Achaogen Inc
Form 10-K
March 16, 2015

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549
FORM 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2014
OR

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE TRANSITION PERIOD FROM ___ TO ___ .
Commission file number 001-36323
ACHAOGEN, INC.
(Exact name of registrant as specified in its charter)

Delaware	68-0533693
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

7000 Shoreline Court, Suite 371
South San Francisco, CA 94080
(Address of principal executive offices including zip code)
650-800-3636
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Name of each exchange on which registered
Common Stock, $0.001 par value	The NASDAQ Global 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 o No x
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 o No x
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.
Yes x No o

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of 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. o.

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

Large accelerated Filer o	Accelerated Filer o
Non-accelerated Filer x	Smaller Reporting Company o

(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in 12b-2 of the Act).

Yes o No x

The aggregate market value of the common stock held by non-affiliates computed by reference to the last reported sale price on June 30, 2014 was approximately $222.9 million. As of March 2, 2015, there were 18,030,027 shares of the registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Certain information required by Part III of the Annual Report on Form 10-K is incorporated by reference to the registrant's definitive proxy statement for the registrant's 2015 annual meeting of stockholders, which will be filed with the Securities and Exchange Commission not later than 120 days after the close of the registrant's fiscal year ended December 31, 2014.

ACHAOGEN, INC.
ANNUAL REPORT ON FORM 10-K
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Part I

Forward-Looking Statements

This Annual Report on Form 10-K, including “Business” in Part I, Item I and “Management's Discussion and Analysis of Financial Condition and Results of Operations” in Part II, Item 7, contains “forward-looking statements” within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended (the “Exchange Act”). All statements other than statements of historical facts contained in this Annual Report on Form 10-K are statements that could be deemed forward-looking statements reflecting the current beliefs and expectations of management with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. These statements are often identified by the use of words such as “may,” “will,” “expect,” “believe,” “anticipate,” “intend,” “could,” “should,” “estimate,” or “continue expressions or variations. The risks and uncertainties referred to above include, without limitation, risks related to our research and development efforts, need for future capital, timely completion of our clinical trials, uncertainty of clinical trial results or regulatory approvals or clearances, manufacturing of our product candidates at scales and costs appropriate for commercialization, enforcement of our patent and proprietary rights, potential competition and other risks that are described herein and that are otherwise described from time to time in our Securities and Exchange Commission (“SEC”) reports including, but not limited to, the factors described in Item 1A, “Risk Factors,” of this Annual Report. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company passionately committed to the discovery, development, and commercialization of novel antibacterials to treat multi-drug resistant ("MDR") gram-negative infections. We are developing plazomicin, our lead product candidate, for the treatment of serious bacterial infections due to MDR Enterobacteriaceae, including carbapenem-resistant Enterobacteriaceae ("CRE"). In 2013, the Centers for Disease Control and Prevention identified CRE as a "nightmare bacteria" and an immediate public health threat that requires "urgent and aggressive action." The first patient was enrolled in our Phase 3 CARE (Combating Antibiotic Resistant Enterobacteriaceae) trial of plazomicin in the third quarter of 2014. Through the Special Protocol Assessment procedure, the U.S. Food and Drug Administration ("FDA") has agreed that the design and planned analyses of our Phase 3 CARE trial adequately address objectives in support of a New Drug Application ("NDA"). In 2012, the FDA granted fast track designation for the development and regulatory review of plazomicin to treat serious and life-threatening CRE infections. In 2014, plazomicin received Qualified Infectious Disease Product ("QIDP") designation from the FDA. The QIDP designation was created by the Generating Antibiotic Incentives Now (GAIN) Act, which was part of the FDA Safety and Innovation Act ("FDASIA") and provides certain incentives for the development of new antibiotics, including priority review and an additional five years of market exclusivity. Our plazomicin program is funded in part with a contract from the Biomedical Advanced Research and Development Authority ("BARDA") for up to $103.8 million. We have global commercialization rights to plazomicin, which has patent protection in the United States extending through 2031. Plazomicin is the first clinical candidate from our gram-negative antibiotic discovery engine, and we have other programs in early and late preclinical stages focused on other MDR gram-negative infections.

According to government agencies and physician groups, including the Centers for Disease Control and Prevention ("CDC") and the Infectious Disease Society of America, one of the greatest needs for new antibiotics is to treat CRE and other drug-resistant gram-negative pathogens. CRE leads to mortality rates of up to 50% in patients with bloodstream infections. We estimate that there were approximately 125,000 cases of CRE infections in the United States and five major markets in the European Union in 2014, with approximately one-fourth of these being bloodstream infections or pneumonia. Based on the significant increase in resistance rates in recent years, we anticipate CRE will continue to be a major health problem. For example, CDC surveillance data indicates that the rate of carbapenem resistance in Klebsiella species, a member of Enterobacteriaceae, increased from 1.6% to 10.4% in the hospital setting in the United States between 2001 and 2011. In Italy, K. pneumoniae carbapenem resistance rates

more than doubled from 16% in 2010 to 36% in 2013. Governments, in collaboration with the private sector, have begun to respond by progressing regulatory reform and economic incentives to spur development of new antibiotics. Plazomicin is a novel intravenous aminoglycoside antibiotic. Aminoglycosides have been used successfully for the treatment of serious infections for more than 50 years. However, the widespread clinical resistance to currently marketed aminoglycosides has increasingly limited their utility. We developed plazomicin by chemically modifying sisomicin, a naturally occurring aminoglycoside, in order to overcome common aminoglycoside resistance mechanisms. In MDR Enterobacteriaceae, including CRE, plazomicin

remains active where most other antibiotics, including the commercially available aminoglycosides, have limited potency due to resistance.

We consider the following to be key attributes that support the clinical utility and commercial value of plazomicin:

- Potent activity in nonclinical studies against MDR Enterobacteriaceae, including CRE.
- Demonstration of comparable efficacy to levofloxacin and acceptable safety in a Phase 2 clinical trial in patients with complicated urinary tract infections caused primarily by non-resistant Enterobacteriaceae.
- Improved dosing strategy as compared to existing aminoglycosides, and individualized patient dosing using our in vitro assay.
- Potential to demonstrate a mortality benefit over currently available therapy in the treatment of life-threatening CRE infections.
- Potential to reduce the healthcare costs associated with the treatment of such infections.

Our Phase 3 CARE trial is a pathogen-specific trial designed to enroll patients with a high risk of mortality and, if successful, provide clinical evidence of the superiority of plazomicin versus the best currently available therapy for life-threatening bloodstream infections and pneumonia due to CRE. We believe that positive efficacy data from this trial would provide the basis for FDA approval and could position plazomicin as a standard of care for the treatment of serious CRE infections.

Our goal is to report top-line data from our Phase 3 CARE trial in 2017. The first patients were enrolled in our Phase 3 CARE trial of plazomicin in September 2014; however, enrollment continues at a rate that has been slower than anticipated. We have been exploring strategies to improve patient recruitment and remain in discussions with the FDA regarding potential modifications to the study design as well as additional clinical trials that could support and, possibly, facilitate regulatory filings for plazomicin. We currently expect to provide an update on our development plans for plazomicin by early in the second quarter of 2015.

CRE are one of many types of MDR gram-negative pathogens threatening patients. Bacteria such as Pseudomonas aeruginosa, Acinetobacter baumannii, and extended-spectrum beta-lactamase producing Enterobacteriaceae, each pose "serious" resistance threats, according to the CDC, and also drive a great need for new, safe, and effective antibiotics. We have assembled the expertise and capabilities required, including chemistry and microbiology, to develop new agents for the treatment of gram-negative infections. Plazomicin was the first clinical candidate from our gram-negative antibiotic discovery engine. In addition, our research and development pipeline includes two programs that specifically target Pseudomonas aeruginosa or Acinetobacter baumannii infections: a program to discover and develop small molecule inhibitors of LpxC, which is an enzyme essential for the synthesis of the outer membrane of gram-negative bacteria, and a therapeutic antibody program.

