Annual Report 2015


ACHILLION

RESEARCH REALIZED

# Research Realized

## A Letter to Our Shareholders

April 2016

Dear Shareholder,

I am pleased to provide to you an update on Achillion's progress during 2015. Throughout the year, our team remained committed to our mission of leveraging our strengths across the drug discovery and development continuum to provide better treatments for people with serious diseases.

During 2015, we achieved two key milestones with that mission in mind.

We announced, in May 2015, a worldwide collaboration with Janssen Pharmaceuticals, Inc. (Janssen), a Johnson & Johnson company, for HCV. The Achillion-Janssen collaboration creates a combined pipeline that has the potential to provide more effective and shorter duration regimens for HCV patients. Importantly, our compounds gained access to the global development and commercial infrastructure at Janssen.

Under the agreement, we provided Janssen with an exclusive, worldwide license to develop and, upon regulatory approval, commercialize HCV products and regimens containing one or more of the HCV assets discovered by Achillion, including odalasvir (also known as ACH-3102), ACH-3422, and sovaprevir. Assuming successful development, and commercialization, Achillion is eligible to receive up to $905 million in clinical, regulatory and commercialization milestone payments. Achillion is also eligible to receive tiered percentage royalties, ranging from the mid-teens to low twenties, on total worldwide revenue. Janssen is responsible for all development and commercialization costs within the collaboration.

Since the start of the collaboration, Janssen has advanced combination all-oral regimens containing odalasvir into a phase 2a trial aiming to establish the safety, pharmacokinetics, and efficacy following dosing durations of eight weeks or shorter for patients with treatment-naïve genotype 1 HCV. Achillion looks forward to reporting top-line results during the first half of 2016, and anticipates that the full study results will be presented at a major medical conference.

The second major achievement during 2015 was the regulatory submission enabling the advancement of ACH-4471, our first orally-administered, small molecule inhibitor of complement factor D for the treatment of rare diseases, toward clinical development.

The complement system is an integral part of the immune system and consists of three pathways: the lectin pathway, the classical pathway, and the alternative pathway. We have chosen to focus on the alternative pathway, as several diseases with high unmet medical need are believed to be associated with its dysregulation or dysfunction. These diseases include paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), C3 glomerulopathies, and dry age-related macular degeneration (AMD). In PNH specifically, the disease is characterized by a genetic mutation that results in a deficiency of complement regulatory proteins, resulting in red blood cells that are susceptible to destruction by the alternative pathway.

Within the alternative pathway, our focus is on factor D, an essential enzyme that plays an important role in amplifying the immune response. Using our internal structural biology and computational chemistry expertise, we have generated 18 high resolution x-ray structures of our factor D inhibitor compounds, and synthesized over 1,400 small molecule factor D inhibitor compounds. Our deep collection of potent factor D molecules allows us to select specific molecules with the right physicochemical properties, not only for oral systemic administration, but also for ophthalmic administration, for diseases like dry AMD, as well as for respiratory indications, where compounds are given by inhalation for diseases such as COPD.

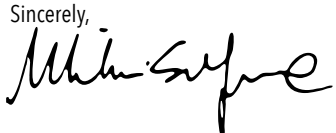
The first of Achillion's factor D inhibitors, ACH-4471, advanced into clinical development in February 2016. The preclinical profile for this compound includes good potency and oral bioavailability, as well as high specificity for factor D. In vitro research conducted by Achillion has shown that ACH-4471 has the ability to inhibit the alternative pathway leading to suppression of membrane attack complex. Membrane attack complexes have been implicated in the destruction of red blood cells in PNH patients. ACH-4471 has also been shown in in vitro studies to prevent C3 deposition on PNH red blood cells, which we believe could lead to improvement in suppression of extra vascular hemolysis observed in a significant number of PNH patients. To date, our on-going clinical and non-clinical studies support further clinical development of ACH-4471.

The initial phase 1 study for ACH-4471 is a single ascending dose study in healthy volunteers in which we are assessing safety, tolerability, and the pharmacokinetic and pharmacodynamic characteristics of the compound. In this study, our objective is to demonstrate inhibition of the complement alternative pathway. We anticipate reporting interim results from this study during the second quarter of 2016. We also plan to initiate a multiple-ascending dose trial of ACH-4471 and plan to report interim results from that trial during the third quarter of 2016. Results from both of these first-in-human trials will position us to begin a phase 2 trial for patients with PNH during the second half of this year with interim results anticipated by year-end.

With the establishment of a global collaboration with Janssen for HCV combined with the significant progress made with ACH-4471, I believe 2015 was a truly transformational year for the Company. Furthermore, Achillion ended the year with a strong balance sheet, including approximately $460 million in cash, cash equivalents and marketable securities, which we expect will advance our internally developed portfolio through clinical development and toward commercialization.

I believe Achillion is rapidly advancing towards its goal of becoming a fully-integrated commercial pharmaceutical company. We are committed to innovative science, novel approaches to treat rare diseases, and most of all, bringing life-saving medicines to patients. We thank you for your continued support.

Sincerely,



**Milind Deshpande, Ph.D.**
President and Chief Executive Officer


# 2015 FORM 10-K

# 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, 2015**

**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, or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

| | |
|---|---|
| Large accelerated filer ☒ | Accelerated filer ☐ |
| Non-accelerated filer ☐ (Do not check if smaller reporting company) | Smaller reporting company ☐ |

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

The aggregate market value of the voting stock held by non-affiliates of the Registrant on June 30, 2015 was approximately $1,014,028,559 based on the closing price of such stock as reported by the NASDAQ Global Select Market on June 30, 2015.

As of February 19, 2016, the registrant had 136,640,019 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, 2015, a definitive proxy statement for our annual meeting of stockholders to be held on May 25, 2016. 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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## PART I

*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 to the effect that we "believe," "expect," "anticipate," "plan," "target," "intend" and similar expressions) should be considered forward-looking statements. 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, and other risk factors. 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.*

### 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 infectious and complement-mediated diseases.

Our current 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 complement system. The complement pathway 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 will initially 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 ultra-rare orphan conditions such as paroxysmal nocturnal hemoglobinuria, or PNH, as well as more prevalent indications such as dry age-related macular degeneration, or dry AMD, and chronic obstructive pulmonary disease, or COPD.

We anticipate that our complement factor D inhibitor compounds may play a role in treating patients with PNH, including patients who have suboptimal response to, or who fail to respond to, currently approved treatments for PNH, atypical hemolytic uremic syndrome, or aHUS, myasthenia gravis, and dry AMD, as well as other therapeutic applications. Our compounds have demonstrated complete suppression of the complement alternative pathway with a single oral dose of our inhibitors in non-human primates. We have initiated a first-in-human phase I clinical trial for our first complement factor D inhibitor, ACH-4471, to assess safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD. We plan to advance this compound to potentially treat patients with PNH and possibly, one additional systemic ultra-rare disease. We may advance other factor D inhibitors for other indications after further characterization.

We also have a collaboration with Janssen Pharmaceuticals, Inc., or Janssen, the pharmaceutical subsidiary of Johnson & Johnson Inc., under which we have granted to Janssen exclusive worldwide rights to develop and commercialize a portfolio of antiviral drug candidates we discovered and developed for the treatment of chronic hepatitis C virus, or HCV, infection in exchange for specified milestone payments and an equity investment in us.

We also intend to continue to leverage our extensive expertise in structural biology and synthetic chemistry to quickly and efficiently discover and develop additional small molecule compounds to meet other significant

unmet medical needs. We believe our drug discovery capabilities will allow us to further expand our drug candidate portfolio, providing us with strong growth potential and, over time, reducing our reliance on the success of any single drug candidate. Our research team has successfully discovered and advanced multiple compounds into clinical development including sovaprevir, odalasvir, also known as ACH-3102, and ACH-3422 in our HCV program, all of which we have licensed to Janssen, and ACH-4471 in our complement factor D inhibitor program.

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 incurred approximately $56.6 million, $53.5 million and $46.7 million in research and development costs for the years ended December 31, 2015, 2014, and 2013, respectively.

**Our Strategy**

Our objective is to become a leading biopharmaceutical company focused on discovering, developing and commercializing small molecule therapies that specifically target the alternative pathway of the human complement system while continuing our interests in HCV through collaboration with our partner, Janssen. Specifically, our near-term strategy includes the following efforts:

- ***Advance our Complement Factor D Portfolio.***
  - ***Advance ACH-4471 in clinical development for rare diseases.*** ACH-4471 entered phase I clinical development in the first quarter of 2016 in a single-ascending dose trial designed to understand the safety and pharmacokinetics of the drug candidate in healthy volunteer subjects. We anticipate next moving into a multiple-ascending dose phase I clinical trial, and in the second half of 2016, into patients with PNH and one additional alternative pathway-mediated rare disease.
  - ***Advance back-up series of compounds for rare diseases.*** We have synthesized and characterized a portfolio of over 1,200 factor D compounds. From this robust program we intend to select back-up compounds for ACH-4471 also for treatment of complement-mediated rare diseases. We plan to nominate at least one additional compound in 2016 for advancement towards clinical trials.
  - ***Discover and develop additional Complement factor D compounds for other complement-mediated disease indications.*** Excessive activation of alternative pathway in the complement system has been implicated in multiple therapeutic areas outside of rare diseases including dry AMD and COPD. We plan to continue to characterize our compounds for potential clinical development in ophthalmic and respiratory indications.
- ***Collaborate with Janssen in HCV.***

In order to access the worldwide development and commercialization expertise of a major pharmaceutical organization to facilitate the advancement of our HCV drug candidate portfolio, we entered into a collaboration with Janssen in June 2015. Despite the fact that Janssen has the deciding vote on collaborative matters, we will seek to maximize the value of this collaboration by leveraging our participation in a joint steering committee, or JSC, with Janssen management for the clinical development of a safe, effective, short-duration combination regimen to treat chronic HCV infection.

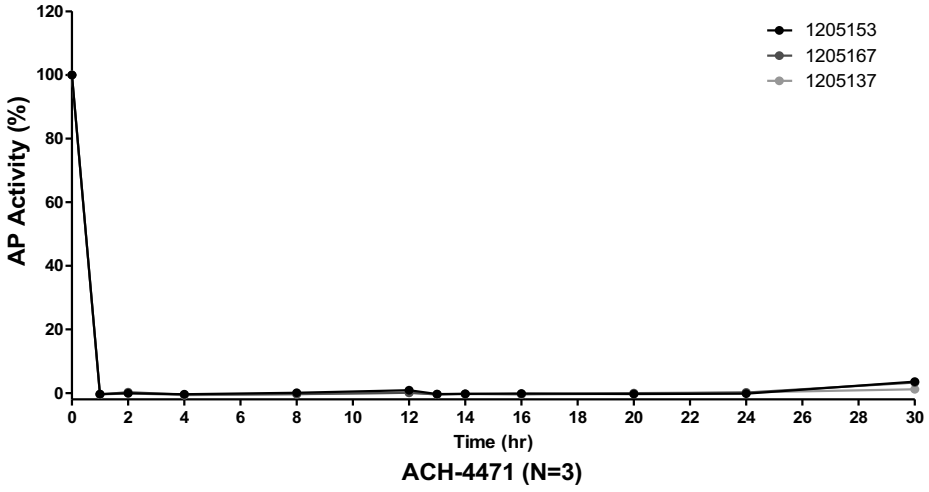
**Our Programs**

Our expertise in structural biology and medicinal chemistry, coupled with our work in antimicrobial discovery research, led us to consider how the immune system plays a part in inhibiting pathogens in the body. This research led us to work in complement system inhibition.

The first clinical compound from our complement inhibitor platform is ACH-4471, which entered phase I clinical development in healthy volunteers in the first quarter of 2016. ACH-4471 is designed to target and inhibit complement factor D, a critical protein in the amplification loop within the alternative pathway of the complement system.

***ACH-4471.*** ACH-4471 is a potent and specific inhibitor of factor D, which has demonstrated complete suppression of the complement alternative pathway with a single oral dose in non-human primates. Further, the compound has demonstrated dose-proportional *in vitro* suppression of red blood cell destruction, or hemolysis, in plasma samples from PNH patients and similar suppression of cell killing in serum from patients with aHUS. ACH-4471 has exhibited the following characteristics in preclinical studies:

- *Potency*. ACH-4471 is highly specific for inhibition of factor D, a protein critical to the amplification of the complement system. In oral administration of ACH-4471 in non-human primates at a dose of 200mg/kg, we noted complete and sustained suppression of alternate pathway activity as shown graphically below.




  In preclinical studies, the compound has demonstrated dose-dependent inhibition of hemolysis and deposit of C3, a complement protein, on blood cells, which can lead to further hemolysis. It has been shown *in vitro* to efficiently block the alternative pathway of the complement system in both PNH and aHUS patients.

- *Pharmacokinetics and Metabolism*. Pharmacokinetic results and activity in preclinical studies suggest that ACH-4471 should be explored in clinical development for potential oral dosing once or twice daily.

- *Safety*. In animal studies we completed in rats for fourteen days and in dogs for twenty eight days, ACH-4471 demonstrated high safety margins with minimal dose-related effects even at high drug exposures. Three month toxicology studies in both rat and dog are on-going.

***Additional Factor D Inhibitors.*** Our research team has synthesized over 1,200 factor D inhibitor compounds from which we plan to select one or more development candidates to advance into the clinic. Our candidate library contains compounds with various pharmacophysical properties that may be advantageous for various routes of administration. Within the library, we are assessing not only additional drug candidates for oral systemic administration but potential candidates for ophthalmic administration via intravitreal injection and for respiratory indications with an inhaled formulation.

**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.

Three biochemical pathways activate the complement system: 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 amplification, or amplification loop. 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 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, the circulatory system. It is estimated that PNH affects 8,000 to 10,000 people in North America and Western Europe. The chronic hemolysis in patients with PNH may be associated with life-threatening thromboses, 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 eculizamab, or Soliris®, 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 $2.6 billion in 2015.

**Benefits of Our Approach**

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

***Targeting Factor D***

In blood serum, factor D has the lowest concentration of all the complement proteins, including targets of other therapies including C5 and C3. It is therefore limited and 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 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 indiscriminant activation of the complement system.

***Small Molecule Inhibitors***

All our complement factor D inhibitor compounds for the potential treatment of rare and ultra-diseases are orally-available small molecule compounds. This is in contrast to biologic compounds that require intravenous or subcutaneous dosing. Other therapies for both PNH and aHUS are dosed intravenously, requiring frequent hospital visits. We believe that oral dosing can provide a more convenient regimen for patients and their care-givers. In addition, small molecule compounds may have dosing advantages in other complement-mediated diseases such as dry AMD and COPD.

***Ability to Treat Patients with Suboptimal Response to Current Therapy***

It is estimated that approximately 30% 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. We believe that our factor D inhibitor has the potential to prevent or reduce the accumulation of C3 fragments such that additional or higher level dosing can be avoided.

**Our Collaboration with Janssen Pharmaceuticals, Inc.**

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. Under the Janssen Agreement, we granted Janssen exclusive worldwide rights to develop and commercialize products that contain 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. The Janssen Agreement became effective June 29, 2015 upon the early termination of applicable waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, or the HSR Act. In addition, upon the closing of the transactions contemplated by the Janssen Agreement, we entered into a stock purchase agreement with JJDC, which we refer to as the JJDC stock purchase agreement. Pursuant to the JJDC stock purchase agreement, on July 1, 2015, we issued 18,367,346 shares of our common stock to JJDC at a price of $12.25 per share for an aggregate purchase price of $225 million. The JJDC stock purchase agreement became effective on July 1, 2015.

Under the terms of the Janssen Agreement, we are eligible to receive (1) up to $115 million of milestone payments based upon achievement of clinical enrollment and dosing in specified studies, substantially all of which is related to dosing in one study, (2) up to an additional $290 million of milestone payments based upon regulatory approvals and first commercial sale in specified territories, the majority of which relates to regulatory approval and the first commercial sale in the U.S., and (3) up to an additional $500 million of milestone payments based upon achieving worldwide sales targets. We are also 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. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after such first commercial sale if there is no such exclusivity. Janssen will bear the future costs of worldwide development and commercialization of licensed products, subject to specified exceptions relating to our ongoing studies and technology transfer.

