to options not yet recognized in the financial statements is approximately $12,312, net of estimated forfeitures, and the weighted average period over which it is expected to be recognized is 2.3 years.

Compensation expense related to option grants made to employees and consultants is included in research and development and general and administrative expense as follows:

	For the Years Ended December 31,		
	2017	2016	2015
Research and development	$ 4,408	$ 4,601	$ 4,346
General and administrative	6,071	6,304	5,567
Total	$ 10,479	$ 10,905	$ 9,913

2006 Employee Stock Purchase Plan

The Company established an Employee Stock Purchase Plan effective December 1, 2006 (the “2006 ESPP Plan”). Eligible employees can purchase common stock pursuant to payroll deductions at a price equal to 85% of

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the lower of the fair market value of the common stock at the beginning or end of each six-month offering period. The Company originally reserved for issuance 250 shares of common stock under the 2006 ESPP Plan. On June 10, 2010, stockholders of the Company approved an amendment to the 2006 ESPP Plan to increase by 250 shares the number of shares of common stock reserved for issuance under the 2006 ESPP Plan from 250 shares to 500 shares. On June 2, 2015, stockholders of the Company approved an amendment to the 2006 ESPP Plan to increase by 1,700 shares the number of shares of common stock reserved for issuance under the 2006 ESPP Plan from 500 to 2,200 shares.

The Company measures the fair value of issuances under the 2006 ESPP Plan using the Black-Scholes option pricing model at the end of each reporting period. The compensation cost for the 2006 ESPP Plan consists of the 15% of the grant date stock price discount and the fair value of the option features.

The Company recorded compensation cost related to the 2006 ESPP Plan of $94, $100 and $160 for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, there were 1,591 shares available for future issuance under the 2006 ESPP Plan.

The assumptions used to value options granted under the 2006 ESPP Plan are as follows:

	For the Years Ended December 31,		
	2017	2016	2015
Expected term of option	6 months	6 months	6 months
Expected volatility	58% – 73%	55% – 66%	57% – 88%
Risk free interest rate	0.05 – 1.3%	0.05 – 0.06%	0.07 – 0.08%
Expected dividend yield	0%	0%	0%

12. Other Income

In August 2015, a stockholder of the Company paid $8,944 to the Company relating to the disgorgement of short swing profits under Section 16(b) of the Securities Exchange Act.

13. Commitments and Contingencies

401(k) Retirement Plan

The Company has a 401(k) defined contribution retirement plan covering substantially all full-time employees. The Company currently matches employee contributions at a rate of $0.50 cents for each dollar contribution, up to 6% of salary deferrals. However, the decision to match any employee contributions is at the sole discretion of the Company. The Company made matching contributions of $415, $406 and $296 for the years ended December 31, 2017, 2016 and 2015, respectively.

Operating Leases

The Company's commitments consist of obligations under operating leases for its facilities and office equipment. The Company leases its operating facility located in New Haven, Connecticut. The lease agreement requires monthly lease payments through March 2020. The Company is recording the expense associated with the lease on a straight-line basis over the expected term of the lease and, as a result, has accrued $149 and $216 at December 31, 2017 and 2016, respectively.

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The future minimum annual lease payments under these operating leases at December 31, 2017 are as follows:

Year Ended December 31,	
2018	$ 925
2019	900
2020	222
Total	$2,047

Rent expense under operating leases was $811, $801 and $629 for the years ended December 31, 2017, 2016 and 2015, respectively.

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 December 31, 2017, there were no active matters.

14. Income Taxes

The Company uses an asset and liability approach for financial accounting and reporting of income taxes. Deferred tax assets and liabilities are determined based on temporary differences between financial reporting and tax basis of assets and liabilities and are measured by applying enacted rates and laws to taxable years in which differences are expected to be recovered or settled. Further, the effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that the rate changes.

The Company applies the provisions of ASC 740, *Income Taxes,* which prescribes a comprehensive model for how a company should recognize, measure, present, and disclose in its financial statements uncertain tax positions that the company has taken or expects to take on a tax return (including a decision whether to file or not file a return in a particular jurisdiction). The Company's financial statements reflect expected future tax consequences of such positions presuming the taxing authorities' full knowledge of the position and all relevant facts.

The Company does not have any interest or penalties accrued related to uncertain tax positions as it does not have any unrecognized tax benefits. In the event the Company determines that accrual of interest or penalties is necessary in the future, the amount will be presented as a component of income taxes.

On December 22, 2017, the President signed into law new legislation, known as the Tax Cuts and Jobs Act of 2017 (the "Tax Act"), that resulted in significant changes to the Internal Revenue Code of 1986, as amended. These changes include a federal statutory rate reduction from 35% to 21%, limitation of the deduction for net operating losses to 80% of taxable income while providing that the net operating loss carryovers for years after 2017 will not expire, limitation on the amount of research and development expenses deductible per year beginning in years after 2021, reduction of the Orphan Drug Credit from 50% to 25% of qualified clinical testing expenditures, increased limitations on certain executive compensation, elimination of the Corporate Alternative Minimum Tax, and modifying or repealing other business deductions and credits.