Strategy

Our strategy is to discover, develop, and commercialize new antibacterials for the treatment of gram-negative bacterial infections. Key elements of our strategy are as follows:

- Complete the studies of plazomicin necessary to obtain regulatory approval in both the United States and the European Union. We have held discussions with the FDA and the EMA regarding additional clinical trials that could support regulatory filings for plazomicin. If the clinical program is successful, we expect to prepare and submit an NDA to the FDA and a Marketing Authorization Application ("MAA") to the EMA. Through the Special Protocol Assessment ("SPA") procedure, the FDA has agreed that the design and planned analyses of our Phase 3 CARE trial could support an NDA. In 2012, the FDA granted fast track designation for the development and regulatory review of plazomicin to treat serious and life-threatening CRE infections. In 2014, plazomicin received QIDP designation from the FDA.
- Demonstrate improved clinical benefit and pharmacoeconomic advantages of our product candidates over existing therapies. By selecting product candidates with potency against MDR pathogens, we have the opportunity to demonstrate superior clinical outcomes against the current standard of care. This is in contrast to most other antibiotics currently marketed or under clinical development, which were tested, or are being tested, in non-inferiority trial designs. We also plan to demonstrate the economic benefits of our product candidates based on pharmacoeconomic outcomes such as fewer days on mechanical ventilation, less time in an intensive care unit

("ICU"), or shorter total hospital stay. For example, our Phase 3 CARE trial of plazomicin is designed to demonstrate improved mortality outcomes of plazomicin over comparator therapy and will allow us to assess improved pharmacoeconomic outcomes from plazomicin treatment.

- Commercialize our products directly, either alone or with support from a commercialization partner, in the United States and through commercialization partners elsewhere. We have global commercialization rights to all of our drug candidates. If approved, we intend to commercialize plazomicin directly, either alone or with support from a commercialization partner, using a targeted hospital-based sales force in the United States, where CRE infections are

concentrated in resistance hotspots, including New York City, Chicago, and other major population centers. Outside the United States, we intend to license full product rights to global and regional commercialization partners who can help us develop and market our products. By collaborating with companies that have an existing commercial presence and experience in targeted geographic markets, we believe we can efficiently maximize the commercial potential of our products.

- Establish and leverage collaborations with non-commercial organizations for scientific expertise and funding support. We collaborate with government agencies and non-profit foundations to support our discovery efforts and advance the product candidates in our pipeline. We are currently receiving funding support for up to $103.8 million from a contract with BARDA for the development of plazomicin as a countermeasure for diseases caused by antibiotic-resistant pathogens and biothreats, such as pneumonic plague and tularemia. We have also received funding support from government agencies such as the U.S. Department of Defense ("DOD"), the U.S. National Institutes of Health ("NIH"), and The Wellcome Trust, a global charitable foundation. We also partner with leading academics, scientists, and clinicians to enhance our internal discovery and development expertise, and to jointly sponsor funding proposals.
- Build a portfolio of differentiated products for the treatment of MDR gram-negative infections. Since we commenced operations in 2004, we have focused on the discovery and development of antibiotics to treat gram-negative infections and have developed proprietary know-how about the relationship between compound structure and potency against gram-negative bacteria through our work on multiple antibiotic classes. We are using this expertise to build a portfolio of product candidates for the treatment of infections due to MDR pathogens. Patients with these infections have limited or inadequate therapeutic options leading to high rates of morbidity and mortality. We believe the greatest unmet medical needs lie among infections due to MDR gram-negative bacteria, where there is a significant and growing problem and the industry pipeline of drug candidates is sparse.

Antibacterials Background

Antibacterials, which we refer to interchangeably as antibiotics, are drugs used to treat infections that are caused by bacteria. The introduction of antibiotics is recognized as one of the most transformative events in medicine. Prior to the introduction of the first antibiotics in the 1930s and 1940s, bacterial infections were often fatal, and invasive surgery was accompanied by a high risk of infectious complications. Today, antibacterials are used routinely to treat and prevent infection. According to IMS Health, antibiotics accounted for $38.8 billion in sales globally in 2012, with healthcare providers prescribing 268 million courses of antibacterials in the United States alone.

There are two main varieties of bacteria, based on a common laboratory staining test known as the "Gram stain." Gram-positive bacteria are surrounded by a single lipid membrane and a thick cell wall. Common gram-positive pathogens include Staphylococcus aureus (including methicillin-resistant strains), Streptococcus species, and Clostridium difficile. In contrast, gram-negative bacteria are encircled by two lipid membranes, an inner membrane and an outer membrane, with a thinner cell wall in between. Gram-negative bacteria include P. aeruginosa, A. baumannii, and the Enterobacteriaceae, a family of related organisms that includes E. coli, K. pneumoniae, Enterobacter, Salmonella, and Shigella species. Drugs that act in the cytoplasm of gram-negative bacteria must cross both the inner and outer membranes, as distinct from drugs that just act on gram-positive bacteria, which only have to cross one membrane. Each membrane in gram-negative bacteria excludes different types of chemical entities, requiring gram-negative active antibiotics to be specifically designed to permeate both membranes. A 2007 study found that in hospital intensive care units worldwide, approximately 54% of bacterial infections were caused by gram-negative organisms and 41% by gram-positive organisms, with the remainder caused by other types of bacteria.

Antibiotics are evaluated according to several criteria:

- Spectrum. Antibiotics that are effective against a wide variety of bacteria, including both gram-negative and gram-positive organisms, are considered to be broad-spectrum, while those that act upon only a limited number of species are considered to be narrow-spectrum. Narrow-spectrum antibiotics are most often selected if a specific pathogen is suspected or confirmed.
- Cidality. Antibiotic action generally falls into two categories: bacteriostatic and bactericidal. Bacteriostatic antibiotics halt the growth of bacteria, requiring the human immune system to clear the infection. Bactericidal antibiotics kill the bacterial pathogen directly and are preferred when the patient’s immune system is not functioning optimally.

In vitro Microbiological activity. This is the ability of the antibiotic to kill or inhibit growth of bacteria in vitro. In vitro experiments and assays do not take into account the complex interactions that occur in animals or human, but are relatively easy to perform in the laboratory and usually constitute the extent of routine microbiological testing in hospital laboratories. Potency, which relates drug concentrations to activity, is commonly expressed as the minimum inhibitory concentration ("MIC") in µg/mL, which is the lowest concentration at which the drug inhibits growth of the bacteria. Antibiotics with lower MICs are considered to be more potent.

- Susceptibility/non-susceptibility. The relationship between microbiological activity and the clinical utility of an antibiotic in the hospital setting can be described in terms of susceptibility or non-susceptibility. A susceptible MIC value indicates a high probability that an antibiotic can be used to treat a particular infection. A non-susceptible MIC value from in vitro testing suggests the antibiotic is unlikely to be effective against the causative pathogen and thus should be use cautiously and under supervision of an infectious disease specialist. The MIC values defining susceptibility are established by FDA on approval of new antibiotics and medical standards organizations including the Clinical Laboratory and Standards Institute ("CLSI"), and the European Committee on Antimicrobial Susceptibility Testing ("EUCAST").
- Resistance. Resistance generally indicates the inability of an antibiotic to effectively treat an infection at usually administered doses. Some bacteria are naturally resistant to certain types of antibiotics. Resistance can also occur due to genetic mutations or changes in gene expression. Mechanisms responsible for resistance are often found together and can be transferred between different bacteria, leading to multi-drug resistance.

New Antibiotics Are Needed for Resistant Gram-negative Infections

According to the CDC, at least two million people each year in the United States acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections, and each year, over 20,000 patients in the United States die from these infections. In the European Union, the annual burden posed by resistant healthcare associated bacterial infections is approximately 2.5 million hospital days and 25,000 deaths. Similar problems exist throughout the world, and the World Health Organization has declared antibiotic resistance a threat to global health security. The development and spread of resistance is driven by the use of antibiotics. Once they arise, resistant bacteria can be transferred between patients and antibiotic resistance mechanisms can be transferred between bacterial species, thus increasing the problem.

Antibiotic-resistant infections not only cause significant morbidity and mortality, but also place a substantial cost burden on the healthcare system. In most cases, antibiotic-resistant infections require prolonged and/or costlier treatments, extend hospital stays, and necessitate additional doctor visits and healthcare expenditures compared with infections that are easily treatable with antibiotics. The CDC estimates that the excess annual cost resulting from these infections in the United States is as high as $20 billion. According to an estimate from a 2012 study of over 5,500 U.S. patients, the average incremental per-patient hospital cost for antibiotic-resistant healthcare-associated infections, as compared to antibiotic-susceptible infections, was over $15,000.