Under the Janssen Agreement, Janssen has agreed to use commercially reasonable efforts to develop a specified licensed product toward regulatory approval in several specified major market countries and, if such development is successful, to seek regulatory approval in such countries. Following regulatory approval (and

pricing and reimbursement approvals, as applicable) of any licensed product in any of the major market countries, Janssen will use commercially reasonable efforts during the applicable royalty term to commercialize such licensed product in each major market country where it has been approved.

The term of the Janssen Agreement will continue, unless earlier terminated, until expiration of the royalty term for licensed products or all payment obligations thereunder.

Janssen may terminate the Janssen Agreement upon sixty days written notice to us at any time prior to submission of the first application for marketing approval for a licensed product in any of the specified major market countries. Janssen may also terminate the Janssen Agreement under specified circumstances relating to the safety or regulatory approvability of a licensed product. Either we or Janssen may terminate the Janssen Agreement if the other party is in material breach of the agreement and fails to cure such breach within specified cure periods. Either we or Janssen may terminate the Janssen Agreement in the event of specified insolvency events involving the other party. Upon any early termination, rights to our licensed drug candidates will revert to us.

In connection with the closing of the transactions contemplated by the JJDC stock purchase agreement, we and JJDC entered into an Investor Agreement on July 1, 2015, which we refer to as the Investor Agreement. Pursuant to the terms of the Investor Agreement the shares of common stock that we issued and sold to JJDC are subject to lock-up restrictions and voting arrangements. In addition, there are specified limitations on JJDC's ability to acquire additional shares of our common stock. We have also agreed to provide JJDC with certain "piggyback" registration rights such that for the seven year period following the expiration of the lock-up, subject to specified conditions, whenever we propose to register shares of our common stock for our own account, JJDC will have the right to include some or all of the shares it acquired from us pursuant to the JJDC stock purchase agreement in such registration.

Pursuant to the Janssen Agreement, the JSC consisting of three members from each of Janssen and our company will provide strategic guidance for the joint HCV program. If the JSC fails to reach a unanimous decision on a matter within its authority, the matter shall be referred to the applicable executive officers of Janssen and our company who shall attempt to reach a mutual decision. If the executive officers cannot reach a mutual decision, then Janssen has the deciding vote with regard to such matter.

We established our HCV drug candidate pipeline entirely through our internal discovery capabilities. Through these efforts, we identified and developed a portfolio of drug candidates including odalasvir, ACH-3422 and sovaprevir. The following compounds from our discovery and development efforts are now licensed for further development to Janssen:

- ***Odalasvir, a NS5A Inhibitor.*** We completed three phase IIa clinical trials with odalasvir including the -007 trial with sovaprevir, the -005 study, which examined the use of odalasvir with ribavirin alone, and the Proxy Doublet study which examined the use of odalasvir in combination with sofosbuvir, a nucleotide NS5B polymerase inhibitor marketed by Gilead Sciences, Inc., or Gilead, under the brand name Sovaldi®. HCV patients treated for both eight weeks and six weeks with the combination of odalasvir and sofosbuvir achieved 100% SVR24, or sustained viral response 24 weeks after cessation of therapy, demonstrating the differentiation of odalasvir within the NS5A class. Based upon clinical data presented at global medical meetings by both us and others, we believe odalasvir is the best-in-class NS5A inhibitor. *In vitro*, odalasvir demonstrated potency at picomolar concentrations in both genotypes 1a and 1b, the genotypes most prevalent in the United States. Other NS5A inhibitors have been challenged to show continued potency against the difficult-to-treat genotype 1a. Odalasvir has also demonstrated activity against all other known genotypes (2, 3, 4, 5 and 6) and has operated synergistically with both NS3 protease and NS5B polymerase inhibitors in *in vitro* studies. We believe odalasvir offers significant benefits, including.
    - *Virology*. Odalasvir is highly specific for inhibition of the NS5A non-structural protein of the hepatitis C virus necessary for viral replication. In clinical studies, the compound has

demonstrated robust antiviral activity as a single agent, and in combination with ribavirin and sofosbuvir, even in the presence of pre-existing resistance mutations, odalasvir has demonstrated rapid viral load reduction in HCV patients. To date, in both clinical and laboratory testing, genotype 1b patients treated with odalasvir have not generated any resistance mutations in the face of treatment.

- *Pharmacokinetics and Metabolism*. Pharmacokinetic results and activity in clinical studies indicate that odalasvir can be dosed once daily and has a low potential for drug-drug interactions, or DDI, based on multiple DDI studies we have conducted.
- *Safety*. In animal studies completed in two species for periods of up to three months, odalasvir demonstrated high safety margins with minimal dose-related effects even at high drug exposures.

- ***ACH-3422, a NS5B Nucleotide Polymerase Inhibitor.*** ACH-3422 has demonstrated excellent potency and was well-tolerated in a phase Ib proof of concept study in which HCV patients receiving a once-daily 700mg dose of ACH-3422 for 14 days demonstrated mean maximal viral load reduction of 4.6 $\log_{10}$.
- ***Sovaprevir, a NS3/4A Protease Inhibitor.*** We have completed a phase II clinical trial that evaluated 12 weeks of treatment consisting of sovaprevir and our NS5A inhibitor, odalasvir, with ribavirin for the treatment of genotype 1 HCV (the -007 trial). In this trial, genotype 1b patients achieved 100% SVR24; however, in genotype 1a patients, the combination regimen results were suboptimal.

In October 2015, we announced that Janssen had initiated phase IIa clinical testing of a triple combination regimen consisting of Olysio®, a protease inhibitor marketed by Janssen, AL-335, a nucleotide polymerase inhibitor in clinical development by Janssen, and odalasvir. The trial will evaluate the safety, pharmacokinetics and efficacy of the combination treatment in patients with genotype 1 chronic hepatitis C virus (HCV). Based on information we have been provided by Janssen and the JSC, we anticipate that this phase IIa trial may be completed in 2016 with interim results available in the first half of 2016.

**The HCV Market**

The hepatitis-C virus is a common cause of viral hepatitis, which leads to inflammation of the liver. HCV infection is contracted by transmission through the blood of an infected person. Hepatitis due to HCV can result in an acute process in which a person is affected for only several months and then the virus is cleared from the body. However, the Department of Health and Human Services Centers for Disease Control, or CDC, estimates that 70% to 85% of newly infected individuals become chronically infected following exposure. HCV disease progression then occurs over a period of 20 to 30 years during which patients are generally asymptomatic, meaning they exhibit no symptoms of the disease, until they experience late-stage disease. Chronic hepatitis can lead to permanent liver damage, which can result in the development of liver cancer, liver failure or death. Estimates by the World Health Organization indicate that approximately 130 million to 150 million individuals worldwide are chronically infected with HCV.

The HCV market has seen significant change in recent years, notably with the 2011-2013 introductions of the first directly acting antivirals (DAAs)—protease inhibitors boceprevir (Victrelis®), telaprevir (Incivek®), simeprevir (Olysio®), and nucleotide polymerase inhibitor, sofosbuvir (Sovaldi®). These were first approved for treatment of patients with HCV genotype 1 in combination with pegylated interferon and ribavirin. Sofosbuvir was also approved for use with ribavirin alone for use in treatment of patients with HCV genotype 2. In 2014, all-oral combination regimens entered the market including the combination of sofosbuvir and ledipasvir (Harvoni®) and the ombitasvir/paritaprevir/ritonavir/dasabuvir/ribavirin combination (Viekira Pak™). In 2016, the oral combination of elbasvir/grazoprevir (Zepatier) also entered the HCV market. These treatment regimens for HCV offer improved SVR rates for patients of the appropriate genotype, who do not have base-line resistant viral variants, and who can tolerate the combination therapy. Sales for marketed HCV regimens were reported at approximately $23 billion in 2015, including sales of boceprevir (Victrelis®), telaprevir (Incivek®) sofosbuvir

(Sovaldi®) and sofosbuvir/ledipasvir (Harvoni™) by Gilead and Viekira Pak™ by Abbvie. Even though the number of patients treated for HCV is anticipated to peak in 2016 through 2020, and competitive pricing may result from the introduction of all-oral combination regimens with broad genotypic coverage in 2015 and beyond, the HCV DAA market is expected to exceed $15 billion annually for the next several years in the combined markets of the United States, the European Union and Japan.

Despite recent improvements in the treatment landscape for HCV infected patients, there remains a goal for a new HCV therapy that addresses the needs of a broader range of HCV patients, both across the spectrum of HCV genotypes 1—6, and across varying stages of liver disease, and that shortens the duration of treatment. We believe our collaboration with Janssen can provide a combination regimen that contains our NS5A inhibitor, odalasvir, in combination with other agents that can effectively address these goals.

**Our Drug Discovery Programs and Capabilities**

To date we have successfully advanced eight drug candidates into human clinical trials, with two additional drug candidates that we advanced into late-stage preclinical studies. We discovered nine of these ten drug candidates in house by applying our expertise in biology and synthetic chemistry. We intend to continue to capitalize on our internal drug discovery and development capabilities to expand our drug candidate portfolio.

From early lead identification through clinical candidate selection, we have coupled our knowledge base in genomic replication targets with an integrated drug discovery infrastructure to aid in the advancement of our discovery programs.

***Target Selection and Assay Development***

We are focused on addressing unmet medical needs with an emphasis on inhibiting essential proteins or enzymes with small molecule inhibitors. We select targets for our drug discovery programs based upon the relevance of the target to key steps within the biological system, our ability to develop appropriate assays for early assessment of potency, selectivity and safety and our ability to identify small molecules that can be optimized within a reasonable time period to become drug candidates.

***Compound Synthesis, Hit Identification and Lead Optimization***

Our focused compound library contains a diverse set of molecules that have been synthesized for specific biological targets. We have developed the following tools that enable us to manage our compounds efficiently and advance our programs:

- AACP (Achillion Automated Chemistry Platform) is a proprietary software that facilitates synthesis of thousands of small molecules in parallel by automating several cumbersome steps involved;
- CART (Compound Acquisition and Repository Tracking) streamlines our scientists' ability to select and acquire compounds for lead identification and optimization;
- CHEM-ACH is a data mining software that allows analysis of our proprietary compounds and their biological activities. Such analysis helps in studying the structure-activity relationships and designing and synthesizing compounds for lead optimization;
- CIDM (Competitive Intelligence & Data Mining) is a web application. It analyzes publicly available information to display competitive information including clinical and preclinical development activities, intellectual property and scientific literature;
- ComplementWiki is an in-house database of ongoing and completed complement- related drug development and clinical trial designs and results. It also has an in-house developed, user friendly interface for accessing and analyzing this data;

- HCVWiki is an in-house database of ongoing and completed HCV therapy clinical trial designs and results. It also has an in-house developed, user friendly interface for accessing and analyzing this data; and
- PSTS (Preclinical Study Tracking System) is a web interface which is used for accessing the details of our preclinical studies. It allows scientists to enter, modify, and query preclinical study documents.

***Preclinical Candidate Selection***

A cornerstone of our approach to drug discovery and development is the early assessment of the drug-like properties associated with optimized lead compounds. Potency and activity against a given target are necessary but not sufficient predictors of eventual successful clinical development of a new drug. In order to perform an early assessment of the potential for successful development, prior to progression of a compound into late-stage preclinical studies in support of clinical trials, we rigorously evaluate compounds in numerous tests relating to safety, metabolism, pharmacokinetic properties and physical properties associated with the feasibility for an oral formulation.

**Competition**

The development and commercialization of new drug products is highly competitive. We expect that we, our collaborators 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 the key complement-mediated disease indications. For example, Alexion's eculizumab (Soliris®) is a marketed therapy for the treatment of PNH and aHUS. Akari, Alexion, Alnylam, Amyndas, Apellis, Bio Cryst, Omeros, Ra Pharma and True North have complement factor inhibitor therapies in development for other hematologic diseases. Additionally, Genentech is developing an anti-factor D antibody treatment for dry AMD. Novartis also has intellectual property rights in the complement area. In the HCV market, there are a number of pharmaceutical companies that currently market and sell products for HCV or are pursuing the development of drug candidates for HCV including Abbvie Pharmaceuticals, Enanta, Gilead Sciences, Merck and Regulus Therapeutics.

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 current or future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we or any current or future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any current or 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.

Our complement inhibitor patent portfolio currently includes a number of pending U.S. provisional and non-provisional applications as well as eight international applications filed under the Patent Cooperation Treaty, referred to as the PCT. These patents and patent applications, if issued, will expire on various dates between 2035 and 2036. The patent applications contain claims directed to classes of compounds, methods of use, mechanisms of action, and research assays.

In 2015, we entered into an exclusive collaboration and license agreement with Janssen and its affiliate. Under the Janssen Agreement, we granted Janssen exclusive worldwide rights to develop and commercialize products that contain 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. Under the Janssen Agreement, we have granted Janssen an exclusive, worldwide license to our intellectual property related to these compounds. Our hepatitis C patent portfolio currently includes ten issued U.S. patents, nine pending applications, as well as a large number of associated foreign patents and pending applications. These patents and patent applications, if issued, will expire on various dates between 2025 and 2034. The patent applications contain claims directed to classes of compounds, methods of use, mechanism of action, and research assays.

Our antibacterial patent portfolio currently includes seven issued United States patents and a number of granted and pending patent applications in foreign jurisdictions. These patents and patent applications, if issued, will expire on various dates between 2026 and 2031. The patent applications contain claims directed to classes of compounds, methods of use, and processes for synthesis pertaining to ACH-702, our antibacterial lead candidate.

In 2012, we entered into a license and development agreement with ORA, Inc. (Ora) for the worldwide development and commercialization of ACH-702 delivered topically or locally. We entered into an amendment to the agreement in April 2013. Under the terms of the agreement, as amended, Ora is responsible for development and regulatory activities and associated costs for ACH-702. We are eligible to receive development and commercialization milestones and royalties on net sales, if any, for ACH-702.

Our HIV patent portfolio currently includes two issued United States patents and several issued foreign patents applications. We either own or hold exclusive worldwide licenses from Yale University and Emory University to these patents. The patents will expire in 2016 and 2023. The issued U.S. patents contain claims directed to elvucitabine chemical compound, method of use, synthesis, and formulation.

In 2010, we entered into a license agreement for elvucitabine with GCA Therapeutics, Ltd. (GCAT) for the treatment of both Hepatitis B, or HBV, and HIV infection. The exclusive license grants GCAT the right, through

its Chinese joint venture with Tianjing Institute of Pharmaceutical Research, or TIPR, to clinically develop and commercialize elvucitabine in mainland China, Hong Kong and Taiwan. Under the terms of the agreement, GCAT, through a sublicense agreement with its Chinese joint venture, T & T Pharma Co., Ltd., formed with TIPR, assumed all development and regulatory responsibility and associated costs for elvucitabine, and we are eligible to receive development milestones and royalties on net sales, if any, in those territories.

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.

We are party to a number of licenses that give us rights to third-party intellectual property that is necessary or useful for our business in the area of HIV and HBV. In particular, we have obtained licenses from Yale University and Emory University with respect to elvucitabine. We may enter into additional licenses for third-party intellectual property in the future. Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for their intellectual property, in particular, those patents to which we have secured exclusive rights.

**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 infectious diseases, hepatology and gastroenterology. Historically, companies have experienced substantial commercial success through the deployment of specialized sales forces which can address a majority of key prescribers, particularly within the infectious disease marketplace. 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 a third party in exchange for one or more of the following: up-front payments, research funding, development funding, milestone payments and royalties on drug sales.

Under the Janssen Agreement, we granted Janssen exclusive worldwide rights to develop and commercialize products that contain 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.

**Regulatory Matters**

***Government Regulation and Product Approval***

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, 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 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.

A drug product candidate must be approved by the FDA through the new drug application, or NDA. 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 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 the potential requirement to conduct post-approval 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 a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. 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 filing 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).

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 continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. 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. 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.

*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 denotes 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 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. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

*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.