As a result of the Tax Act being signed into law, the Company recognized a provisional charge of $52,653 in the fourth quarter of 2017 related to the re-measurement of its U.S. deferred tax assets at the lower enacted corporate tax rate. Due to the history of net operating losses, the Company is in a full valuation allowance

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position. As a result, the additional tax expense due to the Tax Act was offset by an equal reduction to the valuation allowance, resulting in no net tax impact from the Tax Act to the overall financial condition and results of operations of the Company.

The income tax provision (benefit) consists of the following:

	As of December 31,		
	2017	2016	2015
Deferred:			
Federal and state	$ 15,506	$(23,232)	$ 699
Valuation allowance	(15,506)	23,232	(699)
Total deferred	$ —	$ —	$ —

A reconciliation of the statutory tax rates to the effective tax rates is as follows:

	Years Ended December 31,		
	2017	2016	2015
Federal statutory rate	(34.0)%	(34.0)%	(34.0)%
State tax, net of federal benefit	(5.0)	(5.0)	(5.0)
Other	(0.46)	0.06	0.52
Share-based compensation	0.35	0.80	2.84
Change in federal tax rate	61.77	—	—
Valuation allowance	(22.66)	38.14	35.64
	0%	0%	0%

Future tax benefits (deferred tax assets) related to temporary differences are as follows:

	As of December 31,	
	2017	2016
Gross deferred tax assets:		
Net operating losses	$ 115,009	$ 127,376
Tax credits (federal and state)	13,480	10,758
Share-based compensation	9,720	10,725
Other	282	24
	$ 138,491	$ 148,883
Less—valuation allowance	(138,491)	(148,883)
Net deferred tax asset	$ —	$ —

At December 31, 2017 and 2016, the Company had gross deferred income tax assets of approximately $138,491 and $148,883, respectively, which result primarily from net operating loss and tax credit carryforwards. ASC 740 requires that a valuation allowance be established when it is “more likely than not” that all or a portion of deferred tax assets will not be realized. A review of all positive and negative evidence is required when measuring the need for a valuation allowance. The Company’s cumulative loss from inception represents sufficient negative evidence to require a valuation allowance. The Company concluded that it is appropriate to maintain a full valuation allowance for its net deferred tax assets. Additionally, the Company intends to maintain a valuation allowance until sufficient positive evidence exists to support its reversal.

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At December 31, 2017, the Company had the following net operating loss and credit carryforwards available:

	As of December 31, 2017
Federal net operating loss carryforwards	$ 369,929
State net operating loss carryforwards	497,646
Federal research and development credit carryforwards	6,859
State research and development credit carryforwards	6,047

The Company's federal net operating loss carryforwards expire commencing in 2018 through 2037 and state net operating loss carryforwards which expire commencing in 2020 through 2037. The Company's federal research and development credit carryforwards expire commencing in 2028 through 2036. The Connecticut research and development carryforwards have no expiration period.

Deferred tax assets relating to tax benefits of employee stock options have been reduced to reflect exercises. Some exercises resulted in tax deductions in excess of previously recorded benefits based on the option value at the time of grant ("windfalls"). Prior to the adoption of ASU 2016-09 for the year ended December 31, 2017, the additional tax benefit associated with the windfall was not recognized until the deduction reduced taxes payable. Accordingly, the tax benefit of approximately $14,579 of the net operating loss carryforwards available but previously unrecognized, have been recognized upon adoption of ASU 2016-09. There was an offsetting adjustment to the valuation allowance equal to the tax benefit recognized for the windfall, resulting in no net tax impact upon adoption of ASU 2016-09.

Utilization of the net operating losses and research and development credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, or Section 382, due to changes in ownership of the Company that have occurred previously or that could occur in the future. The changes in ownership resulted in net operating loss carryforwards and research and development credits that the Company expects to expire unutilized and thus are not included in gross deferred tax assets disclosed above. The Company will continue to update its analysis of ownership changes and the potential limitations on its deferred tax assets.

The federal and state tax authorities could challenge tax positions taken by the Company for the periods for which there are open tax years. Years subject to audit are years in which unused net operating losses were generated that remain open by the statute of limitations. The Company is open to challenge for the periods of 2006 through 2017 in federal and the State of Connecticut jurisdictions.

The Company did not have any unrecognized tax benefits as of December 31, 2017 and 2016.

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 credits at a rate of 65% of the annual research and development credit, as defined. The Company records the benefit for the estimated proceeds from the exchange as a reduction of research and development expenditures.