According to government agencies and physician groups such as the CDC and the Infectious Disease Society of America, one of the greatest needs is for new antibiotics to treat infections caused by drug-resistant gram-negative pathogens, including CRE, P. aeruginosa, and A. baumannii. These pathogens are associated with significant mortality, as growing antibiotic resistance has left limited effective treatment options. There have been few approvals for new gram-negative antibiotics in recent decades, and there are to our knowledge only a handful of other antibiotics currently in Phase 3 development for infections due to gram-negative pathogens.

Governments, in collaboration with the private sector, have begun to respond to this significant and growing unmet medical need by progressing regulatory reform and offering economic incentives. With the passage of the Generating Antibiotic Incentives Now Act ("GAIN Act") in July 2012, qualifying antibiotics in the United States are eligible for priority review and the potential for a five-year extension of any existing non-patent market exclusivity that has been awarded. Further federal initiatives intended to incentivize new antibiotic development include the proposed Antibiotic Development to Advance Patient Treatment Act (the "ADAPT Act") and the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (the "DISARM Act"). The ADAPT Act, which is pending reintroduction to the U.S. Congress as part of the 21st Century Cures bill, aims to establish a pathway for the prompt approval of antibacterial and antifungal drugs that are intended to treat serious or potentially fatal infections. The DISARM Act, which was reintroduced to the U.S. Congress in January 2015, would reform reimbursement of qualifying antimicrobial products in the hospital setting to allow value-based pricing, thus providing a powerful incentive for manufacturers to develop new antibiotics. Additionally, the FDA has issued a new draft guidance document with proposed approaches to streamline development of new antibiotics addressing serious diseases with limited treatment options. Similar developments are occurring in parallel in other regulatory bodies, most notably in Europe. Government agencies such as BARDA, the DOD’s Defense Threat Reduction Agency ("DTRA") and the NIH

are also providing significant funding to support the discovery and development of new antibiotics.

Our Antibiotic Discovery and Development Engine

The challenge of discovering and developing a new antibacterial for the treatment of gram-negative infections is that such treatments need to overcome resistance mechanisms to existing antibiotics and to permeate the inner and outer membranes of the bacteria. Since we began operations in 2004, we have focused on the discovery and development of antibiotics to treat gram-negative infections and have developed proprietary know-how about the relationship between chemical structure and gram-negative potency through our work on multiple antibiotic classes.

Our progress in discovering and developing gram-negative product candidates has been achieved through:

- Knowledge of gram-negative antibiotic chemistry. We are able to modify the chemical structure of molecules from existing classes, such as the aminoglycosides, to avoid resistance mechanisms that inactivate other members of these classes. Further, by studying the properties of existing antibiotics that are effective against gram-negative bacteria, we believe we elucidated the first set of "rules" for modifying the chemical structure of compounds to increase penetration across both membranes. We are applying these rules in our discovery efforts to engineer molecules to be active against gram-negative bacteria.
- Specialized compound libraries. Our chemistry libraries are designed to contain compounds that have the necessary properties for penetration of gram-negative bacteria and are used in screening campaigns against clinical isolates of MDR gram-negative pathogens.
- Microbiology capabilities in clinically important pathogens. Our current focus is on today’s major unmet needs such as CRE and P. aeruginosa. We have compiled an extensive collection of bacterial isolates, including both clinical and engineered strains, and use them to direct our modifications of compounds. Our molecular genetic expertise with these pathogens allows us to rapidly validate new antibacterial targets and determine the mode of action of our new agents across multiple pathogens.
- Use of nonclinical data to predict clinical outcomes. We leverage in vivo animal data and computational modeling techniques to project the clinical efficacy of our early developmental candidates. In vivo refers to experiments and assays involving complex organisms, such as animals. As compared to other therapeutic areas, animal models of infection treatment are highly predictive of clinical efficacy. Utilizing these results, and pharmacokinetics ("PK"), and safety established in initial clinical trials, we use pharmacometric modeling approaches to estimate clinical efficacy and predict our clinical dosing regimens.
- Collaborations with industry-leading advisors and scientific experts. Our advisors include experts in antibacterial drug development such as Lynn Silver, Ph.D. (former Senior Investigator at Merck Research Laboratories), George H. Talbot, M.D. (Chief Medical Officer, Cerexa, acquired by Forest Laboratories), and Paul Reider, Ph.D. (Former Vice President, Process Chemistry at Merck and Amgen and current faculty member in the Department of Chemistry at Princeton University). We have also established collaborations with academic researchers in the field of antibiotic pharmacology, such as George Drusano, M.D., Henry Heine, Ph.D., and Arnold Louie, M.D., all with the Institute for Therapeutic Innovation, University of Florida. We maintain external collaborations with specialized scientific resources for the conduct of studies with dangerous biodefense pathogens, such as the U.S. Army Medical Research Institute for Infectious Diseases. We leverage these relationships and our own in-house expertise in biodefense countermeasure development to secure funding that supports our antibacterial programs targeting both antibiotic-resistant pathogens and biothreats.

Research and Development Pipeline

The following table summarizes the status of plazomicin and our other research programs:

Plazomicin

Overview

Our most advanced product candidate is plazomicin, a novel aminoglycoside designed by our scientists to overcome most clinically relevant aminoglycoside resistance mechanisms. Aminoglycosides have been used successfully for the treatment of serious bacterial infections for more than 50 years. As a class, aminoglycosides have several important characteristics including rapid bactericidal activity well-characterized PK, a lack of metabolism in humans, and excellent solubility and stability. However, the spread of resistance to currently marketed aminoglycosides has decreased their clinical utility. We developed plazomicin by chemically modifying an existing aminoglycoside, sisomicin, a natural product isolated from bacteria, to shield the regions of the molecule that are targeted by the enzymes responsible for aminoglycoside resistance. As a result of these modifications, plazomicin remains active against multi-drug resistant organisms where most other major drug classes, including commercially available aminoglycosides such as gentamicin and amikacin, have limited activity. Based on this profile, we are developing plazomicin as an intravenous ("IV"), therapy for the treatment of serious bacterial infections due to MDR Enterobacteriaceae, including CRE, which the CDC considers to be one of the top three urgent resistance threats to public health.

We consider the following to be key attributes that support the clinical utility and commercial value of plazomicin:

- Potent in vitro activity and in vivo efficacy in nonclinical studies against MDR Enterobacteriaceae, including CRE. Plazomicin retains activity in nonclinical studies against clinical Enterobacteriaceae isolates possessing most varieties of carbapenem resistance mechanisms, as well as most types of resistance to other key antibiotics, including commercially available aminoglycosides, colistin, and tigecycline.
- Demonstration of comparable efficacy to levofloxacin and acceptable safety in a Phase 2 clinical trial in patients with complicated urinary tract infections caused primarily by susceptible Enterobacteriaceae. We have completed a successful Phase 2 clinical trial of plazomicin in patients with complicated urinary tract infections ("cUTI"), as well as required Phase 1 PK and safety clinical trials. In patients with cUTI, plazomicin demonstrated efficacy that was similar to levofloxacin in microbiological eradication of the causative pathogen of the infection, which were primarily Enterobacteriaceae (but mostly non-MDR Enterobacteriaceae), and in clinical outcome, specifically, resolution of baseline signs and symptoms.