*Review of an NDA by the FDA*

If clinical trials are successful, the next step in the drug development process is the preparation and submission to the FDA of a NDA. The NDA is the vehicle through which drug applicants formally propose that

the FDA approve a new drug for marketing and sale in the United States for one or more indications. The NDA must contain a description of the manufacturing process and quality control methods, as well as results of preclinical tests, toxicology studies, clinical trials and proposed labeling, among other things. Every new drug must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, currently exceeding $2.3 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $114,000 per product and $585,000 per establishment. These fees are typically increased annually. 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, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year, and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway.

Following submission of an NDA, the FDA conducts a preliminary review of an NDA generally within 60 calendar 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 specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process and the Prescription Drug User Fee Act goal date 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 (e.g., 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. 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.

The FDA is required to 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 and Priority Review 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 fast track designation, breakthrough therapy designation and priority review 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 goal for taking action on a marketing application from ten months to six months.

*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 drug, 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 drug.

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, the FDA may require post marketing requirements, 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 marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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.

*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.

*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 drug designation before submitting an NDA for the drug and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation 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 receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication

broader than what was designated in its orphan drug application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product 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.

*Pediatric Studies and Exclusivity*

Under the Pediatric Research Equity Act, 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 Safety and Innovation Act, or the 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 any 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.

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. In order to obtain pediatric exclusivity, a sponsor and the FDA have to agree on a Written Request which details the studies that need to be conducted in order for the product to obtain pediatric exclusivity. The data from these studies does not need to show the product is effective in the pediatric population studied. If reports of the studies outlined in the Written Request 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.

***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*

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, or GCP, an applicant must obtain approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion.

In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will be directly applicable to and binding in all 28 EU Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No 536/2014 will become applicable no earlier than 28 May 2016. It will overhaul the current system of approvals for clinical trials in the EU. Specifically, the new legislation aims at simplifying and streamlining the approval of clinical trials in the EU. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

*Marketing Authorization*

In the EU, marketing authorizations for medicinal products may be obtained through several different procedures founded on the same basic regulatory process.

The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases,. It is optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of a MAA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human use or CHMP. Accelerated evaluation may be granted by the CHMP in exceptional cases. These are defined as circumstances in which a medicinal product is expected to be of a “major public health interest.” Three cumulative criteria must be fulfilled in such circumstances: the seriousness of the disease, such as severely disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In these circumstances, the EMA ensures that the opinion of the CHMP is given within 150 days.

The decentralized procedure provides for approval by one or more other concerned EU Member States of an assessment of an application for marketing authorization conducted by one EU Member State, known as the reference EU Member State. In accordance with this procedure, an applicant submits an application for marketing authorization to the reference EU Member State and the concerned EU Member States. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States which, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one EU Member State. Upon

receipt of this authorization the sponsor can then seek the recognition of this authorization by other EU Member States. Authorization in accordance with either of these procedures will result in authorization of the medicinal product only in the reference EU Member State and in the other concerned EU Member States.

A marketing authorization may be granted only to an applicant established in the EU. Regulation No. 1901/2006 provides that, prior to validating 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, 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.

*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.

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.

***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 and 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 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, which may apply to healthcare items or services that are reimbursed by non-governmental 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 to physicians and other health care providers 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 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 in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs.

This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

**Segment Reporting**

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

**Employees**

As of February 19, 2016, we had 79 full-time employees and one part-time employee, 32 of whom hold doctoral degrees. Approximately 57 of our employees are engaged in research and development, with the remainder engaged in administration, finance and business development functions. 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 and compensation 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. | 59 | President and Chief Executive Officer, Director |
| Mary Kay Fenton | 51 | Executive Vice President and Chief Financial Officer |
| David Apelian, M.D., Ph.D. | 50 | Executive Vice President and Chief Medical Officer |
| Joel Barrish, Ph.D. | 58 | Executive Vice President and Chief Scientific Officer |
| Martha Manning, Esq. | 61 | Executive Vice President, General Counsel and Corporate Secretary |
| Joseph Truitt | 51 | Executive Vice President and Chief Commercial Officer |

*Milind S. Deshpande, Ph.D., President and Chief Executive Officer.* Dr. Deshpande was appointed our President and Chief Executive Officer in May 2013, at which time he was also elected to our board of directors. Prior to that, he was our President of Research and Development and Chief Scientific Officer. 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.* 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 on the Executive Committee 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.

*David Apelian, M.D, Ph.D., Executive Vice President and Chief Medical Officer.* Prior to Joining Achillion in May 2013, Dr. Apelian was Senior Vice President and Chief Medical Officer at GlobeImmune, a biopharmaceutical company, from 2005 to 2013, where he was responsible for clinical development, regulatory affairs, clinical immunology, development of companion diagnostics, as well as target discovery and preclinical research. Prior to GlobeImmune, Dr. Apelian was Clinical Director in the Infectious Diseases Group at Bristol-Myers Squibb, a pharmaceutical company, serving as medical co-lead for the clinical development and NDA submission of entecavir for chronic hepatitis B viral infection. Prior to BMS, Dr. Apelian served as Clinical Director in the Department of Hepatology/Gastroenterology at Schering Plough, a pharmaceutical company, coordinating a supplemental NDA filing for interferon alpha-2b and ribavirin for the treatment of pediatric patients with chronic hepatitis C viral infection. Dr. Apelian completed his residency training in Pediatrics at New York Hospital, Cornell Medical Center. He received his M.D. from the University of Medicine and Dentistry of New Jersey, and his Ph.D. in Biochemistry and B.A. from Rutgers University. He also holds an M.B.A. from Quinnipiac University.

*Joel Barrish. Ph.D. Executive Vice President and Chief Scientific Officer.* Prior to joining Achillion in January 2016, Dr. Barrish was Vice President and Head of Discovery Chemistry at Bristol-Myers Squibb, or BMS, a global pharmaceutical company, from December 2010 to December 2015, leading chemical research on small molecules and other modalities across all therapeutic areas and sites. Prior to that role, from January 1990 to December 2010, he was responsible for teams at BMS that advanced more than 20 compounds into clinical development including SPRYCEL® (dasatinib), a marketed kinase inhibitor used for the treatment of chronic myelogenous leukemia, which he co-invented. He and his co-inventors received the 2008 Thomas Alva Edison Patent Award for its discovery. Dr. Barrish has co-authored over 120 peer-reviewed publications, is a co-inventor on more than 35 issued U.S. patents, and has been invited to give more than 40 lectures at international conferences and universities. In 2010, Dr. Barrish was elected to the Executive Committee of the American Chemical Society Medicinal Chemistry Division and served as its Chair in 2013. He was named an American Chemical Society Fellow in 2012. Dr. Barrish is also a Scientific Advisory Board member for the chemistry departments at the University of Pennsylvania. Dr. Barrish graduated summa cum laude in Chemistry from the University of Pennsylvania and received a doctorate in Organic Chemistry from Columbia University.

*Martha Manning, Esq., Executive Vice President, General Counsel and Corporate Secretary.* 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, 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, Executive Vice President and Chief Commercial Officer.* 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 Our Drug Candidates

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

In addition to our exclusive collaboration with Janssen, we are also 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 pathway that is a part of the human innate immune system. Our complement inhibitor platform is focused on advancing small molecule compounds that inhibit factor D 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, as well as the needs of patients with atypical hemolytic uremic syndrome, or aHUS, myasthenia gravis, dry age-related macular degeneration, or dry AMD, chronic obstructive pulmonary disease, or COPD, as well as other therapeutic uses.

Our approach to the discovery and development of drug candidates that target complement factor D inhibition is unproven. While complement factor D is a clinically validated target in certain ophthalmic diseases, it is unproven in demonstrating efficacy in systemic diseases. 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 discovery phase. Any medicines that we develop may not effectively inhibit complement factor D, and even if they are successful in inhibiting complement factor D, may not 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. Our focus on using our proprietary technology to identify drug candidates targeting complement factor D 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 factor D inhibitor program. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize at least one drug candidate in one or more disease indications based upon our complement inhibition platform.

The success of our complement factor D inhibitor program as well as our HCV program in collaboration with Janssen, will depend on several factors, including the following:

- initiation and 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 our future collaborators, if any;
- 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 launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance of our products, if and when approved, by patients, the medical community and third party payors; and
- our ability to compete with other marketed therapies for complement-mediated disease such as those from Alexion Pharmaceuticals, or Alexion, and other potential therapies in development by Akari Therapeutics, or Akari, Alexion, Alnylam Pharmaceuticals, or Alnylam, Amyndas Pharmaceuticals, or Amyndas, Apellis Pharmaceuticals, or Apellis, Bio Cryst Pharmaceuticals, or Bio Cryst, Omeros, Ra Pharma and True North. Additionally, Genentech is developing a factor D treatment for dry AMD. Novartis also has intellectual property rights in the complement area.

Many of these factors 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 collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize products based on our complement factor D inhibitor program on our own or with any future collaborator, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

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

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

We intend to focus on developing drug candidates for specific indications under our complement inhibitor program that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable drug candidates. 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.

**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.

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 current or 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 current or 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 current or future collaborators, may never receive such approvals. We, and any current or 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. Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any current or future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if (1) we, or any current or 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 current or 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 current or 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 current or 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 the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If any of our drug candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any current or 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 current or future collaborators, experience any of a number of possible unforeseen 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 current or future collaborators, may experience numerous unforeseen 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 current or 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 current or future collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any current or future collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any current or 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 current or 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 current or future collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any current or future collaborators in a timely manner or at all;
- regulators or institutional review boards may not authorize us, any current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or future collaborators, may have the exclusive right to commercialize our drug candidates or allow our competitors, or the competitors of any current or future collaborators, to bring products to market before we, or any current or future collaborators, do and impair our ability, or the ability of any current or 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 current or 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 current or 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. 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, aHUS, myasthenia gravis, and dry AMD;
- 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 new 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 any 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 companies that currently market and sell products for HCV or are pursuing the development of

additional drug candidates for HCV including Abbvie Pharmaceuticals, Enanta, Gilead Sciences, Merck and Regulus Therapeutics. Some of these marketed products have demonstrated good efficacy rates and safety profiles. We and our collaborator, Janssen, would have to demonstrate similar efficacy and safety profiles in order to be competitive, which cannot be assured.

In addition, there are also 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's eculizumab (Soliris®) is a marketed therapy for the treatment of PNH and aHUS. Akari, Alexion, Alnylam, Amyndas, Apellis, Bio Cryst, Omeros, and Ra Pharma have complement factor inhibitor therapies in development for other hemotologic diseases. Additionally, Genentech is developing a factor D treatment for dry AMD. Novartis also has intellectual property rights in the complement area.

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 current or future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we or any current or future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any current or 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 an 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. It is unclear whether the FDA will treat the active ingredients in our drug candidates as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 current or 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 recent 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 current or 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 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 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. 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 increasing 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 increasing net operating losses for at least the next several years. Our net losses were $5.0 million, $69.0 million and $58.9 million for the years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, we had an accumulated deficit of $455.7 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. In May 2015, we entered into an exclusive collaboration and license agreement with Janssen pursuant to which we granted Janssen exclusive worldwide rights to develop and commercialize products based upon our portfolio of HCV drug candidates. We do not intend to further the development of our HCV drug candidates internally. Going forward, we will focus solely on our complement inhibitor platform, which will initially focus on complement factor D. We are currently only in the early clinical testing stages for our most advanced drug candidate under this program 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 research and initiate preclinical and clinical development efforts for our drug candidates, including ACH-4471;

- seek regulatory and marketing approvals for our drug candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure to commercialize various products for which we may obtain marketing approval, if any;
- contract for the manufacture of larger quantities of drug candidates for clinical development and potentially commercialization;
- maintain, expand and protect our intellectual property portfolio; and
- hire and retain additional personnel, such as clinical, quality control and scientific 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 current or 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 of our current or current or 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 current or future collaborators may never succeed in these activities and, even if we do, or any current or future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. We are currently only in the early clinical testing stages for our most advanced drug candidates under our complement factor D inhibitor program. 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 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. A decline in the value of our company could cause you to lose all or part of your investment.

**We may 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 current or future collaborator. Accordingly, we may 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 program. 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.

We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2015, will enable us to fund our operating expenses, debt service and capital expenditure requirements through 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 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 current or future 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 expand our research and development and establish a commercial infrastructure; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims.

**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 addition, debt financing, if available, would 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.

**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, 2011, and determined that we had three ownership changes since inception. The changes of ownership will result in net operating loss and research and development credit carryforwards that we expect to expire 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, 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 depend on our collaboration with Janssen and may depend on collaborations with additional 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.**

In May 2015, we entered into an exclusive collaboration and license agreement with Janssen. Under the Janssen Agreement, we granted Janssen exclusive worldwide rights to develop and commercialize products based on certain of our HCV drug candidates. We may in the future seek other third-party collaborators for the development and commercialization of product candidates based on our complement inhibitor program. 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 the collaboration and license agreement with Janssen or any future arrangements 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.

Collaborations involving our drug candidates, including our collaboration with Janssen, 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. For example, under our collaboration with Janssen, development plans and strategies for all licensed products will be conducted in accordance with a plan and budget approved by a joint committee comprised of equal numbers of representatives from each of us and Janssen, as to which Janssen generally has final decision-making authority, and, subject to specified diligence requirements, Janssen has full discretion over commercialization plans and strategies for all licensed products;

- 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;
- 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. For example, under specified circumstances Janssen has the first right to maintain or defend certain of our intellectual property rights under our collaboration agreement and, although we may have the right to assume the maintenance or defense of such intellectual property rights if Janssen does not, our ability to do so may be compromised by Janssen's actions;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- 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. For example, Janssen can terminate its agreement with us in its entirety upon sixty days' notice at any time prior to submission of the first application for marketing approval for a licensed product in any specified major market country, and can terminate the entire agreement with us in connection with any undisputed material breach of the agreement by us that remains uncured for a specified period of time; and
- collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner or at all. If any current or 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 additional 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 additional 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 several issued patents U.S. and pending U.S. provisional and non-provisional patent applications, as well as pending PCT applications and associated non-US 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 the issued patents that are licensed to us, and the claims of any patents which have already issued or may issue in the future and are owned 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.

Further, 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.

**As a result of our collaboration with Janssen, Janssen has received certain rights in our HCV patents which affect how our patents are prosecuted and litigated, and any lack of validity or enforceability of our patents licensed to Janssen, or third party competition, can affect our royalty income.**

Under the Janssen Agreement, we have granted Janssen an exclusive, worldwide license to all of our intellectual property pertaining to odalasvir, sovaprevir and ACH-3422. Janssen will pay us royalties on a country by country basis during the later of (i) the term during which we have a valid claim covering the product or where the market is protected by regulatory data exclusivity or (ii) ten years from first commercialization. If neither of these conditions exist in a country, our royalties will be reduced. Even if one of these conditions do exist, however, if there is generic competition in a country, Janssen can reduce our royalties in that country until the generic sales are abated.

A patent working group which reports to the joint steering committee has been established to coordinate all prosecution and litigation activities. Under this arrangement, we will continue to prosecute the HCV patents owned by us, at Janssen's expense, and Janssen has primary responsibility for patent prosecution of all jointly created patent rights under the Janssen Agreement.

Janssen has the initial right to bring and control any enforcement actions under our and jointly owned patent rights, and thus we do not have the primary right to enforce our HCV patents. If Janssen declines to enforce a patent, then we have the right to do so at our expense. If Janssen or we do not elect to enforce a patent, our commercial market, and thus our product revenues, if any, can be negatively affected by third party competition. If the Janssen Agreement is terminated, we and Janssen shall each have the right to use joint patent rights without the consent of the other.

**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 assets 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.

As the commercializing entity of our HCV candidates odalasvir, sovaprevir and ACH-3422, Janssen will be primarily responsible for handling any issues pertaining to asserted infringement by third parties of their patents through the development, offer for sale, sale, importation or exportation of these products in the U.S. and other countries. Under our Agreement, Janssen can offset part of the cost of any licenses with third parties required for commercialization against our royalties.

**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. Under our license agreements with Yale University we have the right, but not an obligation, to bring actions against an infringing third party. If we do not bring an action within a specified number of days, the licensor may bring an action against the infringing party. 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.

For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. 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 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, 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.