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15. Related Party Transactions

Nicole Vitullo

In connection with Domain Associates, LLC's ("Domain") agreement to invest in the Company, the board of directors of the Company elected Nicole Vitullo of Domain as a Class II member of the board of directors on September 30, 2010 to serve until her successor is duly elected and qualified. Ms. Vitullo is a partner at Domain.

In August 2010, Domain purchased 8,032 shares of common stock and warrants to purchase 2,811 shares of common stock for an aggregate purchase price of $20.4 million.

In August 2017, Domain exercised the 2,811 warrants purchased in August 2010 by means of a cashless exercise of the warrants, resulting in the issuance of 1,084 shares of common stock.

As of December 31, 2017, Domain was the beneficial owner of approximately 2.5% of the Company's total issued and outstanding shares of common stock.

16. Unaudited Quarterly Results

The following tables summarize unaudited quarterly financial data for the years ended December 31, 2017 and 2016. This data has been derived from unaudited financial statements that, in the Company's opinion, include all adjustments necessary for a fair statement of such information. The operating results for any quarter are not necessarily indicative of results for any future period.

	2017 Quarters			
	First	Second	Third	Fourth
Total operating revenue	$ —	$ —	$ —	$ —
Total operating expenses	21,143	23,616	20,463	24,354
Net income (loss)	(20,152)	(22,543)	(19,338)	(23,203)
Net income (loss) per share—basic and diluted	$ (0.15)	$ (0.16)	$ (0.14)	$ (0.17)
Weighted average number of shares outstanding—basic and diluted	136,722	136,736	137,375	137,870

	2016 Quarters			
	First	Second	Third	Fourth (1)
Total operating revenue	$ —	$ —	$ —	$ 15,000
Total operating expenses	18,718	19,309	21,549	20,289
Net income (loss)	(18,054)	(18,493)	(20,730)	(4,429)
Net income (loss) per share—basic and diluted	$ (0.13)	$ (0.14)	$ (0.15)	$ (0.03)
Weighted average number of shares outstanding—basic and diluted	136,640	136,680	136,681	136,693

(1) In May 2015, the Company entered into an exclusive collaboration and license agreement with Janssen, and its affiliate, Johnson & Johnson Innovation-JJDC, Inc., or JJDC, which we refer to as the Janssen Agreement for the further clinical advancement of a portfolio of antivirals the Company discovered and developed for the treatment of HCV. In addition, upon the closing of the transactions contemplated by the Janssen Agreement, the Company entered into a stock purchase agreement with JJDC. Pursuant to the JJDC Stock Purchase Agreement, on July 1, 2015, the Company issued 18,367 shares of common stock to JJDC at a price of $12.25 per share for

an aggregate purchase price of $225,000. The Company recorded revenue of $66,122 during the year ended December 31, 2015 associated with this transaction. The Company also recorded revenue of $15,000 during the year ended December 31, 2016 related to the achievement of a clinical enrollment milestone under the Janssen Agreement. On September 9, 2017, the Company received notice from Janssen of Janssen's termination of the Janssen Agreement effective November 8, 2017. As a result of the termination of the Janssen Agreement, the Company will not receive any future milestone-based or royalty payments under the agreement. Also refer to footnote 5.

17. Subsequent Events

In February 2018, the Company implemented a restructuring plan that will reduce employee headcount by approximately 20% to approximately 70 employees in March 2018. 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 and late-stage preclinical compounds. The Company assessed the staffing levels required to accomplish its revised strategic goals and determined to reduce its staff across several functional areas.

In connection with this reduction, the Company offered individuals whose employment was terminated a severance package that included severance pay, continuation of benefits and outplacement services. The Company will recognize expense relating to the restructuring in the first quarter of 2018 and estimates that the costs will be approximately $1,500.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (Nos. 333-206276, 333-183152, 333-168902, 333-158241, 333-149729, 333-141661 and 333-138984) and Form S-3 (No. 333-216197) of Achillion Pharmaceuticals, Inc. of our report dated February 22, 2018 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Hartford, Connecticut
February 22, 2018

EXHIBIT 31.1

Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Milind S. Deshpande, certify that:

1. I have reviewed this Annual Report on Form 10-K of Achillion Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ MILIND S. DESHPANDE

Milind S. Deshpande
Chief Executive Officer

Dated: February 22, 2018

EXHIBIT 31.2

Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002

I, Mary Kay Fenton certify that:

1. I have reviewed this Annual Report on Form 10-K of Achillion Pharmaceuticals, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ MARY KAY FENTON

Mary Kay Fenton
Chief Financial Officer

Date: February 22, 2018

EXHIBIT 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Achillion Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Milind S. Deshpande, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350 as adopted by Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 22, 2018

/s/ MILIND S. DESHPANDE

Milind S. Deshpande
Chief Executive Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

EXHIBIT 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Achillion Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Mary Kay Fenton, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350 as adopted by Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 22, 2018

/s/ MARY KAY FENTON

Mary Kay Fenton
Chief Financial Officer

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.