- Improved dosing strategy compared to existing aminoglycosides, and individualized patient dosing using our in vitro assay. We have used recent innovations in PK and pharmacodynamic ("PD"), modeling to create dosing regimens designed to achieve the drug exposures in the body we project to be efficacious in treating serious CRE infections. As a consequence, plazomicin is dosed in higher amounts relative to MIC than other commercially available aminoglycosides. Patient dosing in the Phase 3 CARE trial population will also be individualized by using a proprietary in vitro assay to measure levels of plazomicin in the bloodstream and adjusting the dose to achieve the targeted drug exposure.
- Potential to demonstrate a mortality benefit over currently available therapy in the treatment of life-threatening CRE infections. We have designed our Phase 3 CARE trial for plazomicin as a superiority trial with a primary efficacy endpoint of all-cause mortality at 28 days. The trial will compare a plazomicin-based regimen versus a colistin-based regimen for the treatment of CRE bloodstream infections and pneumonia. Through the SPA procedure, the FDA has agreed that the design and planned analyses of the trial adequately address objectives in support of an NDA. Most antibiotics are approved based on demonstrating non-inferiority to the current standard of care in the treatment of a specific type of infection (such as cUTI, intra-abdominal infection, and pneumonia) caused by a range of pathogens against which both the treatment and comparator are active. By focusing the Phase 3 CARE trial on patients with a high unmet medical need where the efficacy of the current standard of care is poor, and enrolling based on infections caused by the target pathogen (CRE), we have the opportunity to demonstrate differentiated efficacy of plazomicin in the clinical setting.
- Potential to reduce the healthcare costs associated with the treatment of serious infections. Treatment of antibiotic-susceptible infections is associated with lower overall costs as compared to the treatment of antibiotic-resistant infections. Our Phase 3 CARE trial of plazomicin will permit us to document improved pharmacoeconomic outcomes from plazomicin treatment of MDR Enterobacteriaceae, which may include fewer days on mechanical ventilation, less time in the ICU, and shorter total hospital stay.

Based on these attributes, we believe that plazomicin has the potential to become the new standard of care for the treatment of CRE.

Carbapenem-Resistant Enterobacteriaceae Pose an Urgent Threat to Patients

The need for new antibiotics to treat CRE is particularly acute, as CRE are one of the top global threats in infectious disease. In 2013, the CDC labeled CRE as "nightmare bacteria" and indicated that CRE pose a public health threat requiring "urgent and aggressive action." These bacteria are commonly MDR, exhibiting resistance not only to carbapenems, but also to nearly all antibiotics commonly used to treat gram-negative infections, including cephalosporins, beta-lactam/beta-lactamase inhibitor combinations, fluoroquinolones, and currently-marketed aminoglycosides. Resistance to carbapenems, has been highlighted because these drugs are one of the last lines of defense against resistant gram-negative infections. Most CRE express enzymes called carbapenemases which break down the carbapenem antibiotic molecule before it can kill the bacteria. Due to the lack of effective therapies, CRE infections are associated with significant mortality, with up to 50% mortality observed in patients with bloodstream infections and >70% in patients with cancer or receiving a liver transplant.

With limited treatment options available for CRE infections, physicians have resorted to previously abandoned drugs such as colistin or more recently approved drugs such as tigecycline. However, there is evidence that these antibiotics are failing patients. For example, in bloodstream infections due to carbapenemase-producing K. pneumoniae, all-cause mortality for treatment with colistin, tigecycline, or combinations of antibiotics that do not include a carbapenem active in vitro against the infecting isolate were reported to be 46%, 47%, and 37%, respectively. Recently, resistance to even these last-resort treatments has begun to be reported, further increasing the urgency for new therapeutic options.

The CRE problem is global and the incidence has increased significantly over the last decade. For example, CDC surveillance data indicates that the rate of carbapenem resistance among Klebsiella species increased from 1.6% to 10.4% in the United States between 2001 and 2011. In Italy, 36% of K. pneumoniae strains were carbapenem-resistant in 2013, a sharp increase from 2010 when the rate was 16%. The problem is even more pronounced in Greece, with more than 60% of K. pneumoniae strains exhibiting resistance in 2013. In Latin America, 17-18% of Klebsiella

species were resistant to carbapenems in Brazil and 11-12% in Argentina, according to surveillance data gathered in 2011.

We estimate that there were approximately 125,000 cases of CRE infections in the United States and five major markets in the European Union in 2014, which we refer to as the EU 5, with approximately one-fourth of these being bloodstream infections or pneumonia. We believe that CRE incidence will continue to increase in the future. A key driver of resistance growth, the use of carbapenems, is increasing. Once restricted in use to limit the emergence of resistance, hospitals are changing their policies due to the pressing need for carbapenems to treat the growing number of MDR infections. In a recent survey, two-thirds of U.S. hospital pharmacy directors reported that carbapenems are now unrestricted on their hospital formularies, likely a reflection of the increasing incidence of difficult-to-treat gram-negative infections. Additionally, the spread of CRE among patients, between healthcare facilities, and across geographic regions is exacerbated by the ability of Enterobacteriaceae to readily transfer their resistance genes from one

bacterium to another. Especially concerning is the potential of CRE to spread in the outpatient setting, which could lead to an epidemic of community-based CRE infections. Among outpatients in the United States, almost 2% of K. pneumoniae isolates were resistant to carbapenems in 2010, up from a negligible rate in 2005 and a recent study in 2012-2013 concluded that approximately 20% of CRE infections in hospitalized patients were community acquired. Finally, CRE are very difficult to eradicate once they establish a foothold in the healthcare setting.

Commercial Strategy for Plazomicin in CRE

Our overall goal is to establish plazomicin as the standard of care for the treatment of serious CRE infections. Through our clinical development approach to demonstrate plazomicin's superiority to the current standard of care, and our regulatory filing strategy under an SPA, we plan to establish the utility of plazomicin in treating bloodstream infections and pneumonia caused by gram-negative bacteria. This strategy is intended to support plazomicin's differentiated profile from both approved and development-stage antibacterials.

We believe that the commercial opportunity for plazomicin will be significant if our Phase 3 CARE trial demonstrates a mortality benefit against currently available antibacterial treatment. To our knowledge, plazomicin would be the first antibiotic to be approved on the basis of such a design. We anticipate that the expected mortality benefit of plazomicin will create significant physician demand for plazomicin based on our primary market research. A demonstrated mortality benefit in a patient population with a high risk of death, and a potential to circumvent spread of CRE in the hospital setting, will be key product differentiators that drive adoption. We intend to achieve our pricing and reimbursement objectives through demonstration of a mortality benefit in CRE patients as well as through demonstration of significant pharmacoeconomic cost savings to the healthcare system with the use of plazomicin. At a 2013 forum sponsored by The Pew Charitable Trusts, a nonprofit organization, which brought together payors, the FDA, and industry, panelists supported an approximate price point of $15,000 per treatment course for new antibacterial agents for resistant infections as long as clinical and economic benefits were clearly demonstrated. We will collect data in our Phase 3 CARE trial that is designed to enable us to compare medical resource utilization between patients treated with plazomicin and those treated with comparator therapy. For example, we will determine whether plazomicin-based therapy results in fewer days on mechanical ventilation, less time in the ICU, and shorter total hospital stays. As a reference for the potential cost-savings that could accumulate, a study using 2002 cost data estimated that the total cost of a single day in the ICU without mechanical ventilation was over $3,000, and that the incremental cost of a day of mechanical ventilation in the ICU was over $1,500. Accordingly, we believe an effective treatment for CRE infections has the potential to yield substantial cost-savings relative to existing therapy based on these key cost drivers.

We expect physicians will use plazomicin for definitive treatment of patients with CRE infections, as well as for empiric treatment, or treatment prior to definitive confirmation of the pathogen, of patients who are at risk of CRE. Definitive treatment for CRE begins when the infecting pathogen has been confirmed as CRE. Assuming success of our Phase 3 CARE trial as currently designed, definitive treatment with plazomicin is expected to last between 7 to 14 days. We estimate that there were approximately 125,000 cases of confirmed CRE infections in the United States and the EU 5 in 2014, with approximately one-fourth of these cases being bloodstream infections or pneumonia. Given the importance of providing effective CRE therapy as soon as possible in order to reduce the risk of death, we believe physicians will use plazomicin empirically to treat patients who are at a high risk of CRE infection. Empiric treatment continues until the pathogen is confirmed, which typically takes 2 to 3 days. Following pathogen confirmation, definitive treatment begins either with the same drug(s) used for empiric treatment or with different drug(s), depending on numerous factors including the identity and susceptibility of the pathogen, as well as patient response to empiric therapy. We estimate the total number of pneumonia or bloodstream infections treated empirically in the US and the EU 5 was approximately four million in 2013. We estimate that approximately 850,000 of these empirically treated cases involved consultation with an infectious disease physician, a proxy for the number of more complicated cases or serious infections, including suspected MDR infections. This smaller subset of empirically treated patients is a more relevant population in which plazomicin might be prescribed to provide empiric treatment for CRE, depending on a number of CRE risk factors, including patient colonization with CRE and high incidence of CRE in the hospital unit.