**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, including certain countries in Asia, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, most 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, which could materially diminish the value of the patent. Compulsory licensing of life-saving products is also becoming increasingly popular in developing countries, either through direct legislation or international initiatives. Such compulsory licenses could be extended to include some of our drug candidates, which may limit our potential revenue opportunities.

**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. 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. 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. 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.

**We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.**

Over time, we expect to experience significant 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. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional drug candidates. If we are unable to effectively manage our expected growth, 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 our 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 and our collaborators 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 our 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 our 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 our third party 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 be approved for reimbursement before the product

can be approved for sale in that country. We or our third party 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.

**We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our drug candidates and, even if we do, that exclusivity many not prevent the FDA or the EMA 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. 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.

**Fast track designation by the FDA 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 may not lead to a faster regulatory review or approval process and, in any event, does not assure FDA 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. 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 six-month review cycle or thereafter.

**Even if we, or any current or 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 current or 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 current or 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 current or 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 current or future collaborators, receive marketing approval for one or more of our drug candidates, we, and any current or 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 current or future collaborators, are not able to comply with post-approval regulatory requirements, we, and any current or future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any current or 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 our 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 our 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 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.

**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 $5,500 to $11,000 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 report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013; 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 non-governmental 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 physicians and other healthcare providers 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 and the curtailment or restructuring of our operations. Any penalties, damages, fines, 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, imprisonment, exclusion of products 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 exclusions from government funded healthcare programs.

**Current and future legislation may increase the difficulty and cost for us and any 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 other 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 collaborators, may receive for any approved products.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our drug 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;
- 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;
- 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 of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- 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;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new 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; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

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, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several 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 drug candidates for which regulatory approval is obtained.

We expect that the PPACA, 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 in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. 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 collaborators to more stringent product 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 current or 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 19, 2016, our directors, executive officers and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, beneficially own, in the aggregate, greater than approximately 70% 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, 2015, 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 our current and planned clinical trials of drug candidates under our complement factor D inhibitor program;
- the timing and amount of proceeds received from milestones achieved and royalties earned, if any, by us under the Janssen agreement;
- 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 key agreements, or any new collaboration agreement we may enter;
- market expectations about the timeliness of our entry into, or failure to enter, 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 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 of our common stock;
- 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.

**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 further, or do not improve, 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 these 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 38,632 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 |
|---|---|---|
| **2014** | | |
| First Quarter | $ 4.36 | $2.98 |
| Second Quarter | $ 8.61 | $2.45 |
| Third Quarter | $13.80 | $6.61 |
| Fourth Quarter | $16.87 | $9.32 |
| **2015** | | |
| First Quarter | $16.54 | $9.75 |
| Second Quarter | $11.05 | $8.13 |
| Third Quarter | $ 9.62 | $6.46 |
| Fourth Quarter | $10.95 | $6.41 |

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 19, 2016, there were approximately 71 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.

### *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*

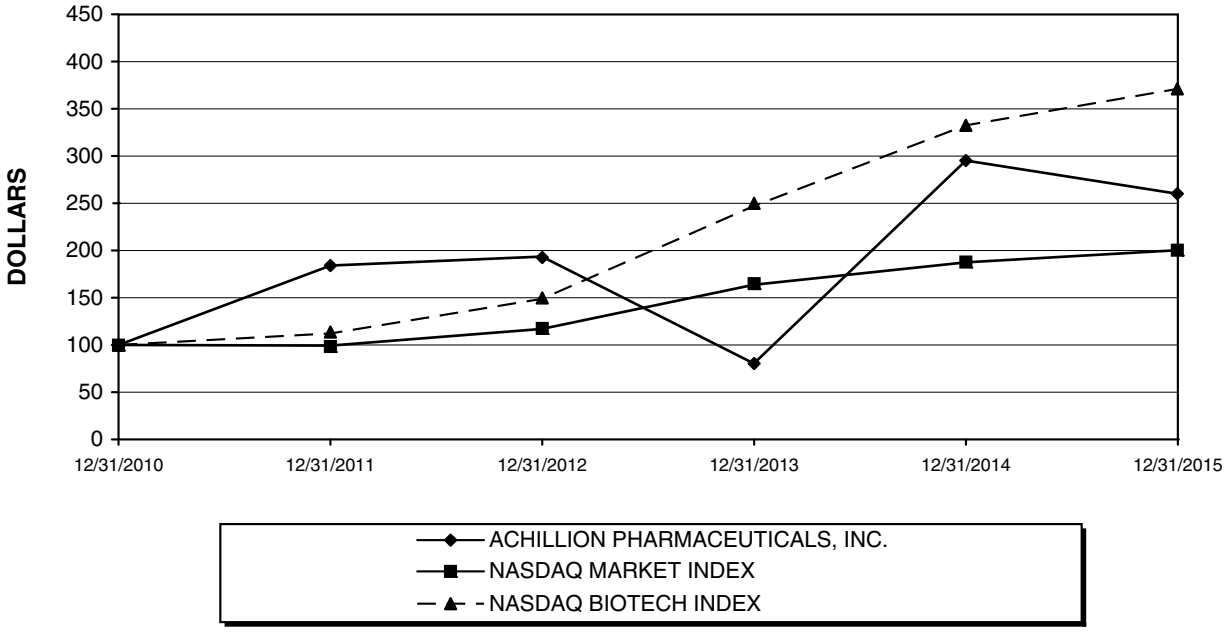
Neither we nor any affiliated purchaser or anyone acting on behalf of us or an affiliated purchaser made any purchases of shares of our common stock in the fourth quarter of 2015.

### *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, 2010 to December 31, 2015 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, 2010 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.

**COMPARISON OF CUMULATIVE TOTAL RETURN**
**AMONG ACHILLION PHARMACEUTICALS, INC.,**
**NASDAQ MARKET INDEX AND NASDAQ BIOTECH INDEX**




ASSUMES $100 INVESTED ON JAN. 01, 2011
ASSUMES DIVIDEND REINVESTED
FISCAL YEAR ENDING DEC. 31, 2015

## 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, 2015, 2014 and 2013 and balance sheet data as of December 31, 2015 and 2014 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, 2012 and 2011 and balance sheet data as of December 31, 2013, 2012 and 2011 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, | | | | |
|---|---|---|---|---|---|
| | 2015 | 2014 | 2013 | 2012 | 2011 |
| | (in thousands, except per share amounts) | | | | |
| **Statement of Comprehensive Loss Data:** | | | | | |
| Total revenue (1) | $ 66,122 | $ — | $ — | $ 2,607 | $ 247 |
| Research and development | 56,553 | 53,515 | 46,736 | 38,999 | 35,441 |
| General and administrative | 24,676 | 15,911 | 12,741 | 10,901 | 9,153 |
| Total operating expenses | 81,229 | 69,426 | 59,477 | 49,900 | 44,594 |
| Loss from operations | (15,107) | (69,426) | (59,477) | (47,293) | (44,347) |
| Interest income (expense), net | 1,188 | 418 | 530 | 166 | 141 |
| Net loss | (5,030) | (69,008) | (58,947) | (47,127) | (44,206) |
| Net loss per share—basic and diluted | $ (0.04) | $ (0.70) | $ (0.63) | $ (0.64) | $ (0.69) |
| Weighted average number of shares outstanding—basic and diluted | 125,592 | 98,367 | 93,983 | 73,965 | 64,248 |

| | As of December 31, | | | | |
|---|---|---|---|---|---|
| | 2015 | 2014 | 2013 | 2012 | 2011 |
| **Balance Sheet Data:** | | | | | |
| Cash and cash equivalents (1)(2) | $ 81,725 | $ 73,664 | $ 33,457 | $ 18,526 | $ 16,110 |
| Short-term marketable securities (1)(2) | 377,616 | 79,215 | 88,393 | 46,884 | 37,456 |
| Long-term marketable securities | — | — | 36,139 | 12,008 | 26,377 |
| Working capital | 447,930 | 141,816 | 115,379 | 58,731 | 46,148 |
| Total assets | 464,525 | 156,807 | 162,417 | 81,530 | 82,630 |
| Long-term liabilities | 231 | 279 | 56 | 347 | 2,718 |
| Total liabilities | 14,889 | 13,338 | 9,459 | 9,483 | 11,662 |
| Total stockholders' equity | 449,636 | 143,469 | 152,958 | 72,047 | 70,968 |

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. 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 infectious and complement-mediated diseases.

Our current 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 complement system. The complement pathway 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 will initially 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 ultra-rare orphan indications such as paroxysmal nocturnal hemoglobinuria, or PNH, as well as more prevalent conditions such as dry age-related macular degeneration, or dry AMD, and chronic obstructive pulmonary disease, or COPD.

We anticipate that our complement factor D inhibitor compounds may play a role in treating patients with PNH, including patients who have suboptimal response to, or who fail to respond to, currently approved treatments for PNH, atypical hemolytic uremic syndrome, or aHUS, myasthenia gravis, and dry AMD, as well as other therapeutic applications. Our compounds have demonstrated complete suppression of the complement alternative pathway with a single oral dose of our inhibitors in non-human primates. We have initiated a first-in-human phase I clinical trial for our first complement factor D inhibitor, ACH-4471, to assess safety, tolerability, pharmacokinetics, or PK, and pharmacodynamics, or PD. We plan to advance this compound to potentially treat patients with PNH and possibly, one additional systemic ultra-rare disease. We may advance other factor D inhibitors for other indications after further characterization.

We also have a collaboration with Janssen Pharmaceuticals, Inc., or Janssen, the pharmaceutical subsidiary of Johnson & Johnson Inc., under which we have granted to Janssen exclusive worldwide rights to develop and commercialize a portfolio of antiviral drug candidates we discovered and developed for the treatment of chronic hepatitis C virus, or HCV, infection in exchange for specified milestone payments and an equity investment in us.

We also intend to continue to leverage our extensive expertise in structural biology and synthetic chemistry to quickly and efficiently discover and develop additional small molecule compounds to meet other significant unmet medical needs. We believe our drug discovery capabilities will allow us to further expand our drug candidate portfolio, providing us with strong growth potential and, over time, reducing our reliance on the success of any single drug candidate. Our research team has successfully discovered and advanced multiple compounds into clinical development including sovaprevir, odalasvir, also known as ACH-3102, and ACH-3422 in our HCV program, all of which we have licensed to Janssen, and ACH-4471 in our complement factor D inhibitor program.

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 incurred approximately $56.6 million, $53.5 million and $46.7 million in research and development costs for the years ended December 31, 2015, 2014, and 2013, respectively.

**Collaboration with Janssen Pharmaceuticals, Inc.**

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. Under the Janssen Agreement, we granted Janssen exclusive worldwide rights to develop and commercialize products that contain 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. We have completed the transfer of our portfolio of drug candidates for the treatment of chronic HCV to Janssen. The Janssen Agreement became effective June 29, 2015 upon the early termination of applicable waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, or the HSR Act. In addition, upon the closing of the transactions contemplated by the Janssen Agreement, we entered into a stock purchase agreement with JJDC, which we refer to as the JJDC stock purchase agreement. 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 $225.0 million. The JJDC stock purchase agreement became effective on July 1, 2015.

Under the terms of the Janssen Agreement, we are eligible to receive (1) up to $115.0 million of milestone payments based upon achievement of clinical enrollment and dosing in specified studies, substantially all of which is related to dosing in one study, (2) up to an additional $290.0 million of milestone payments based upon regulatory approvals and first commercial sale in specified territories, the majority of which relates to regulatory approval and the first commercial sale in the U.S., and (3) up to an additional $500.0 million of milestone payments based upon achieving worldwide sales targets. We are also 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. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after such first commercial sale if there is no such exclusivity. Janssen will bear the future costs of worldwide development and commercialization of licensed products, subject to specified exceptions relating to our ongoing studies and technology transfer.

**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, 2015, we recognized revenue of $66.1 million under the Janssen Agreement. We did not recognize any revenue during the years ended December 31, 2014 and 2013.

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 to180 days after the effective date of the Janssen Agreement. We have completed this transfer. 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.

The development, regulatory and sales milestones represent non-refundable amounts that would be paid by Janssen to us if certain milestones are achieved in the future. These milestones, if achieved, are substantive as they relate solely to past performance and are commensurate with estimated enhancement of value associated with the achievement of each milestone. However, there can be no assurance that Janssen will achieve the milestones or that we will receive the related revenue.

***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 laboratories; and clinical development space and operating supplies.

***Complement Factor D Inhibitor Program***

Our current 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 complement system. We are advancing novel small molecules from this platform which will initially 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 ultra-rare orphan indications such as PNH, as well as more prevalent indications such as dry AMD.

We anticipate that our complement factor D inhibitors may play a role in addressing needs of patients with PNH, including patients who have suboptimal response to, or who fail to respond to, currently approved treatments for PNH, aHUS, myasthenia gravis, dry AMD, and COPD as well as other therapeutic applications. Our compounds have demonstrated complete suppression of the complement alternative pathway with a single oral dose of our inhibitors in non-human primates. We have initiated a first-in-human clinical trial for our first complement factor D inhibitor, ACH-4471.

***HCV Program***

We established our HCV drug candidate pipeline entirely through our internal discovery capabilities. Through these efforts, we identified and developed a portfolio of drug candidates including odalasvir, ACH-3422 and sovaprevir. The following compounds from our discovery and development efforts are now licensed for further development to Janssen:

- ***Odalasvir, a NS5A Inhibitor.*** We completed three phase IIa clinical trials with odalasvir including the -007 trial with sovaprevir, the -005 study, which examined the use of odalasvir with ribavirin alone, and the Proxy Doublet study which examined the use of odalasvir in combination with sofosbuvir, a nucleotide NS5B polymerase inhibitor marketed by Gilead Sciences, Inc., or Gilead, under the brand name Sovaldi®. HCV patients treated for both eight weeks and six weeks with the combination of odalasvir and sofosbuvir achieved 100% SVR24, or sustained viral response 24 weeks after cessation of therapy, demonstrating the differentiation of odalasvir within the NS5A class.
- ***ACH-3422, a NS5B Nucleotide Polymerase Inhibitor.*** ACH-3422 has demonstrated excellent potency and was well-tolerated in a phase Ib proof of concept study in which HCV patients receiving a once-daily 700mg dose of ACH-3422 for 14 days demonstrated mean maximal viral load reduction of 4.6 $\log_{10}$.
- ***Sovaprevir, a NS3/4A Protease Inhibitor.*** We have completed a phase II clinical trial that evaluated 12 weeks of treatment consisting of sovaprevir and our NS5A inhibitor, odalasvir, with ribavirin for the treatment of genotype 1 HCV (the -007 trial). In this trial, genotype 1b patients achieved 100% SVR24; however, in genotype 1a patients, the combination regimen results were suboptimal.

In October 2015, we announced that Janssen had initiated phase IIa clinical testing of a triple combination regimen consisting of Olysio®, a protease inhibitor marketed by Janssen, AL-335, a nucleotide polymerase inhibitor in clinical development by Janssen, and odalasvir. The trial will evaluate the safety, pharmacokinetics and efficacy of the combination treatment in patients with genotype 1 chronic hepatitis C virus (HCV). Based on information we have been provided by Janssen and the joint steering committee, we anticipate that this phase IIa trial may be completed in 2016 with interim results available in the first half of 2016.

We also intend to continue to focus on the discovery and development of new drug candidates through our extensive expertise in structural biology and synthetic chemistry. Although significant additional funding and research and development will be required to support these efforts, we believe our drug discovery capabilities will allow us to further expand our product candidate portfolio, providing us with strong growth potential and, over time, reducing our reliance on the success of any single drug candidate.

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, 2015, 2014 and 2013 were as follows:

| | For the Years Ended December 31, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| | (in thousands) | | |
| Direct external costs: | | | |
| Complement factor D compounds | $13,320 | $ 2,676 | $ — |
| HCV compounds and combination trials | 20,956 | 31,959 | 31,314 |
| Other | 47 | 205 | 387 |
| | 34,323 | 34,840 | 31,701 |
| Direct internal personnel costs | 17,605 | 14,607 | 11,489 |
| Sub-total direct costs | 51,928 | 49,447 | 43,190 |
| Indirect costs and overhead | 5,265 | 4,746 | 3,729 |
| Connecticut research and development tax credit | (640) | (678) | (183) |
| Total research and development | $56,553 | $53,515 | $46,736 |

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.