We intend to focus our initial commercial efforts on the U.S. market, which we believe represents the largest single market opportunity for plazomicin. We plan to use a targeted U.S. sales force to promote plazomicin to hospital-based healthcare professionals in resistance hotspots either alone or with support from a commercialization partner. In key markets outside of the United States, including Europe, Asia, and Latin America, we believe we can maximize the value of plazomicin through licensing full product rights to one or more commercialization partners who have local market expertise.

Plazomicin Development Program

We are developing plazomicin, our lead product candidate, for the treatment of serious bacterial infections due to MDR Enterobacteriaceae, including CRE. We have not conducted a clinical trial of plazomicin in patients with CRE infections, and we have no direct clinical evidence that plazomicin is effective in treating CRE infections in humans. However, the successful Phase 2 trial evaluating the efficacy of plazomicin compared with levofloxacin in patients with cUTI provides evidence of efficacy and safety

against Enterobacteriaceae infections in general and because CRE have similar susceptibility to plazomicin, the Phase 2 results predict efficacy against CRE. Based on the strength of our nonclinical data against CRE, and supported by the clinical pharmacokinetic, efficacy and safety data generated by our completed clinical trials, including our successful Phase 2 trial, the FDA agreed through the SPA procedure and other communications that our Phase 3 CARE trial, a total safety database of approximately 300 patients, and additional nonclinical studies would be acceptable to support an NDA for plazomicin. While we were originally developing plazomicin for a broad range of gram-negative infections, including cUTI, we recognized it had exciting potential to address the urgent public health threat of CRE that has emerged in recent years. We also received FDA fast track designation for plazomicin for the treatment of serious and life-threatening CRE infections and QIDP designation in multiple indications. We believe our currently planned development program, if successful, will also be acceptable to support a marketing application for plazomicin in the EU, based on feedback obtained through the EMA scientific advice procedure.

Key elements of our current program to develop plazomicin for the treatment of CRE infections are outlined in the table below:

CRE Clinical Program

Phase	Objectives	Planned Enrollment (approximate)	Initiation— Target Receipt of Top-Line Data
3	Primary: Demonstrate superiority of plazomicin as compared to colistin with respect to all-cause mortality at 28 days in patients with serious CRE infections Secondary : Safety, PK of plazomicin	360	2014 – 2017

Nonclinical Studies Supporting Success of CRE Program

Study	Methods	Key Result
In vitro activity against CRE	Standard microbiology assays	Plazomicin demonstrated strong potency against CRE isolates resistant to other antibiotics.
In vivo efficacy against CRE	Mouse models of lung and thigh muscle infection	Plazomicin demonstrated strong efficacy against CRE, including improved killing compared to colistin or tigecycline.
In vivo efficacy against plague and tularemia	Non-human primate models of pneumonic plague and tularemia	Animals receiving plazomicin demonstrated survival at doses below the level equivalent to our current Phase 3 CARE clinical dose.
In vivo and in vitro toxicology studies	In vitro and animal model studies of toxicities and potential side effects	Plazomicin demonstrated impacts on kidney function similar to other aminoglycosides. No other significant effects were observed.

Completed Phase 1 and Phase 2 Clinical Studies

Study No.	Objectives	Number Enrolled	Key Result
001	Phase 1 trial of safety and PK after single and multiple doses in healthy subjects	39	Plazomicin was well tolerated at doses of up to 15 mg/kg for 3 days.
003	Phase 1 trial of safety, plasma PK and lung penetration in healthy subjects	40	Plazomicin was well tolerated at doses of up to 15 mg/kg for 5 days. Plazomicin penetrated into the lung to a similar degree as other aminoglycosides.
004	Phase 1 trial of safety and PK in healthy and impaired kidney function subjects	24	As with other aminoglycosides, plazomicin's dose needs to be adjusted in patients with

			moderately or severely impaired kidney function.
006	Phase 1 thorough QT/QTc trial in healthy subjects[1]	64	Plazomicin showed no clinically relevant potential to increase risk for cardiac arrhythmias at single doses of up to 20 mg/kg.
002	Phase 2 safety, efficacy, and PK in patients with cUTI	145	Plazomicin displayed efficacy similar to the comparator antibiotic treatment (levofloxacin). Plazomicin was generally well tolerated at doses of up to 15 mg/kg for 5 days.

1 The "thorough QT/QTc study" is used to determine whether or not the effect of a drug on the QT/QTc interval in target patient populations should be studied intensively during later stages of drug development. The QT/QTc interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart’s electrical cycle.

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Phase 3 CARE Trial of Plazomicin for the Treatment of CRE

Given the critical need for new drugs to treat infections caused by CRE and given plazomicin's differentiated in vitro activity and in vivo efficacy against this pathogen, we have designed our Phase 3 CARE trial to position plazomicin as a superior drug for the treatment of CRE. By focusing on a difficult-to-treat pathogen against which plazomicin has excellent nonclinical activity, instead of a broader population of pathogens, we believe we have a greater probability of demonstrating the clinical differentiation of plazomicin. In addition, unlike most antibiotic trials that are designed to show non-inferiority to the current standard of care, this trial is a superiority study with a primary efficacy endpoint of all-cause mortality at 28 days. This superiority approach is consistent with recent FDA draft guidance regarding the development of antibacterial therapies to treat patients with unmet medical need. We have reached agreement with the FDA through the SPA procedure on the design and planned analyses of this Phase 3 CARE trial.

The first patient in our global Phase 3 CARE trial for the treatment of serious CRE infections was enrolled in September 2014. Our goal is to have top-line data from this Phase 3 CARE trial and to have gathered requisite safety data in 2017. If the trial is successful, we expect to submit an NDA to the FDA and an MAA to the EMA, and subsequently submit marketing applications in other global regions. Enrollment in the Phase 3 CARE trial continues at a rate that has been slower than anticipated. We have been exploring strategies to improve patient recruitment and remain in discussions with the FDA regarding potential modifications to the study design as well as additional clinical trials that could support and, possibly, facilitate regulatory filings for plazomicin. We currently expect to provide an update on our development plans for plazomicin by early in the second quarter of 2015. Our Phase 3 CARE trial for plazomicin is being funded in part by BARDA, which has awarded us an option for $60.4 million in funding for the trial, as part of our $103.8 million contract.

Trial Design

Our Phase 3 CARE trial is a randomized, open-label superiority trial of the efficacy and safety of plazomicin as compared to colistin when each is combined with a second antibiotic in the treatment of patients with bloodstream infections or hospital-acquired pneumonia due to CRE. The trial is enrolling patients whose causative pathogen is either presumed or confirmed to have an MIC ≥ 4 μg/mL for the broadest spectrum carbapenems, which are referred to as type 2 carbapenems. These patients are reported to have high mortality rates when treated with currently available therapeutic options, including colistin, the comparator in this study, providing us with the opportunity to demonstrate a statistically significant improvement in mortality with plazomicin.

The following figure provides an overview of our Phase 3 CARE trial:

Patients with presumed or confirmed infection with CRE based on local laboratory testing are being enrolled and randomized 1:1 to a plazomicin- or colistin-based regimen. Presumed CRE infections are those with a high probability of being CRE based on diagnostic testing (for example, preliminary susceptibility testing or demonstration of the presence of a carbapenemase), while confirmed CRE infections for purposes of our Phase 3 CARE trial are those with isolates confirmed to have an MIC ≥ 4 μg/mL to a type 2 carbapenem. At the time of randomization, one adjunctive antibiotic, either tigecycline or meropenem, is being selected by the investigator to be combined with plazomicin or colistin.

The trial is enrolling patients with serious CRE infections that are associated with significant mortality. The enrollment criteria, also referred to as inclusion/exclusion criteria, seek to identify patients most likely to derive a survival benefit from efficacious antibacterial therapy. Only patients who have received less than 72 hours of empirical therapy for presumed or confirmed CRE infection are eligible for the trial. The trial excludes patients with colistin resistant infections, refractory septic shock, or specified clinical syndromes that require more than 14 days of antibiotic therapy. We are also using the Acute Physiology and Chronic Health Evaluation II ("APACHE II"), score, a measure of the severity of disease that ranges from 0 to 71, as part of our enrollment criteria. Higher APACHE II scores correspond to more severe disease and a higher risk of death. Patients are eligible for enrollment with an APACHE II score from 15 to 30.