Janssen will bear the future costs of worldwide development and commercialization of products under the Janssen Agreement. Accordingly, we do not expect to incur significant research and development costs associated with our HCV compounds or combination trials in the future.

We expect research and development expenses associated with our complement inhibitor program and the development of other preclinical programs that we may initiate 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 impact the development of our complement inhibitor program and plans over time.

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

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

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. We have completed this transfer. 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 represent a single unit of accounting because they were not viewed to have standalone value. The Janssen Agreement entered into by us and Janssen, the JJDC stock purchase agreement, and the Investor Agreement were entered into by us and Janssen's affiliate 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 our common stock 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.

The development, regulatory and sales milestones represent non-refundable amounts that would be paid by Janssen to us if certain milestones are achieved in the future. We have elected to apply the guidance in ASC 605-28 to the milestones. These milestones, if achieved, are substantive as they relate solely to past performance and are commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of our performance; however, there can be no assurance that Janssen will achieve the milestones or that we will receive the related revenue.

***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 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. To the extent that the amount of the aggregate fair market value of qualified stock options that become exercisable for an individual exceeds $100,000 during any tax year, those stock options are treated as non-qualified stock options. 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.

For the years ended December 31, 2015 and 2014, we based our estimate of the expected term of historical data for similar stock option grants. We utilized the simplified method in developing an estimate of the expected term of “plain vanilla” share options for the year ended December 31, 2013. This method was considered appropriate given our limited exercise history. For the years ended December 31, 2015, 2014 and 2013, we calculated volatility based on actual volatility for the expected term of the option. We are also required to 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, 2015. 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, 2015 we recognized revenue of $66.1 million under the Janssen Agreement. We did not recognize any revenue during the years ended December 31, 2014 and 2013.

***Comparison of the Years Ended December 31, 2015 and 2014***

The increase in collaboration revenue in 2015 is related to the recognition of revenue under the Janssen Agreement.

***Comparison of the Years Ended December 31, 2014 and 2013***

We did not recognize any revenue during the years ended December 31, 2014 and 2013.

**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 | | | |
|---|---|---|---|---|---|---|---|
| | 2015 | 2014 | 2013 | 2015 vs. 2014 | | 2014 vs. 2013 | |
| | (in thousands) | | | | | | |
| Personnel costs | $13,130 | $11,894 | $ 9,342 | $1,236 | 10% | $2,552 | 27% |
| Stock based compensation | 4,500 | 2,713 | 2,146 | 1,787 | 66% | 567 | 26% |
| Outsourced research and supplies | 31,214 | 31,706 | 30,326 | (492) | (2)% | 1,380 | 5% |
| Professional and consulting fees | 5,287 | 5,263 | 2,720 | 24 | 0% | 2,543 | 93% |
| Facilities costs | 2,505 | 2,083 | 2,028 | 422 | 20% | 55 | 3% |
| Travel and other costs | 557 | 534 | 357 | 23 | 4% | 177 | 50% |
| Research and development tax credit | (640) | (678) | (183) | 38 | (6)% | (495) | 270% |
| Total | $56,553 | $53,515 | $46,736 | $3,038 | 6% | $6,779 | 15% |

***Comparison of the Years Ended December 31, 2015 and 2014***

The increase in research and development costs from 2014 to 2015 was primarily due to increased preclinical and manufacturing costs related to our complement inhibitor program. These amounts were partially offset by decreased clinical trial costs related to our ACH-3422 clinical trials, our odalasvir and sofosbuvir combination trial and ACH-2684 clinical and manufacturing costs. Personnel and non-cash stock-based compensation costs also increased due to the addition of personnel in our drug development group.

We expect research and development expenses will increase somewhat over the next year as we continue to advance ACH-4471 through clinical trials, enhance our manufacturing and formulation processes for ACH-4471 and other complement factor D inhibitors, advance our broader complement factor D portfolio to address additional indications, and pursue additional discovery opportunities for creating small molecule therapies that address significant patient needs.

***Comparison of the Years Ended December 31, 2014 and 2013***

The increase in research and development expenses from 2013 to 2014 was primarily due to increased clinical and manufacturing costs related to ACH-3422, and increased costs related to our odalasvir and sofosbuvir combination trial, as well as increased costs related to our complement inhibitor program. Consulting, intellectual property and medical affairs related costs also increased. Additionally, personnel costs and non-cash stock-based compensation increased due to the addition of personnel in our development group and increased incentive compensation as the result of exceeding achievement of corporate goals. These amounts were primarily offset by decreased costs related to combination and drug interaction studies of sovaprevir and odalasvir.

**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 | | | |
|---|---|---|---|---|---|---|---|
| | 2015 | 2014 | 2013 | 2015 vs. 2014 | | 2014 vs. 2013 | |
| | (in thousands) | | | | | | |
| Personnel costs | $ 5,099 | $ 4,339 | $ 3,533 | $ 760 | 18% | $ 806 | 23% |
| Stock based compensation | 5,572 | 4,560 | 3,774 | 1,012 | 22% | 786 | 21% |
| Professional and consulting fees | 11,038 | 4,983 | 3,681 | 6,055 | 122% | 1,302 | 35% |
| Facilities costs | 875 | 729 | 655 | 146 | 20% | 74 | 11% |
| Travel and other costs | 2,092 | 1,300 | 1,098 | 792 | 61% | 202 | 18% |
| Total | $24,676 | $15,911 | $12,741 | $8,765 | 55% | $3,170 | 25% |

***Comparison of the Years Ended December 31, 2015 and 2014***

The increase in general and administrative costs from 2014 to 2015 was primarily due to increased business consulting and corporate legal fees related to the Janssen Agreement, increased corporate fees and taxes, and increased personnel and non-cash stock-based compensation costs due to the addition of personnel.

We expect that general and administrative costs during the next year will be consistent with 2015 costs.

***Comparison of the Years Ended December 31, 2014 and 2013***

The increase in general and administrative expenses from 2013 to 2014 was primarily due to increased professional consulting and corporate legal fees as well as insurance costs. Personnel costs and non-cash stock-based compensation also increased primarily due to increased incentive compensation as a result of exceeding achievement of corporate goals.

**Other Income and Expense:**

***Comparison of the Years Ended December 31, 2015 and 2014***

Other income was $8.9 million and $0 for the years ended December 31, 2015 and 2014, respectively. The $8.9 million increase was due to the receipt of a payment by a stockholder representing the disgorgement of short swing profits under Section 16(b) of the Securities Exchange Act.

Interest income was $1.2 million and $455,000 for the years ended December 31, 2015 and 2014, respectively. The $733,000, or 161%, increase from 2014 to 2015 was primarily due to increased average cash balances.

Interest expense was $55,000 and $37,000 for the years ended December 31, 2015 and 2014, respectively. The increase of $18,000, or 49%, was primarily due to higher average debt balances outstanding in 2015.

***Comparison of the Years Ended December 31, 2014 and 2013***

Interest income was $455,000 and $582,000 for the years ended December 31, 2014 and 2013, respectively. The $127,000, or 22%, decrease from 2013 to 2014 was primarily due to decreased average cash balances.

Interest expense was $37,000 and $52,000 for the years ended December 31, 2014 and 2013, respectively. The decrease of $15,000, or 29%, was primarily due to lower average debt balances outstanding in 2014.

**Liquidity and Capital Resources**

Since our inception, we have financed our operations primarily through proceeds from the sale of equity securities. Through December 31, 2015, 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 the equity investment by JJDC.

In October 2014, we entered into a Master Security Agreement for a $1.0 million Capital Expenditure Line of Credit, or 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 bear 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.

As of December 31, 2015, our debt balance due to borrowings was $454,000 with a weighted average interest rate of 6.26%. As of December 31, 2015, the following amounts remain outstanding under the following debt facilities:

| Lender | Date | Interest Rate (per annum) | Principal Amount | Outstanding Balance | Maturity Date |
|---|---|---|---|---|---|
| Webster Bank | October 2014 | 6.30% | $440,000 | $278,667 | October 2017 |
| Webster Bank | March 2015 | 6.20% | $228,962 | $175,662 | March 2018 |

We had $459.3 million and $152.9 million in cash, cash equivalents and marketable securities as of December 31, 2015 and 2014, respectively. We regularly review our investments and monitor the financial markets. As of December 31, 2015, 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.

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. Cash used in operating activities was $55.5 million for the year ended December 31, 2014 and was primarily attributable to our $69.0 million net loss primarily offset by $9.7 million non-cash charges related to depreciation, amortization of premiums on marketable securities and stock -based compensation combined with a $3.8 million increase in accounts payable and accrued expenses. Cash used in operating activities was $53.6 million for the year ended December 31, 2013 and was primarily attributable to our $58.9 million net loss combined with $3.4 million in premiums paid on the purchase of marketable securities, primarily offset by $8.7 million in non-cash charges related to depreciation, amortization of premiums on marketable securities and stock -based compensation.

Cash used in investing activities was $298.7 million for the year ended December 31, 2015 and was primarily attributable to purchase of marketable securities partially offset by maturities of marketable securities. Cash provided by investing activities was $43.3 million for the year ended December 31, 2014 and was primarily attributable to maturities of marketable securities partially offset by purchases of marketable securities. Cash used in investing activities was $65.0 million for the year ended December 31, 2013 and was primarily attributable to purchases of marketable securities partially offset by maturities of marketable securities.

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 Fitzgerald. Cash provided by financing activities was $52.4 million for the year ended December 31, 2014 and was primarily attributable to $42.6 million in net proceeds from the sale of 3,236,497 shares of our common stock pursuant to our at-the-market sales agreement with Cantor Fitzgerald, combined with $9.4 million in proceeds from the exercise of stock options and warrants. Cash provided by financing activities was $133.6 million for the year ended December 31, 2013 and was primarily attributable to $133.2 million in net proceeds from our public offering of common stock in February 2013.

We expect to incur substantial and increasing losses for at least the next several years as we seek to continue preclinical and initiate clinical development of our complement inhibitor program and identify and progress any potential 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 costs involved in the preclinical and clinical development of our complement inhibitor drug candidates;
- the costs involved in obtaining regulatory approvals for our drug candidates;
- the scope, prioritization and number of programs we pursue;
- the costs involved in preparing, filing, prosecuting, maintaining, enforcing and defending patent and other intellectual property claims;
- the timing and amount of proceeds received from milestones achieved and royalties earned, if any, by us under the Janssen agreement;
- 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 currently unknown to us.

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. In connection with capital raising activities, we may be required to dilute our existing stockholders substantially. There can be no assurance that we will be able to obtain adequate levels of additional funding or favorable terms, if at all, or that we will achieve the milestone-based payments pursuant to the Janssen Agreement. If we are unable to obtain adequate levels of additional funding or if we do not achieve the milestone-based payments pursuant to the Janssen Agreement, in whole or in part, 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, ownership interest 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, 2015:

| | Payment Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less Than 1 Year | 1-3 Years | 3-5 Years | More than 5 Years |
| | | | (in thousands) | | |
| Debt, including interest | $ 485 | $ 245 | $ 240 | $ — | $ — |
| Operating lease obligations | 3,415 | 770 | 1,628 | 1,017 | — |
| Clinical research obligations | 14,206 | 14,154 | 51 | 1 | — |
| Research obligations and licenses | 1,092 | 852 | 240 | — | — |
| Other professional obligations | 100 | 20 | 40 | 40 | — |
| Total | $19,298 | $16,041 | $2,199 | $1,058 | $ — |

Clinical research obligations consists 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. Upon the achievement of specified development milestones for elvucitabine we will be required to make milestone payments to Yale University and Emory University. We will also be required to pay Yale University and Emory University royalties on net sales of elvucitabine and a specified share of sublicensing fees that we receive under any sublicenses that we grant. The timing and achievement of such milestones is uncertain and potential payments under these agreements have been excluded from the above amounts.

**Off-Balance Sheet Arrangements**

We do not have any off-balance sheet arrangements as of December 31, 2015.

**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. We are currently evaluating the impact ASU No. 2014-09 will have on our financial position and results of operations.

In August 2014, FASB issued ASU No. 2014-15, "Presentation of Financial Statements – Going Concern." ASU No. 2014-15 provides guidance regarding management's responsibility to evaluate whether there exists substantial doubt about a company's ability to continue as a going concern and to provide related footnote disclosures in certain circumstances. ASU No. 2014-15 is effective for annual reporting periods beginning after December 15, 2016, and interim periods thereafter. We do not believe ASU No. 2014-15 will have a material effect on our financial position and results of operations.

In April 2015, FASB issued ASU No. 2015-03, "Interest – Imputation of Interest." ASU No. 2015-03 requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. ASU 2015-03 is effective for financial statements issued for fiscal years beginning after December 15, 2015 (and interim periods within those fiscal years) with early adoption permitted and retrospective application required. We do not believe ASU No. 2015-03 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, government sponsored bond obligations and government-backed 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, 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.

## 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, 2015. 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, 2015, 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, 2015. 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, 2015, 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, 2015 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, 2015 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

## ITEM 9B. OTHER INFORMATION

None.

## 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, 2015. 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 26 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, 2015. 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-30 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

The exhibits which are filed with this report or which are incorporated herein by reference are set forth in the Exhibit Index hereto.

## 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 25, 2016.

**ACHILLION PHARMACEUTICALS, INC.**

By: /s/ MILIND S. DESHPANDE
**Milind S. Deshpande**
**President and 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<br>**Milind S. Deshpande** | President and Chief Executive Officer and Director (Principal executive officer) | February 25, 2016 |
| /s/ MARY KAY FENTON<br>**Mary Kay Fenton** | Executive Vice President and Chief Financial Officer (Principal financial and accounting officer) | February 25, 2016 |
| /s/ DAVID SCHEER<br>**David Scheer** | Chairman of the Board | February 25, 2016 |
| /s/ JASON FISHERMAN, M.D.<br>**Jason Fisherman, M.D.** | Director | February 25, 2016 |
| /s/ GARY E. FRASHIER<br>**Gary E. Frashier** | Director | February 25, 2016 |
| /s/ KURT GRAVES<br>**Kurt Graves** | Director | February 25, 2016 |
| /s/ MICHAEL D. KISHBAUCH<br>**Michael D. Kishbauch** | Director | February 25, 2016 |
| /s/ ROBERT VAN NOSTRAND<br>**Robert Van Nostrand** | Director | February 25, 2016 |
| /s/ NICOLE VITULLO<br>**Nicole Vitullo** | Director | February 25, 2016 |
| /s/ FRANK VERWIEL<br>**Frank Verwiel** | Director | February 25, 2016 |

## INDEX TO FINANCIAL STATEMENTS

## Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of
Achillion Pharmaceuticals, Inc.:

In our opinion, the accompanying balance sheets and the related statements of comprehensive loss, of stockholders' equity, and of cash flows present fairly, in all material respects, the financial position of Achillion Pharmaceuticals, Inc. at December 31, 2015 and December 31, 2014, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2015 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, 2015, based on criteria established in *Internal Control—Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). 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 the Management's Annual Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. 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.

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 25, 2016

**Achillion Pharmaceuticals, Inc.**

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

| | As of December 31, | |
|---|---|---|
| | **2015** | **2014** |
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 81,725 | $ 73,664 |
| Marketable securities | 377,616 | 79,215 |
| Accounts and other receivables | 506 | 95 |
| Prepaid expenses and other current assets | 2,741 | 1,901 |
| Total current assets | 462,588 | 154,875 |
| Fixed assets, net | 1,735 | 1,726 |
| Other assets | 50 | 54 |
| Restricted cash | 152 | 152 |
| Total assets | $ 464,525 | $ 156,807 |
| **Liabilities and Stockholders' Equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 4,133 | $ 6,418 |
| Accrued expenses | 10,302 | 6,446 |
| Current portion of long-term debt | 223 | 195 |
| Total current liabilities | 14,658 | 13,059 |
| Long-term debt | 231 | 279 |
| Total liabilities | 14,889 | 13,338 |
| Commitments (Notes 14 and 15) | | |
| Stockholders' Equity: | | |
| Common Stock, $.001 par value; 200,000 shares authorized at December 31, 2015 and 2014; 136,640 and 103,594 shares issued and outstanding at December 31, 2015 and 2014, respectively | 137 | 104 |
| Additional paid-in capital | 905,256 | 599,796 |
| Stock subscription receivable | — | (5,737) |
| Accumulated deficit | (455,712) | (450,682) |
| Accumulated other comprehensive loss | (45) | (12) |
| Total stockholders' equity | 449,636 | 143,469 |
| Total liabilities and stockholders' equity | $ 464,525 | $ 156,807 |

*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, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| Revenue | $ 66,122 | $ — | $ — |
| Operating expenses | | | |
| Research and development | 56,553 | 53,515 | 46,736 |
| General and administrative | 24,676 | 15,911 | 12,741 |
| Total operating expenses | 81,229 | 69,426 | 59,477 |
| Loss from operations | (15,107) | (69,426) | (59,477) |
| Other income (expense) | | | |
| Interest income | 1,188 | 455 | 582 |
| Interest expense | (55) | (37) | (52) |
| Other income | 8,944 | — | — |
| Net loss | $ (5,030) | $(69,008) | $(58,947) |
| Unrealized loss on marketable securities | (33) | (18) | (13) |
| Total other comprehensive loss | (33) | (18) | (13) |
| Total comprehensive loss | $ (5,063) | $(69,026) | $(58,960) |
| Basic and diluted net loss per share attributable to common stockholders (Note 4) | $ (0.04) | $ (0.70) | $ (0.63) |
| Weighted average shares used in computing basic and diluted net loss per share attributable to common stockholders | 125,592 | 98,367 | 93,983 |

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

**Achillion Pharmaceuticals, Inc.**

**Statements of Stockholders' Equity for the Years Ended December 31, 2013, 2014 and 2015**
**(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, 2012 | 79,626 | $ 80 | $394,675 | $(322,727) | — | $ 19 | $ 72,047 |
| Net loss | — | — | — | (58,947) | — | — | (58,947) |
| Other comprehensive loss | — | — | — | — | — | (13) | (13) |
| Stock compensation | — | — | 5,920 | — | — | — | 5,920 |
| Issuance of common stock upon exercise of warrants | 4 | — | — | — | — | — | — |
| Issuance of common stock upon exercise of stock options | 224 | — | 555 | — | — | — | 555 |
| Issuance of common stock under the Employee Stock Purchase Plan | 44 | — | 185 | — | — | — | 185 |
| Issuance of common stock in connection with the public offering, net of issuance costs | 16,894 | 17 | 133,194 | — | — | — | 133,211 |
| Balances at December 31, 2013 | 96,792 | $ 97 | $534,529 | $(381,674) | — | $ 6 | $152,958 |
| Net loss | — | — | — | (69,008) | — | — | (69,008) |
| Other comprehensive loss | — | — | — | — | — | (18) | (18) |
| Stock compensation | — | — | 7,273 | — | — | — | 7,273 |
| Issuance of common stock upon exercise of warrants | 2,099 | 2 | 5,249 | — | — | — | 5,251 |
| Issuance of common stock upon exercise of stock options | 1,364 | 1 | 4,192 | — | (126) | — | 4,067 |
| Issuance of common stock under the Employee Stock Purchase Plan | 102 | 1 | 240 | — | — | — | 241 |
| Issuance of common stock in connection with the public offering, net of issuance costs | 3,237 | 3 | 48,313 | — | (5,611) | — | 42,705 |
| 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 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 | 138,859 | — | — | — | 158,877 |
| Balances at December 31, 2015 | 136,640 | $137 | $905,256 | $(455,712) | $ — | $ (45) | $449,636 |

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

**Achillion Pharmaceuticals, Inc.**

**Statements of Cash Flows**
**(in thousands)**

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| **Cash flows from operating activities** | | | |
| Net loss | $ (5,030) | $ (69,008) | $ (58,947) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Depreciation and amortization | 694 | 489 | 399 |
| Noncash stock-based compensation | 10,072 | 7,273 | 5,920 |
| (Gain)/loss on disposal of equipment | 2 | (2) | — |
| Premium on purchases of marketable securities | (2,486) | (947) | (3,387) |
| Amortization of premium on marketable securities | 2,002 | 1,959 | 2,360 |
| Changes in operating assets and liabilities: | | | |
| Accounts and other receivables | (411) | 385 | (203) |
| Prepaid expenses and other current assets | (837) | 575 | (104) |
| Accounts payable | (2,285) | 1,827 | 315 |
| Accrued expenses | 3,856 | 1,925 | 11 |
| Net cash provided by (used in) operating activities | 5,577 | (55,524) | (53,636) |
| **Cash flows from investing activities** | | | |
| Purchase of fixed assets | (704) | (947) | (408) |
| Purchase of marketable securities | (692,525) | (79,338) | (168,117) |
| Maturities of marketable securities | 394,575 | 123,625 | 103,491 |
| Net cash provided by (used in) investing activities | (298,654) | 43,340 | (65,034) |
| **Cash flows from financing activities** | | | |
| Proceeds from issuance of common stock in connection with public offerings, net of issuance costs | 138,260 | 42,705 | 133,211 |
| Proceeds from issuance of common stock in connection with the JJDC stock purchase agreement | 158,878 | — | — |
| Proceeds from exercise of stock options | 3,730 | 4,067 | 555 |
| Proceeds from exercise of warrants | — | 5,251 | — |
| Proceeds from sale of stock under the Employee Stock Purchase Plan | 290 | 241 | 185 |
| Borrowings of debt | 229 | 440 | — |
| Repayments of debt | (249) | (313) | (350) |
| Net cash provided by financing activities | 301,138 | 52,391 | 133,601 |
| Net increase in cash and cash equivalents | 8,061 | 40,207 | 14,931 |
| Cash and cash equivalents, beginning of period | 73,664 | 33,457 | 18,526 |
| Cash and cash equivalents, end of period | $ 81,725 | $ 73,664 | $ 33,457 |
| **Supplemental disclosure of cash flow information** | | | |
| Cash paid for interest | $ 50 | $ 35 | $ 46 |
| **Supplemental disclosure of noncash financing activities** | | | |
| Cashless exercise of warrants | $ 53 | $ 2,848 | $ 47 |

*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 seeking to transform innovation into novel treatments that address the needs of patients by discovering and developing small molecule therapeutics for the treatment of infectious diseases and immune system disorders. The Company is devoting substantially all of its efforts towards product research and development.

The Company incurred losses of $441,850 from inception through December 31, 2015 and had an accumulated deficit of $455,712 at December 31, 2015, 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 clinical 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 costs involved in the preclinical and clinical development of the Company's complement inhibitor drug candidates;
- the costs involved in obtaining regulatory approvals for the Company's drug candidates;
- the scope, prioritization and number of programs the Company pursues;
- the costs involved in preparing, filing, prosecuting, maintaining, enforcing and defending patent and other intellectual property claims;
- the timing and amount of proceeds received from milestones achieved and royalties earned, if any, by the Company under its exclusive collaboration and license agreement with Janssen Pharmaceuticals, Inc. ("Janssen");
- 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 currently unknown to the Company.

## 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.

In May 2015, the Company entered into parallel transactions with Janssen and its affiliate, Johnson & Johnson Innovation-JJDC, Inc. ("JJDC"), consisting of (i) an exclusive collaboration and license agreement with Janssen (the "Janssen Agreement") pursuant to which, upon the closing of the transactions contemplated by the Janssen Agreement on June 29, 2015, the Company granted Janssen exclusive worldwide rights to develop and commercialize products that contain one or more of the Company's drug candidates for the treatment of chronic hepatitis C virus ("HCV") infection, namely odalasvir, a second-generation NS5A inhibitor, ACH-3422, a NS5B HCV polymerase inhibitor, and sovaprevir, a NS3/4A HCV protease inhibitor, and (ii) a stock purchase

agreement with JJDC (the "Stock Purchase Agreement") pursuant to which, upon the closing of the transactions contemplated by the Stock Purchase Agreement, JJDC purchased 18,367 shares of the Company's common stock (the "Shares") at a price of $12.25 per share, for an aggregate purchase price of $225,000. The Janssen Agreement became effective on June 29, 2015 upon the early termination of applicable waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended (the "HSR Act"). The Stock Purchase Agreement became effective July 1, 2015. In connection with the closing of the transactions contemplated by the Stock Purchase Agreement, the Company and JJDC entered into an Investor Agreement (the "Investor Agreement") on July 1, 2015.

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 represent a single unit of accounting because they were not viewed to have standalone value. The Janssen Agreement entered into by the Company and Janssen, the Stock Purchase Agreement, and the Investor Agreement were entered into by the Company and Janssen's affiliate 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.

The development, regulatory and sales milestones represent non-refundable amounts that would be paid by Janssen to the Company if certain milestones are achieved in the future. The Company has elected to apply the guidance in ASC 605-28 to the milestones. These milestones, if achieved, are substantive as they relate solely to past performance and are commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of the Company's performance; however, there can be no assurance that Janssen will achieve the milestones or that the Company will receive the related revenue.

***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 qualified 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. To the extent that the amount of the aggregate fair market value of qualified stock options that become exercisable for an individual exceeds $100 during any tax year, those stock options are treated as non-qualified stock options. 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.

For the years ended December 31, 2015 and 2014, the Company based its estimate of the expected term on historical data for similar stock option grants. The Company utilized the simplified method in developing an estimate of the expected term of "plain vanilla" share options for the year ended December 31, 2013. This method was considered appropriate given the Company's limited exercise history. For the years ended December 31, 2015, 2014 and 2013, the Company calculated 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, 2015 and 2014, the Company had $81,725 and $73,664, 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 $377,616 and $79,215 as of December 31, 2015 and 2014, respectively, was valued based on level 2 inputs. The Company's investments consist mainly of corporate debt securities and government sponsored bond obligations. 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, 2015, 2014, and 2013, 100%, 0% and 0%, respectively, of the Company's revenue was generated from the Janssen Agreement. At December 31, 2015, 79% of the Company's accounts receivable was from one collaboration partner.

***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.

The Company did not have any unrecognized tax benefits as of December 31, 2015. 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. The Company is currently evaluating the impact ASU No. 2014-09 will have on its financial position and results of operations.

In August 2014, FASB issued ASU No. 2014-15, "Presentation of Financial Statements – Going Concern." ASU No. 2014-15 provides guidance regarding management's responsibility to evaluate whether there exists substantial doubt about an organization's ability to continue as a going concern and to provide related footnote disclosures in certain circumstances. ASU No. 2014-15 is effective for annual reporting periods beginning after December 15, 2016, and interim periods thereafter. The Company does not believe ASU No. 2014-15 will have a material effect on its financial position and results of operations or disclosures.

In April 2015, FASB issued ASU No. 2015-03, "Interest – Imputation of Interest." ASU No. 2015-03 requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. ASU 2015-03 is effective for financial statements issued for fiscal years beginning after December 15, 2015 (and interim periods within those fiscal years) with early adoption permitted and retrospective application required. The Company does not believe ASU No. 2015-03 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.

Between December 22, 2014 and December 31, 2014, the Company sold 3,236 shares of its common stock pursuant to the Sales Agreement, dated November 8, 2012, between the Company and Cantor Fitzgerald & Co.

(the "Cantor Sales Agreement"). In connection with these sales, the Company received $48,316 in net proceeds. As of December 31, 2014, the Company had $5, 611 in subscriptions receivable, as a portion of the sales under the Cantor Sales Agreement closed in January 2015. In January 2015, the Company received the remaining $5,611 in net proceeds from the portion of the sales that closed in January 2015.

In February 2013, the Company entered into an underwriting agreement (the "Underwriting Agreement") with Citigroup Global Markets, Inc. and Leerink Swann LLC as representatives of the several underwriters named therein (the "Underwriters"), related to a public offering of shares of the Company's common stock, par value $0.001 per share, at a price of $8.40 per share less underwriting discounts and commissions. The Company issued and sold to the Underwriters an aggregate of 16,894 shares of common stock in connection with the Offering. The offering resulted in net proceeds to the Company of $133,211.

## 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, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| | | (in thousands) | |
| Net loss (numerator) | $ (5,030) | $(69,008) | $(58,947) |
| Weighted-average shares, in thousands (denominator) | 125,592 | 98,367 | 93,983 |
| Basic and diluted net loss per share | $ (0.04) | $ (0.70) | $ (0.63) |

Potentially dilutive securities outstanding as of December 31, 2015, 2014 and 2013 are as follows:

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| | | (in thousands) | |
| Stock Options | 8,501 | 9,493 | 9,083 |
| Warrants | 2,833 | 2,844 | 5,338 |

## 5. Collaboration Arrangements

### *Janssen Pharmaceuticals, Inc.*

In May 2015, the Company entered into parallel transactions with Janssen and its affiliate, JJDC, Inc. , consisting of (i) an exclusive collaboration and license agreement with Janssen pursuant to which, upon the closing of the transactions contemplated by the Janssen Agreement on June 29, 2015, the Company granted Janssen exclusive worldwide rights to develop and commercialize products that contain one or more of the Company's 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, and (ii) a stock purchase agreement with pursuant to which, upon the closing of the transactions contemplated by the Stock

Purchase Agreement, JJDC purchased 18,367 shares of the Company's common stock at a price of $12.25 per share, for an aggregate purchase price of $225,000. The Janssen Agreement became effective on June 29, 2015 upon the early termination of applicable waiting periods under the HSR Act. The Stock Purchase Agreement became effective July 1, 2015. In connection with the closing of the transactions contemplated by the Stock Purchase Agreement, the Company and JJDC entered into the Investor Agreement on July 1, 2015.

Under the terms of the Janssen Agreement, the Company is eligible to receive (1) up to $115,000 of milestone payments based upon achievement of clinical enrollment and dosing in specified studies, substantially all of which is related to dosing in one 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 relates to regulatory approval and the first commercial sale in the U.S., and (3) up to an additional $500,000 of milestone payments based upon achieving worldwide sales targets. The Company is also 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. The royalty term is determined on a licensed-product-by-licensed-product and country-by-country basis and begins on the first commercial sale of a licensed product in a country and ends on the expiration of the last to expire of specified patents or regulatory exclusivity covering such licensed product in such country or, with a customary royalty reduction, ten years after such first commercial sale if there is no such exclusivity. Janssen will bear the future costs of worldwide development and commercialization of licensed products, subject to specified exceptions relating to the Company's ongoing studies and technology transfer.

The term of the Janssen Agreement will continue, unless earlier terminated, until expiration of the royalty term for licensed products or all payment obligations under the Janssen Agreement. Janssen may terminate the Janssen Agreement upon 60 days' written notice to the Company at any time prior to submission of the first application for marketing approval for a licensed product in any of the specified major market countries. Janssen may also terminate the Janssen Agreement under specified circumstances relating to the safety or regulatory approvability of a licensed product. Either the Company or Janssen may terminate the Janssen Agreement if the other party is in material breach of the agreement and fails to cure such breach within specified cure periods. Either the Company or Janssen may terminate the Janssen Agreement in the event of specified insolvency events involving the other party. Upon any early termination, rights to the Company's licensed drug candidates will revert to the Company.

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, 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 has determined that license and technology transfer services represent a single unit of accounting because they were not viewed to have standalone value. The Janssen Agreement entered into by the Company and Janssen, the Stock Purchase Agreement, and the Investor Agreement were entered into by the Company and Janssen's affiliate 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 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, 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.

The development, regulatory and sales milestones represent non-refundable amounts that would be paid by Janssen to the Company if certain milestones are achieved in the future. The Company has elected to apply the guidance in ASC 605-28 to the milestones. These milestones, if achieved, are substantive as they relate solely to past performance and are commensurate with estimated enhancement of value associated with the achievement of each milestone as a result of the Company's performance; however, there can be no assurance that Janssen will achieve the milestones or that the Company will receive the related revenue.