We are stratifying patients for factors that could independently impact mortality in order to minimize the risk for a baseline imbalance between the treatment arms. Patients are being stratified by infection type (bloodstream or pneumonia), APACHE II score, and time from the initiation of empirical therapy for the patient's infection to randomization for this trial.

Patients randomized to plazomicin are receiving an initial dose up to 15 mg/kg as a 30-minute IV infusion. The initial dose and dosing interval is being determined by baseline renal function. Subsequent plazomicin doses are being individualized based on changes in renal function and by therapeutic drug management ("TDM"), using our in vitro assay.

Colistin is being administered in the form of its IV prodrug as a 5 mg/kg IV loading dose followed by maintenance dosing of 5 mg/kg divided every eight or every 12 hours for up to 14 days. Colistin dosing is being adjusted according to renal function.

The trial comprises a screening period of up to 72 hours, an active-treatment period of 7 to 14 days, and a post-treatment period through the end of study on Day 28. Efficacy will be determined by assessments of survival, clinical response, and microbiological response. The primary efficacy endpoint is all-cause mortality at 28 days. Secondary efficacy parameters include time to death through Day 28, all-cause mortality at 14 days after randomization and assessment of clinical response at end of treatment, test of cure, and end of study. Additional efficacy endpoints include early assessment of the resolution of fever, improvement of oxygenation in pneumonia patients, and clearance of bacteremia in patients with bloodstream infections. Microbiological assessments include the evaluation of microbiological response and the incidence of development of decreased susceptibility to plazomicin or colistin.

Prior to the completion of enrollment, an independent data monitoring committee will conduct and review two unblinded interim analyses of efficacy and futility. The interim analyses will occur when approximately 33% and 67% of the required patients in the primary analysis population have reached the end of study on Day 28, which we anticipate to occur in 2015 and 2016, respectively. The interim analyses will determine whether the trial should be stopped early based on either efficacy or futility criteria.

Dosing Strategy for Phase 3 Using Pharmacometric Modeling

We used recent innovations in PK/PD modeling to predict that the plazomicin dosing regimen in the Phase 3 CARE trial will be adequate for efficacious treatment of CRE infections. This approach integrates information on the distribution of MICs for the target pathogen, based on recent microbiology surveillance data, exposure-response assessments in animal models, and PK data from our Phase 1 and 2 trials to define the appropriate dosing regimen for efficacy. Based on this analysis, we predict that with our Phase 3 CARE dosing regimen 92% of patients will achieve the levels of plazomicin in their blood or lung tissue predictive of successful treatment of CRE infection in vivo. This level is considerably greater than what can be achieved with current dosing of other aminoglycosides or other therapies such as colistin and tigecycline.

In addition, dosing of plazomicin in our Phase 3 CARE trial is being individualized for each patient based on changes in renal function and by TDM. The use of TDM for currently marketed aminoglycosides, combined with real-time PK assessments, has been shown to help achieve target drug exposures, leading to improved patient outcomes and reduced length of hospital stays. Plazomicin concentration in plasma will be determined using an investigational in vitro assay. In November 2013, we received an Investigational Device Exemption approval from the FDA for use of the assay in the trial.

Projected Mortality Benefit of Plazomicin

To estimate the potential size of the treatment effect for plazomicin over colistin in our Phase 3 CARE trial, we performed a meta-analysis of data from three observational studies describing the clinical outcome of 309 patients with bloodstream infections due to carbapenemase-producing Enterobacteriaceae. We segregated patients into two groups:

- "High MIC": Patients whose infections were caused by an isolate with a carbapenem MIC ≥ 4 μg/ml, our target MIC for inclusion in our Phase 3 CARE trial, and who received combination antibiotic therapy.
- "Low MIC": Patients whose infections were caused by an isolate with a carbapenem MIC < 4 μg/ml, and who received combination antibiotic therapy containing a carbapenem.

We observed a 35% mortality rate in the High MIC group and a lower 14% mortality rate in the Low MIC group. We interpret the absolute mortality difference of 21% (95% confidence interval: 11%-30%) between the two groups to be an indication of the potential magnitude of the treatment effect that might be observed when an effective (e.g., plazomicin) versus less effective (e.g., colistin) antibiotic therapy is used to treat patients whose isolates have a carbapenem MIC ≥ 4 μg/ml.

The size of our trial is based on the assumption of a smaller treatment effect size than suggested by this meta-analysis. Specifically, we assumed that a plazomicin-based regimen would result in a 12% absolute reduction in mortality from a baseline mortality rate of 35% in the colistin comparator group. Based on this projection, as well as additional statistical considerations, we estimate that the trial will need to enroll 286 treated patients with laboratory confirmed CRE infections to complete the primary analysis population. We estimate that it will require approximately 360 randomized patients over a 36-month period to reach this enrollment target.

We will continue to monitor changes in the competitive landscape and new opportunities that may result from regulatory reform regarding approval pathways for new antibiotics and from direct interactions we have with regulatory authorities. As appropriate, we may consider performing additional clinical trials if we believe such trials might result in faster regulatory approval or a greater probability of success.

Nonclinical Data Support the Use of Plazomicin for the Treatment of CRE Infections

Plazomicin has been tested extensively in vitro, in animal efficacy models, and in safety pharmacology and toxicology studies. As noted above, nonclinical assays are generally predictive of clinical efficacy for antibacterials, particularly in the case of a well understood class such as aminoglycosides.

In vitro Activity Against MDR Enterobacteriaceae, Including CRE

Results from multiple susceptibility testing studies against MDR Enterobacteriaceae demonstrate that plazomicin remains potent against strains resistant to several other classes of antibiotics, including carbapenems and other aminoglycosides. We can determine the likely activity of plazomicin against MDR Enterobacteriaceae, including CRE, encountered in the hospital setting globally by testing a large number of clinical isolates collected from unique patients with different types of infections from hospitals around the world.

In these studies, we measured the potency of each drug by determining the concentration of drug required to inhibit the growth of 50% and 90% of the isolate set. We refer to these measurements as the MIC 50 and MIC 90, respectively. The table below summarizes the in vitro activity of plazomicin and several other commercially-available antibiotics from various different drug classes commonly used to treat Enterobacteriaceae infections against a large number of clinical CRE isolates.

Compound	Class	N	MIC 50 (μg/mL)	MIC 90 (μg/mL)
Plazomicin	Aminoglycoside	807	0.5	2
Gentamicin	Aminoglycoside	807	4	128
Amikacin	Aminoglycoside	806	32	64
Ciprofloxacin	Fluoroquinolone	767	8	8
Ceftazidime	Cephalosporin	510	64	>128
Piperacillin/tazobactam	Beta-lactam/Beta-lactamase inhibitor	731	>128	>128
Tigecycline	Glycycline	723	1	2
Colistin/polymyxin B	Polymyxin	692	1	4

Key:

Susceptible Non-susceptible

N=number of strains within the overall set of 807 strains tested vs. the given antibiotic.

Notes: CLSI 2012 susceptibility criteria were used except for tigecycline and colistin, for which EUCAST 2013 criteria were used because CLSI criteria were not available. Isolates selected had an MIC ≥ 2 μg/mL for any type 2

carbapenem, a value defined as non-susceptible for this class according to CLSI 2012 susceptibility criteria. Plazomicin has not yet been assigned susceptibility criteria by these organizations.

As shown in this table, at least 50% of the tested isolates were non-susceptible to all of the marketed drugs except for gentamicin, tigecycline, and colistin, while plazomicin remained potent (MIC of 0.5 μg/mL or less). This shows the high degree of multi-drug resistance in CRE and the reason tigecycline and colistin are considered among the only options for treatment of infections

caused by CRE. All of the MIC90 values of the marketed drugs were non-susceptible, meaning that a significant percentage of infections caused by these isolates would be untreatable with available antibiotics. Plazomicin maintained an MIC90 of 2, meaning that at least 90% of these isolates were inhibited by a concentration of 2 μg/mL or less. Overall, 96% of these isolates had a plazomicin MIC of 2 μg/mL or less. Such concentrations are easily achievable in humans.