Pursuant to the terms of the Investor Agreement, the Shares are subject to a lock-up restriction, such that JJDC agreed it will not, and will also cause its affiliates not to, without the prior approval of the Company, sell, transfer or otherwise dispose of the Shares until the earliest to occur of (i) a specified period after July 1, 2015, (ii) the expiration or earlier termination of the Janssen Agreement or (iii) other specified events. In addition, for the seven year period following the expiration of the lock-up period, subject to specified conditions, the Company has agreed to file a registration statement in order to register all or a portion of the Shares. The Company will not be required to effect more than two such demand registrations for JJDC in the aggregate and is not required to effect more than one such demand registration in any 12 month period. The Company has also agreed to provide JJDC with certain "piggyback" registration rights such that for the seven year period following the expiration of the lock-up period, subject to specified conditions, whenever the Company proposes to register shares of its common stock for its account, JJDC will have the right to include some or all of its Shares in such registration. The Investor Agreement also contains other customary terms and conditions of the parties with respect to the registration of the Shares.

Pursuant to the terms of the Investor Agreement, the Shares are subject to a voting agreement, such that until the earliest to occur of (i) a specified period after July 1, 2015, (ii) the expiration or earlier termination of the Janssen Agreement or (iii) other specified events, and subject to specified conditions and excluding specified extraordinary matters, JJDC will, and will cause its permitted transferees to, vote in accordance with the recommendation of the Company's Board of Directors, or in the case of a meetings of stockholders, if JJDC or a permitted transferee has delivered written notice to the Company at any time prior to the vote on any given matter (but in any event not less than five business days prior to such vote), setting forth its intent to vote on such matter, vote in the same proportion as the votes cast by all other holders of all classes of voting securities of the Company, and JJDC has granted the Company an irrevocable proxy with respect to the foregoing.

In addition, pursuant to the terms of the Investor Agreement, the Shares are subject to a standstill agreement, such that until the earliest to occur of (i) a specified period after July 1, 2015 or (ii) other specified events, neither JJDC nor any of its affiliates, except as expressly approved in writing by the Company, will, subject to specified conditions, directly or indirectly, acquire shares of the Company's outstanding common stock, seek to have called any meeting of the stockholders of the Company, solicit proxies or consents in opposition to the recommendation of a majority of the Company's Board of Directors with respect to any matter or undertake other specified actions related to the potential acquisition of additional equity interests in the Company.

***GCA Therapeutics, Ltd.***

In February 2010, the Company entered into a license agreement (the "Agreement") with GCA Therapeutics, Ltd. ("GCAT") for elvucitabine, the Company's nucleoside reverse transcriptase inhibitor for the treatment of both hepatitis B virus ("HBV") infection and human immunodeficiency virus ("HIV") infection. The

Agreement was amended and restated in March 2010. The exclusive license grants GCAT the right, through a Chinese joint venture with Tianjing Institute of Pharmaceutical Research, to clinically develop and commercialize elvucitabine in mainland China, Hong Kong and Taiwan.

Under the terms of the Agreement, GCAT, through a sublicense agreement with a Chinese joint venture, T&T Pharma Co., Ltd., will assume all development and regulatory responsibility and associated costs for elvucitabine. The Company did not receive any payment upon the signing of the agreement. Upon the first commercial sale of a licensed product GCAT is obligated to pay $100 to the Company. Further, the Company will be eligible to receive royalties up to 15% of net sales in those territories.

The Company does not believe that the milestone specified under the Agreement is substantive as achievement of the milestone is based solely on the performance of GCAT and does not relate to any past or future performance by the Company. Because the Company has no performance obligations under the Agreement, it intends to recognize revenue related to the milestone payment upon achievement of the milestone by GCAT. However, there can be no assurance that GCAT will achieve the milestone or that the Company will receive the related revenue. This Agreement shall be effective, unless earlier terminated, until the expiration of the last to expire royalty term.

***Ora, Inc.***

In October 2012, the Company entered into a license and development agreement (the "Ora Agreement") with Ora, Inc. ("Ora") for the worldwide development and commercialization of ACH-702 delivered topically or locally. The Ora Agreement was amended in April 2013. Under the terms of the Ora Agreement, Ora has assumed development and regulatory responsibility and associated costs for ACH-702. Upon initiation of the agreement, the Company received a one-time license fee of $100, which was recognized as revenue upon the completion of the technology transfer by the Company. The Company is eligible to receive up to $4,000 in development milestones and up to $7,000 in commercialization milestones as well as royalties up to 3.5% of net sales. The Company has no further obligations under the Ora Agreement.

The Ora Agreement includes the right to sublicense any or all of the licensed rights, subject to the Company's approval. Ora has agreed to pay the Company 15% of all up-front licensing payments and any other payment allocated to or received by Ora pursuant to any sublicense agreement granted by Ora under the Ora Agreement; provided that such payment is not a royalty on net sales and not a development or commercial milestone already due to Achillion. In December 2012, Ora entered into a sublicense agreement with Taejoon Pharmaceutical Co. for the development of ACH-702.

The Company does not believe that the milestones specified under the Ora Agreement are substantive as achievement of the milestones is based solely on the performance of Ora and its sublicensee(s) and does not relate to any past or future performance by the Company. Because the Company has no performance obligations under the Ora Agreement, it intends to recognize revenue related to any milestone payments upon achievement of the milestone by Ora or its sublicensee(s). The Ora Agreement shall be effective and, unless earlier terminated, will continue until the last sale of each and every licensed product to an unrelated third party by Ora, its affiliate or sublicensee.

**6. Marketable Securities**

The fair value of the Company's marketable securities of $377,616 and $79,215 as of December 31, 2015 and 2014, respectively, is valued based on level 2 inputs. The Company's investments consist mainly of corporate debt securities and government sponsored bond obligations. Fair value is determined by taking into

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

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, 2014 and 2015. 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 $(45), $(12) and $6 at December 31, 2015, 2014 and 2013, respectively.

As of December 31, 2015, none of the Company's investments were determined to be other than temporarily impaired.

The following table summarizes the Company's investments:

| | December 31, 2015 | | | | December 31, 2014 | | | |
|---|---|---|---|---|---|---|---|---|
| | Amortized Cost | Unrealized Gain | Unrealized (Loss) | Estimated Fair Value | Amortized Cost | Unrealized Gain | Unrealized (Loss) | Estimated Fair Value |
| Commercial Paper | $137,483 | $158 | (6) | $137,635 | $ 4,747 | $3 | — | $ 4,750 |
| Corporate Debt Securities | 164,884 | — | (205) | 164,679 | 58,452 | 1 | (16) | 58,437 |
| Government and Agency Securities | 75,294 | 16 | (8) | 75,302 | 16,028 | 1 | (1) | 16,028 |
| Total | $377,661 | $174 | (219) | $377,616 | $79,227 | $5 | (17) | $79,215 |

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

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| Government | 75,301 | 16,028 |
| Banking | 93,040 | 18,925 |
| Industrial | 209,275 | 44,262 |
| Total | $377,616 | $79,215 |

## 7. Prepaid Expenses and Other Current Assets

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

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| Prepaid research and development costs | $ 487 | $ 221 |
| Tax credit receivable | 640 | 678 |
| Maintenance agreements | 269 | 387 |
| Interest receivable | 1,199 | 551 |
| Other prepaid expenses | 146 | 64 |
| Total | $2,741 | $1,901 |

(in thousands, except per share amounts)

## 8. Fixed Assets, net

A summary of property and equipment is as follows:

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| Laboratory equipment | $ 3,642 | $ 3,461 |
| Office equipment | 1,302 | 989 |
| Leasehold improvements | 3,083 | 3,017 |
| Construction in process | 6 | — |
| | 8,033 | 7,467 |
| Less—accumulated depreciation and amortization | (6,298) | (5,741) |
| Total | $ 1,735 | $ 1,726 |

Depreciation expense was $693, $488 and $390 for the years ended December 31, 2015, 2014 and 2013, respectively.

## 9. Accrued Expenses

Accrued expenses consist of the following:

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| Accrued compensation | $ 4,326 | $ 846 |
| Accrued research and development expenses | 4,743 | 4,727 |
| Accrued professional expenses | 846 | 649 |
| Other accrued expenses | 387 | 224 |
| Total | $10,302 | $6,446 |

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.

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

## 10. Debt

Debt consists of the following:

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| 2011 Credit Facility, payable in equal monthly installments through March 2015, with fixed interest of 6.44% per annum | $ — | $ 56 |
| 2014 Credit Facility, payable in equal monthly installments through October 2017, with fixed interest of 6.30% per annum | 279 | 418 |
| 2014 Credit Facility, payable in equal monthly installments through March 2018, with fixed interest of 6.20% per annum | 175 | — |
| Total long-term debt | 454 | 474 |
| Less: current portion | (223) | (195) |
| Total long-term debt, net of current portion | $ 231 | $ 279 |

In March 2011, the Company entered into a Master Security Agreement for a $2,000 Capital Expenditure Line of Credit, (the "2011 Credit Facility") with Webster Bank ("Webster"). Under the 2011 Credit Facility, the Company could draw down equipment loan advances for the purchase of new laboratory equipment through March 2013. In connection with the Master Security Agreement, the Company granted Webster a security interest in equipment to be purchased under the Credit Facility

In October 2014, the Company entered into a Master Security Agreement for a $1,000 Capital Expenditure Line of Credit (the "2014 Credit Facility") with Webster. Under the 2014 Credit Facility, the Company can draw down equipment loan advances for the purchase of new laboratory equipment through October 2015. In connection with the Master Security Agreement, the Company granted Webster a security interest in equipment to be purchased under the Credit Facility. In October 2014 and March 2015, Webster advanced $440 and $229, respectively, to the Company under the 2014 Credit Facility.

The fair value for this debt is classified as a level 2 measurement. Fair value is computed using a discounted cash flow model based on current interest rates. At this time, the carrying value approximates fair value.

## 11. Capital Structure

### *Preferred Stock*

At December 31, 2015, the Company had 5,000 authorized shares of undesignated preferred stock of which no shares were issued and outstanding.

### *Common Stock*

At December 31, 2015, the Company had 200,000 authorized shares of $0.001 par value common stock of which 136,640 shares were issued and outstanding and 21,813 shares were reserved for future issuance.

### *Warrants*

At December 31, 2015, there were 2,833 warrants outstanding with a weighted average exercise price of $3.12 and a weighted average remaining contractual life of 1.64 years.

***Stock Subscription Receivable***

In December 2014, the Company issued 3,236 shares of common stock under a sales agreement with Cantor Fitzgerald. Sales of the Company's common stock under the agreement with Cantor Fitzgerald were deemed to be "at-the-market" equity offerings as defined in Rule 415 under the Securities Act of 1933, as amended, or the Securities Act. The offering resulted in net proceeds to the Company of $48,316. Of the total proceeds, $5,611 was not received until January 2015 and was recorded as a stock subscription receivable as of December 31, 2014.

In December 2014, the Company issued 19 shares of common stock upon the exercise of stock options. The proceeds of $126 were not received until January 2015 and were recorded as a stock subscription receivable as of December 31, 2014.

**12. 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.

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 Stock Incentive Plan, as amended, (the "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.

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

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 and 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, and other stock-based awards. The Company's officers, employees, consultants, advisors and directors are eligible to receive awards under the 2015 Plan; however, incentive stock options may only be granted to employees.

Options granted under the Company's 1998 Stock Option Plan, 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 ratably over four years.

As of December 31, 2015, there were 8,773 shares available to be granted under the 2015 Plan.

A summary of the status of the Company's stock option activity for the year ended December 31, 2015 is presented in the table and narrative below:

| | 2015 | |
|---|---|---|
| | Options | Weighted Average Exercise Price |
| Outstanding at January 1, 2015 | 9,493 | $ 6.88 |
| Granted | 213 | 9.14 |
| Exercised | (835) | 4.47 |
| Forfeited | (297) | 7.93 |
| Cancelled | (73) | 12.60 |
| Outstanding at December 31, 2015 | 8,501 | $ 7.08 |
| Options exercisable at December 31, 2015 | 5,642 | $ 6.39 |
| Options vested and expected to vest at December 31, 2015 | 8,083 | $ 7.05 |

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

The following table summarizes information about stock options outstanding at December 31, 2015:

| | 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 | 137 | 3.0 | $ 1.05 | 137 | $ 1.05 |
| $2.01 – $4.00 | 3,279 | 6.6 | 3.07 | 2,288 | 3.08 |
| $4.01 – $6.00 | 367 | 2.2 | 5.16 | 364 | 5.15 |
| $6.01 – $8.00 | 1,754 | 6.8 | 7.45 | 1,347 | 7.42 |
| $8.01 – $10.00 | 1,033 | 7.3 | 8.73 | 742 | 8.68 |
| $10.01 – $12.00 | 125 | 8.6 | 10.51 | 41 | 10.70 |
| $12.01 – $14.00 | 1,502 | 8.9 | 13.44 | 419 | 13.43 |
| $14.01 – $16.00 | 301 | 1.0 | 14.75 | 301 | 14.75 |
| $16.01 – $20.00 | 3 | 1.1 | 19.00 | 3 | 19.00 |
| | 8,501 | 6.7 | $ 7.08 | 5,642 | $ 6.39 |

As of December 31, 2015, the intrinsic value of the options outstanding and options vested was $36,733 and $27,139, respectively. 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, 2015, 2014 and 2013 was $5,302, $7,855 and $790, respectively.

The weighted-average, grant-date fair value of options granted during the years ended December 31, 2015, 2014 and 2013 was $6.66, $8.50 and $3.29, respectively. The weighted-average, grant-date fair value of options vested at December 31, 2015, 2014 and 2013 was $4.64, $4.13 and $3.52, respectively.

The weighted average remaining contractual life is 5.9 years for options exercisable and 6.7 years for options vested and expected to vest.

*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 is also required to estimate forfeitures at the grant date and recognize compensation costs for only those awards that are expected to vest. Judgment is required in estimating the amount of stock-based awards that are expected to be forfeited. For the years ended December 31, 2015 and 2014, the Company based its estimate of the expected term on historical data for similar stock option grants. The Company utilized the simplified method in developing an estimate of the expected term of "plain vanilla" share options for the year ended December 31, 2013. This method was considered appropriate given the Company's limited exercise history. For the years ended December 31, 2015, 2014 and 2013, the Company calculated volatility based on actual volatility for the expected term of the option.

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

The assumptions used to value options granted are as follows:

| | For the Years Ended December 31, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| Expected term of option | 6.25 years | 5.0 – 6.25 years | 5.0 – 6.1 years |
| Expected volatility | 84% – 91% | 92% – 96% | 87% – 94% |
| Risk free interest rate | 1.54 – 1.93% | 1.81 – 2.02% | 1.01 – 2.10% |
| 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, 2015, 2014 and 2013 was $9,887, $7,177 and $5,760, 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, 2015, 2014 and 2013 was $25, $0 and $69, 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, 2015, the total compensation cost related to options not yet recognized in the financial statements is approximately $15,333, net of estimated forfeitures, and the weighted average period over which it is expected to be recognized is 1.4 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, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| Research and development | $4,346 | $2,713 | $2,146 |
| General and administrative | 5,567 | 4,464 | 3,682 |
| Total | $9,913 | $7,177 | $5,828 |

*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 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 Plan consists of the 15% of the grant date stock price discount and the fair value of the option features.

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

The Company recorded compensation cost related to 2006 ESPP Plan of $160, $96 and $92 for the years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, there were 1,706 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, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| Expected term of option | 6 months | 6 months | 6 months |
| Expected volatility | 57% – 88% | 67% – 130% | 47% – 141% |
| Risk free interest rate | 0.07 – 0.08% | 0.06 – 0.08% | 0.11 – 0.14% |
| Expected dividend yield | 0% | 0% | 0% |

## 13. 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.

## 14. Other License and Research and Development Agreements

The Company has entered into certain non-exclusive HCV license and collaborative research agreements with third parties relating to the Company's drug discovery and development initiatives. Under these agreements, the Company has been granted certain worldwide non-exclusive licenses to use the licensed compounds or technologies. Included in the accompanying 2015, 2014 and 2013 statements of comprehensive loss is $115, $140 and $140, respectively, of research and development expense resulting from these arrangements. In order to maintain its rights under these agreements, provided that the Company does not terminate such agreements, the Company will also be required to pay an additional $100 of aggregate minimum payments over the next five years.