The graphs below display the activity of each of plazomicin and two commercially available aminoglycosides, amikacin and gentamicin, against clinical isolates of Enterobacteriaceae that are resistant to carbapenems due to the expression of two of the three main types of carbapenemases, serine carbapenemase and oxacillinase. The MIC of each of the tested drugs is expressed along the horizontal axis of the graph and the percent of the strains inhibited by the tested drug at a given MIC is expressed along the vertical axis. The number specified in the title indicates the number of strains that were included in each study.

As exemplified in the above graphs, plazomicin retained activity against 90% or more of the tested isolates at an MIC of less than or equal to 1 μg/mL. Amikacin and gentamicin display poor activity overall because the tested strains also expressed aminoglycoside resistance mechanisms.

The following set of graphs displays the activity of each of plazomicin, amikacin, and gentamicin against clinical isolates of Enterobacteriaceae that are resistant to carbapenems due to the expression of the third main type of carbapenemase, metallo-beta-lactamase, or MBL. Activity against isolates with NDM-1, which is a particular type of MBL, is shown separately from isolates with other MBLs.

Plazomicin retained activity with an MIC of less than or equal to 1 μg/mL against 90% or more of the tested isolates with an MBL, except for those with NDM-1, where plazomicin was only active against one of the 17 isolates tested. Plazomicin, amikacin, and gentamicin each display very poor activity against the NDM-1 isolates because this resistance mechanism and a particular aminoglycoside resistance mechanism, ribosomal methyltransferase, commonly occur together in the same isolate. Ribosomal methyltransferase, which renders plazomicin and most commercially available aminoglycosides inactive, and NDM-1 are generally limited to some countries in Asia, including India, although there have been isolated cases of infections by bacteria carrying such resistance mechanisms elsewhere, including the United States.

We also studied the activity of plazomicin in vitro against eight clinical CRE isolates in combination with meropenem and tigecycline, as we are planning to use plazomicin in combination with these two antibiotics during our Phase 3 CARE trial. In our studies, we did not observe any reduced activity of plazomicin in combination with either of these antibiotics.

In vivo Efficacy Against CRE

Plazomicin has demonstrated efficacy against CRE in multiple efficacy studies in animal models, and was consistently more potent than either tigecycline or colistin at doses equivalent to the clinical dose for each drug. In these studies, the PK of plazomicin was measured so the effect of its concentration in blood or lung tissue could be evaluated. Because animals and humans metabolize

and excrete drugs at different rates, the dose of plazomicin was "humanized" so the concentration of plazomicin over time in the animal closely matched the human concentration over time measured from our clinical studies. We used two different mouse models of bacterial infection in which a measured amount, or inoculum, of a CRE strain was introduced into either the thigh muscle or lung of the animal, allowed to grow for two hours, and then treated with an antibiotic for one day. We determined efficacy in the animal model by measuring the amount of bacteria, expressed as colony-forming units per gram (CFU/g), in treated as compared to untreated tissues, and then comparing either the increase or decrease in the amount of bacteria versus the original inoculum, or stasis.

The graph below shows the results of plazomicin, colistin administered as its prodrug used in the treatment of patients, and tigecycline against eight CRE strains in a mouse thigh infection model.

For these thigh infection studies, we selected CRE isolates from hospitalized patients that were primarily susceptible (MIC ≤ 1 μg/mL) to colistin and tigecycline by EUCAST criteria. The MICs of the antibiotics against the eight tested CRE isolates are shown in the table below.

	Number of Strains with the Given MIC	
	≤ 1 μg/mL	≥ 2 μg/mL
Plazomicin	8	0
Colistin	6	2
Tigecycline	7	1

Plazomicin demonstrated efficacy by reducing the amount of bacteria by up to 100 times compared to the original inoculum at doses lower than the equivalent clinical dose. In contrast, colistin and tigecycline displayed poor efficacy, despite having MICs against most of the isolates at or below the value considered to be susceptible. This result is consistent with the high mortality rates observed when colistin and tigecycline are used to treat serious CRE infections.

Efficacy Against Rapidly Lethal Plague and Tularemia Pneumonia in Non-Human Primate Models

Plazomicin has demonstrated efficacy in non-human primate models against infections caused by the biothreat pathogens Yersinia pestis and Francisella tularensis. These two bacteria species are considered potential bioweapons and are the causative agents for plague and tularemia, respectively. The primary site of infection in these models is the lung, and the pathogens cause a rapidly lethal pneumonia that spreads to other organs in the absence of effective therapy. In these models, animals were exposed to an aerosol spray of the pathogen and monitored for signs of fever indicating an active infection. PK was also measured. Once fever was detected, treatment was started with either a fixed dose of plazomicin (six animals for each treatment group) or a placebo and continued for 10 days. In one arm of the tularemia study, treatment was withheld until 24 hours after fever was observed allowing additional time for the infection to establish and worsen. Across these studies, almost all plazomicin-treated animals were cleared of their bloodstream and lung infections even when dosed below levels equivalent to our Phase 3 CARE clinical dose. However, in the plague studies some plazomicin-treated animals died due to infections that spread to the central nervous system ("CNS"), where we believe plazomicin does not penetrate. Like other aminoglycosides, intravenous plazomicin would not be suitable for the treatment of CNS infections. In contrast, none of the placebo control-treated animals in these studies survived. The strong efficacy of plazomicin against these diseases in a primate model suggests that it would likely be effective in similar serious infections in humans. Our BARDA contract

includes an unexercised option for funding, among other things, additional non-human primate studies of plazomicin's efficacy against Yersinia pestis and Francisella tularensis. The dollar value of this unexercised option has not yet been determined.

Nonclinical Safety Studies

We have studied plazomicin in industry-standard in vitro and in vivo toxicology models designed to characterize the potential side effects and safety parameters of drugs. These studies are typically required by regulatory agencies such as the FDA prior to use of the drug in humans. In our studies, plazomicin's primary toxicological effect was on the kidney. In animals, damage to the kidney increased and organ function deteriorated in proportion to plazomicin dose. This effect was observed to be reversible. After plazomicin dosing ceased, kidney function returned to normal or near normal, and the kidney damage was repaired. These results are consistent with the nonclinical toxicity and clinical safety of other aminoglycosides. Reversible kidney toxicity is a known side effect of these drugs. In head to head studies in animals, we observed the relationship between plazomicin dose and effect on the kidney and its function to be similar to that of gentamicin.

Aminoglycosides are also associated with hearing loss and impaired balance. Both of these functions are controlled by organs in the inner ear. To evaluate the potential for hearing loss with plazomicin treatment, we studied plazomicin in an animal model designed to detect hearing loss associated with drug treatment. In this study, plazomicin did not impact hearing function or cause detectable damage to the inner ear. The ability of this model or other available nonclinical models to predict drug-related hearing loss has not been firmly established. Therefore, we carefully monitored hearing and balance in our completed clinical trials of plazomicin.

Additional Nonclinical Studies to Support an NDA

We intend to conduct additional nonclinical studies to support an NDA for plazomicin. We plan to perform further microbiological studies of plazomicin in order to assess its activity against contemporary clinical isolates of Enterobacteriaceae and other bacterial species from the United States and other countries. We plan to conduct these studies no earlier than three years prior to the NDA filing. Our BARDA contract includes an unexercised option for additional funding to support these studies. The FDA has agreed that these additional nonclinical studies, when combined with our Phase 3 CARE trial and a total safety database of approximately 300 patients, would be acceptable to support an NDA for plazomicin. Other studies we plan to conduct include industry-standard experiments to characterize the distribution and excretion of plazomicin in vivo, as well as in vitro studies of the potential for plazomicin to interact with enzymes associated with drug distribution and metabolism.

Plazomicin Clinical Data Are Supportive of Further Trials of Plazomicin in Patients with CRE

Our clinical trial data to date for plazomicin indicate an acceptable safety profile, predictable PK, and lung penetration that is similar to other aminoglycosides. In addition, our Phase 2 trial demonstrates that plazomicin has microbiological and clinical efficacy in treating cUTI that is similar to levofloxacin, an approved antibiotic in the fluoroquinolone class commonly used in hospitals for the treatment of this infection.