In February 2000, the Company entered into a license agreement with Vion Pharmaceuticals, ("Vion"), pursuant to which it obtained a worldwide exclusive sublicense from Vion on the composition of matter and use of elvucitabine. Vion's license rights were granted to it by Yale University, ("Yale"). Upon the dissolution of Vion in a 2011 bankruptcy, the Company became a direct licensee of Yale. This license covers the use of elvucitabine alone, as a pharmaceutical composition containing elvucitabine alone, or its use as monotherapy to treat HIV. Yale has retained rights to utilize the intellectual property licensed by this agreement for its own noncommercial purposes. Through December 31, 2015, the Company has made aggregate payments of $35 to Yale under this agreement, including a $10 initial license fee and a $25 development milestone payment. Under the terms of the agreement, the Company may be required to make additional milestone payments to Yale of up to an aggregate of $850 for each licensed product based on the achievement of specified development and regulatory approval milestones. The Company is also required to pay Yale specified royalties on net product sales and a specified share of sublicensing fees that it receives under any sublicenses that it grants. No other payments are included in the Company's financial statements as these payments are contingent on the achievement of certain milestones that have not yet been reached.

In July 2002, the Company entered into a license agreement with Emory University ("Emory"), pursuant to which it obtained a worldwide exclusive license under specified licensed patents to use elvucitabine in combination with other antivirals. Under the license, Emory retains a right to use the intellectual property for educational and research purposes only and also retains the right to approve sublicenses under specified

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

circumstances. Through December 31, 2015, the Company has made aggregate payments of $150 to Emory under this agreement, including an initial license fee of $100 and a development milestone payment of $50. The Company may also be required to make additional payments of up to an aggregate of $400 based on the achievement of specified development and regulatory approval milestones. Under this agreement, the Company is also required to pay Emory specified royalties on net product sales and a specified share of sublicensing fees that it receives under any sublicenses that it grants. As these payments are contingent on the achievement of certain milestones that have not yet been reached, the related amounts are not recognized as expense in the accompanying financial statements.

## 15. 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 $296, $262 and $238 for the years ended December 31, 2015, 2014 and 2013, respectively.

### *Operating Leases*

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 $72 and $83 at December 31, 2015 and 2014, respectively.

The future minimum annual lease payments under this operating lease at December 31, 2015 are as follows:

| **Year Ended December 31,** | |
|---|---|
| 2016 | $ 770 |
| 2017 | $ 814 |
| 2018 | $ 814 |
| 2019 | $ 814 |
| 2020 | $ 203 |
| Total | $3,415 |

Rent expense under operating leases was $629, $617, and $617, for the years ended December 31, 2015, 2014 and 2013, 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, 2015, there are no active matters.

On May 5, 2014, without any settlement payment by the Company, any individual defendant or any third party on their behalf, the lead plaintiffs in the previously disclosed consolidated class action lawsuit originally filed in October 2013 against the Company and certain of its current and former officers in the United States District Court for the District of Connecticut voluntarily dismissed all of their claims without prejudice. The Court approved the voluntary dismissal and closed the case on May 6, 2014. A dismissal without prejudice does not prevent the litigation of the same claims in a subsequent action.

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

## 16. 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.

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

| | As of December 31, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| Deferred: | | | |
| Federal and state | $ 699 | $ 29,287 | $ 28,554 |
| Valuation allowance | (699) | (29,287) | (28,554) |
| Total deferred | $ — | $ — | $ — |

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

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2015 | 2014 | 2013 |
| Federal statutory rate | (34.0)% | (34.0)% | (34.0)% |
| State tax, net of federal benefit | (5.0) | (5.0) | (5.0) |
| Other | 0.52 | 0.07 | 0.07 |
| Share-based compensation | 2.84 | (0.56) | 2.90 |
| Valuation allowance | 35.64 | 39.49 | 36.03 |
| | 0% | 0% | 0% |

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

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

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| **Gross deferred tax assets:** | | |
| Net operating losses | $ 151,076 | $ 154,019 |
| Tax credits (federal and state) | 12,977 | 11,419 |
| Share-based compensation | 7,643 | 5,378 |
| Other | 419 | 601 |
| | $ 172,115 | $ 171,417 |
| Less—valuation allowance | (172,115) | (171,417) |
| Net deferred tax asset | $ — | $ — |

At December 31, 2015 and 2014, the Company had gross deferred income tax assets of approximately $172,115 and $171,417, 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.

At December 31, 2015 and 2014, the Company had available the following net operating loss and credit carryforwards:

| | As of December 31, | |
|---|---|---|
| | 2015 | 2014 |
| Federal net operating loss carryforwards | $351,977 | $360,598 |
| State net operating loss carryforwards | 418,720 | 418,879 |
| Federal research and development credit carryforwards | 8,337 | 7,007 |
| State research and development credit carryforwards | 4,640 | 4,412 |

The Company's federal net operating loss carryforwards expire commencing in 2018 through 2035 and state net operating loss carryforwards which expire commencing in 2020 through 2035. The Company's federal research and development credit carryforwards expire commencing in 2028 through 2034. 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"). Although these windfalls are reflected in net operating loss carryforwards, the additional tax benefit associated with the windfall is not recognized until the deduction reduces taxes payable. Accordingly, approximately $14,345 of the net operating loss carryforwards available, if realized, would be credited to additional paid-in capital.

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. These ownership changes may limit the amount of net operating losses and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. The Company completed a review of its changes in ownership through December 31, 2011, and determined that it had three ownership changes since inception. The changes of ownership will result in approximately $55,429 of net operating loss carryforwards that the Company expects to expire unutilized and approximately $4,066 of research and development credit carryforwards that the Company expects to expire unutilized. The Company had historically recorded a valuation allowance against the net operating losses and research and development carryforwards. This resulted in no change to the income statement, with a change to footnote disclosure only. 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 2004 through 2015 in federal and the State of Connecticut jurisdictions.

The Company did not have any unrecognized tax benefits as of December 31, 2014 and 2015.

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. During the years ended December 31, 2015, 2014 and 2013, the Company recorded a benefit of approximately $640, $678 and $183, respectively, for the estimated proceeds from this exchange. This benefit is recorded as a reduction of research and development expenditures.

## 17. 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.

As of December 31, 2015, Domain was the beneficial owner of approximately 4% of the Company's total issued and outstanding shares of common stock.

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

## 18. Unaudited Quarterly Results

The following tables summarize unaudited quarterly financial data for the years ended December 31, 2015 and 2014. 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.

| | 2015 Quarters | | | |
|---|---|---|---|---|
| | First | Second | Third (1) | Fourth (1) |
| Total operating revenue | $ — | $ 711 | $ 33,820 | $ 31,591 |
| Total operating expenses | 19,399 | 29,899 | 16,839 | 15,092 |
| Net income (loss) | (19,263) | (28,978) | 26,259 | 16,952 |
| Net loss per share—basic and diluted | $ (0.17) | $ (0.25) | $ 0.19 | $ 0.12 |
| Weighted average number of shares outstanding—basic | 111,202 | 117,770 | 136,438 | 136,558 |
| Weighted average number of shares outstanding—diluted | 111,202 | 117,770 | 140,024 | 140,475 |

| | 2014 Quarters | | | |
|---|---|---|---|---|
| | First | Second | Third | Fourth |
| Total operating revenue | $ — | $ — | $ — | $ — |
| Total operating expenses | 16,235 | 15,766 | 15,764 | 21,661 |
| Net loss | (16,088) | (15,657) | (15,667) | (21,596) |
| Net loss per share—basic and diluted | $ (0.17) | $ (0.16) | $ (0.16) | $ (0.21) |
| Weighted average number of shares outstanding—basic | 96,792 | 97,017 | 99,031 | 100,579 |
| Weighted average number of shares outstanding—diluted | 96,792 | 97,017 | 99,031 | 100,579 |

(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. Also refer to footnote 5.

## EXHIBIT INDEX

| | Exhibit No. | Description | Incorporated by Reference | | | Filed with this 10-K |
|---|---|---|---|---|---|---|
| | | | Form | SEC Filing date | Exhibit Number | |
| | 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 | License Agreement, dated as of February 3, 2000, by and between Vion Pharmaceuticals, Inc. and the Registrant, as amended on January 28, 2002. | S-1 | 03/31/06 | 10.2 | |
| | 10.2 | Letter Agreement, dated as of September 22, 2006, by and between the Registrant and Yale University. | S-1/A | 10/10/06 | 10.2.1 | |
| † | 10.3 | Collaboration and License Agreement, dated May 19, 2015, between the Registrant and Janssen Pharmaceuticals, Inc. | 10-Q | 08/10/15 | 10.2 | |
| | 10.4 | Stock Purchase Agreement, dated May 19, 2015, between the Registrant and Johnson & Johnson Innovation-JJDC, Inc. | 10-Q | 08/10/15 | 10.3 | |
| † | 10.5 | Investor Agreement, dated July1, 2015, between the Registrant and Johnson & Johnson Innovation-JJDC, Inc. | 10-Q | 08/10/15 | 10.4 | |
| | 10.6 | Form of Common Warrant issued by the Registrant pursuant to the Securities Purchase Agreement dated as of August 18, 2010. | S-3 | 09/17/10 | 10.2 | |
| | 10.7 | 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 | |
| | 10.8 | Master Security Agreement between the Registrant and Webster Bank, National Association, dated as of October 3, 2014. | 8-K | 10/03/14 | 10.1 | |
| | 10.9 | 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 | |
| | 10.10 | 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 | |
| | 10.11 | 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 | |
| # | 10.12 | 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 | |
| # | 10.13 | Form of Nonstatutory Stock Option Agreement under the 2006 Stock Incentive Plan. | 8-K | 12/22/10 | 99.1 | |

| | Exhibit No. | Description | Incorporated by Reference | | | Filed with this 10-K |
|---|---|---|---|---|---|---|
| | | | Form | SEC Filing date | Exhibit Number | |
| # | 10.14 | Form of Incentive Stock Option Agreement under the 2006 Stock Incentive Plan. | 8-K | 12/22/10 | 99.2 | |
| # | 10.15 | 2015 Stock Incentive Plan, dated June 2, 2015. | 8-K | 06/08/15 | 10.1 | |
| # | 10.16 | Form of Incentive Stock Option Agreement under the 2015 Stock Incentive Plan. | | | | X |
| # | 10.17 | Form of Nonstatutory Stock Option Agreement under the 2015 Stock Incentive Plan. | | | | X |
| # | 10.18 | Second Amended and restated Employment Agreement and Supplemental Severance Agreement, dated March 9, 2010, and Supplemental Terms of Compensation, dated April 5, 2011, between the Registrant and Mary Kay Fenton. | 8-K | 04/08/11 | 10.2 | |
| # | 10.19 | Employment Agreement, dated April 5, 2011, between the Registrant and Joseph Truitt. | 8-K | 04/08/11 | 10.6 | |
| # | 10.20 | Employment Agreement, dated May 6, 2013 between the Registrant and David Apelian. | 8-K | 05/30/13 | 10.1 | |
| # | 10.21 | Employment Agreement, dated May 28, 2013 between the Registrant and Milind Deshpande. | 8-K | 05/30/13 | 10.2 | |
| # | 10.22 | Letter Agreement, dated May 23, 2014, between the Registrant and Milind Deshpande. | 10-Q | 08/07/14 | 10.1 | |
| # | 10.23 | Employment Agreement, dated January 2, 2016 between the Registrant and Joel Barrish. | | | | X |
| # | 10.24 | Employment Agreement, dated February 1, 2016 between the Registrant and Martha Manning. | | | | X |
| # | 10.25 | Non-Executive Directors Compensation Policy, dated January 23, 2016. | | | | X |
| | 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 |

| | | Incorporated by Reference | | | |
|---|---|---|---|---|---|
| Exhibit No. | Description | Form | SEC Filing date | Exhibit Number | Filed with this 10-K |
| 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, 2015 and December 31, 2014, (ii) Statements of Comprehensive Loss for the years ended December 31, 2015, 2014 and 2013, (iii) Statements of Stockholders' Equity and Comprehensive Loss for the years ended December 31, 2013, 2014 and 2015, (iv) Statements of Cash Flows for the years ended December 31, 2015, 2014 and 2013 and (v) Notes to Financial Statements.

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**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**
**President and Chief Executive Officer**

Dated: February 25, 2016

**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 25, 2016

**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, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Milind S. Deshpande, President and 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 25, 2016

/s/ MILIND S. DESHPANDE

**Milind S. Deshpande**
**President and 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, 2015 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 25, 2016

/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.

# Corporate Information

## EXECUTIVE MANAGEMENT AND CORPORATE OFFICERS

**Milind Deshpande, Ph.D.**
President and Chief Executive Officer

**David Apelian, M.D., Ph.D.**
Executive Vice President and
Chief Medical Officer

**Joel C. Barrish, Ph.D.**
Executive Vice President and
Chief Scientific Officer

**Mary Kay Fenton**
Executive Vice President and
Chief Financial Officer

**Martha E. Manning, Esq.**
Executive Vice President,
General Counsel and Corporate Secretary

**Joseph Truitt**
Executive Vice President and
Chief Commercial Officer

**Michael Banks, Ph.D.**
Senior Vice President,
Pharmaceutical Sciences

**Amy Jennings, Ph.D.**
Senior Vice President, Regulatory Affairs

**Ky Nam-Wortman**
Vice President, Head of Human Resources

**Maira Rieger**
Vice President, Portfolio Management

## BOARD OF DIRECTORS

**David I. Scheer, Chairman of the Board**
President
Scheer & Co., Inc.

**Milind Deshpande, Ph.D.**
President and Chief Executive Officer
Achillion Pharmaceuticals, Inc.

**Jason Fisherman, M.D.**
President and Chief Executive Officer
C4 Therapeutics, Inc.

**Gary E. Frashier**
President
Management Associates

**Kurt Graves**
Chief Executive Officer
Intarcia Therapeutics

**Michael D. Kishbauch**
Former President and
Chief Executive Officer of
Achillion Pharmaceuticals, Inc.

**Robert L. Van Nostrand**
Former Chief Financial Officer
of Aureon Laboratories,
AGI Dermatics and
OSI Pharmaceuticals

**Frank Verwiel, M.D.**
Former President and
Chief Executive Officer of
Aptalis Pharma

**Nicole Vitullo**
Partner
Domain Associates

## CORPORATE COUNSEL
Wilmer Cutler Pickering Hale and Dorr LLP
New York, NY

## INDEPENDENT AUDITORS
PricewaterhouseCoopers LLP
Hartford, CT

## TRANSFER AGENT & REGISTRAR
Computershare Shareholder Services, Inc.
(781) 575-2879
P.O. Box 30170
College Station, TX 77842-3170

## CORPORATE HEADQUARTERS
300 George Street
New Haven, CT 06511
Main: 203.624.7000

## INVESTOR RELATIONS
Glenn Schulman, Pharm.D., M.P.H.
gschulman@achillion.com
Direct: 203.752.5510

## COMMON STOCK
Achillion Pharmaceuticals, Inc.
common stock trades on the
NASDAQ Global Select Market
under the symbol ACHN

## ANNUAL MEETING
Wednesday, May 25, 2016
9:00 a.m. Eastern Daylight Time
300 George Street
New Haven, CT 06511

### Important Note About Forward-Looking Statements

This report contains forward looking statements regarding our research and development programs, operating results, financial condition, business strategies and prospects. You can identify these forward looking statements by such terms as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "project," "should," "will," "would" or other words that convey uncertainty of future events or outcomes. Our actual results may differ materially from those indicated by these forward-looking statements as a result of various important factors, including: our ability to complete the development of our drug candidates under the timelines we anticipate in current and future clinical trials; our ability to obtain requisite marketing approvals for our product candidates, whether alone or in collaboration with others; our ability to obtain patent protection for our drug candidates and freedom to operate under third party intellectual property; our ability to identify, enter into and successfully maintain collaboration agreements with appropriate third-parties, including our current agreement with Janssen; our ability to raise the additional capital needed to achieve our business objectives; our ability to manage competition; and other risks we describe from time to time in our SEC filings. These and other risks are described in greater detail under the heading "Risk Factors" in the accompanying Annual Report on Form 10-K.

Achillion does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

Achillion Pharmaceuticals, Inc.
300 George Street
New Haven, CT 06511

**www.achillion.com**