Plazomicin has been studied in four Phase 1 clinical trials and one Phase 2 clinical trial. To date, a total of 239 healthy subjects and patients have received plazomicin at doses ranging between 1 and 20 mg/kg administered as an IV infusion. In the Phase 1 trials, 82 subjects received 15 mg/kg administered either as a single dose or once daily for up to five days. In the Phase 2 trial, 74 patients with cUTI received 15 mg/kg of plazomicin administered once daily for up to five days.

Phase 1 Clinical Trials

In our Phase 1 trials we demonstrated that plazomicin displays good tolerability and safety in single doses up to 20 mg/kg and multiple doses of up to 15 mg/kg of plazomicin administered once daily for five days. Common adverse events in the Phase 1 studies (occurring at a frequency greater than 5% in all subjects) were headache, numbness or tingling, dizziness, nausea, and drowsiness. All adverse events were mild or moderate in severity, and the overall frequency of events was similar between the plazomicin and placebo groups. In a substudy of our second Phase 1 trial (003) that investigated lung penetration of plazomicin, five subjects experienced mild to moderate transient hypotension at the end or soon after a single dose, consisting of a 10-minute infusion of 15 mg/kg of plazomicin. Following this trial, the infusion period was increased to 30 minutes for all subsequent trials. In a focused cardiovascular trial, plazomicin showed no clinically significant potential to cause arrhythmias, and all adverse events

were mild or moderate in severity.

Pharmacokinetic data collected in these trials showed dose proportionality and linearity in plasma within the tested plazomicin dose range. Lung penetration of plazomicin based on epithelial lining fluid levels was similar to the range of values reported for amikacin, another aminoglycoside agent, in bronchial secretions of normal and infected subjects. Phase 1 trials also showed that, as with other aminoglycosides, plazomicin is mainly cleared through the kidneys. A trial in subjects with moderate or severe kidney function impairment confirmed that plazomicin PK is significantly altered in these subjects relative to subjects with mild or normal kidney function. This trial demonstrated that, as with other aminoglycosides, dose adjustment will be necessary in patients with moderate or severe impairment.

Phase 2 Clinical Trial

Our Phase 2 multicenter, double-blind, randomized, active comparator-controlled trial, evaluated the efficacy of plazomicin compared with levofloxacin in 145 patients with cUTI including acute pyelonephritis. We selected cUTI as the target infection for our Phase 2 trial because cUTIs are one of the most common hospital-acquired infections, and the majority of cUTIs across all geographic regions are caused by Enterobacteriaceae, most commonly E. coli. We selected levofloxacin as the comparator drug for this trial since it is considered an empiric standard of care for cUTI and it shares many similar properties to plazomicin, such as concentration-dependent killing of bacteria, once-daily dosing, and achievement of high urinary concentrations.

During the first phase of the trial, patients were randomized 1:1:1 to 10 mg/kg plazomicin, 15 mg/kg plazomicin, or 750 mg levofloxacin, each treatment being administered once daily for five consecutive days. During the second phase of the trial, the 10 mg/kg treatment arm was eliminated and patients were randomized 2:1 to 15 mg/kg plazomicin or levofloxacin 750 mg.

Efficacy was assessed through microbiological and clinical outcomes at end of treatment, at test of cure, and at a long-term follow-up visit. The primary efficacy endpoint was the proportion of patients who attained microbiological eradication at the test of cure visit. This endpoint was determined for two analysis populations: a modified intent-to-treat ("MITT") population which included all randomized patients with at least one causative pathogen isolated from an acceptable urine specimen before treatment; and a microbiologically evaluable, or ME, population which was a smaller subset of the MITT population and included patients who met key study inclusion criteria, received study treatment for a pre-specified duration and had an acceptable urine specimen at test of cure.

As shown in the table below, the proportion of patients who achieved microbiological eradication was similar for each of the plazomicin (10 mg/kg and 15 mg/kg) and levofloxacin treatment groups in both analysis populations. Microbiological eradication rates for the MITT population in our Phase 2 trial were lower than the ME population. This is in part due to the fact that the MITT population, but not the ME population, had a proportion of patients with an unknown/indeterminate microbiologic outcome primarily because samples at the test of cure visit were not obtained.

By-Patient Microbiological Response [1]	Plazomicin 10 mg/kg	Plazomicin 15 mg/kg	Levofloxacin 750 mg
Microbiologically Evaluable (ME)			
N	7	35	21
Eradication, n (%)	6 (85.7%)	31 (88.6%)	17 (81.0%)
95% CI	42.1%–99.6%	73.3%–96.8%	58.1%–94.6%
Difference (95% CI) [2]			–7.6% (–31.3%, 16.0%)
Modified Intent-to-Treat (MITT)			
N	12	51	29
Eradication, n (%)	6 (50.0%)	31 (60.8%)	17 (58.6%)
95% CI	21.1%–78.9%	46.1%–74.2%	38.9%–76.5%
Difference (95% CI) [2]			–2.2% (–27.2%, 22.9%)

[1] N = number of patients in the treatment group; n=number of patients within a specified microbiological response category.

[2] Difference in microbiological eradication rates between levofloxacin 750 mg and plazomicin 15 mg/kg as calculated by the levofloxacin eradication percentage minus the plazomicin 15 mg/kg eradication percentage. The 95% CI for the difference is based on a normal approximation with a continuity correction.

The secondary efficacy endpoint of the trial was clinical outcome. In the plazomicin and levofloxacin treatment groups, a majority of the clinically evaluable patients (66.7%–78.6%) were assessed as cured, with resolution of baseline signs and symptoms of infections. Results for the ME and MITT groups were similar. The majority of isolates collected from patients in these populations during the trial were non-MDR Enterobacteriaceae.

Overall in the Phase 2 trial, plazomicin administered at doses of 10 or 15 mg/kg once daily for five days was generally well tolerated. There were no serious adverse events assessed as related to treatment with plazomicin. Five patients (four in the plazomicin 15 mg/kg group and one in the levofloxacin group) prematurely discontinued study drug due to adverse events. Overall, adverse events were experienced by 7 of 22 patients (31.8%) in the plazomicin 10 mg/kg groups, 26 of 74 patients (35.1%) of patients in the plazomicin 15 mg/kg group, and 21 of 44 patients (47.7%) in the levofloxacin 750 mg group. Most of these were assessed as mild or moderate in severity. Adverse events occurring in at least two patients are shown in the table below.

Adverse Event, number of patients (%)	Plazomicin 10 mg/kg (22 patients)	Plazomicin 15 mg/kg (74 patients)	Levofloxacin 750 mg (44 patients)
Headache	2 (9.1%)	6 (8.1%)	3 (6.8%)
Diarrhoea	0 (0.0%)	4 (5.4%)	2 (4.5%)
Dizziness	0 (0.0%)	4 (5.4%)	0 (0.0%)
Nausea	0 (0.0%)	4 (5.4%)	0 (0.0%)
Vomiting	0 (0.0%)	4 (5.4%)	1 (2.3%)
Gastritis	1 (4.5%)	2 (2.7%)	0 (0.0%)
Abdominal pain upper	0 (0.0%)	1 (1.4%)	1 (2.3%)
Cough	1 (4.5%)	1 (1.4%)	1 (2.3%)
Dyspepsia	1 (4.5%)	1 (1.4%)	1 (2.3%)
Dyspnoea	1 (4.5%)	1 (1.4%)	0 (0.0%)
Hypokalaemia	0 (0.0%)	1 (1.4%)	2 (4.5%)
Insomnia	0 (0.0%)	1 (1.4%)	1 (2.3%)
Dysgeusia	0 (0.0%)	0 (0.0%)	2 (4.5%)
Hypertension	1 (4.5%)	0 (0.0%)	1 (2.3%)
Pruritus	1 (4.5%)	0 (0.0%)	2 (4.5%)
Tachycardia	1 (4.5%)	0 (0.0%)	1 (2.3%)
Upper respiratory tract infection	0 (0.0%)	0 (0.0%)	2 (4.5%)

The hearing and balance of patients were closely assessed, as aminoglycosides are known to have safety liabilities associated with these functions. One plazomicin-treated patient reported mild transient vertigo and another plazomicin-treated patient reported mild unilateral tinnitus that persisted and was considered permanent. Neither patient tested positive for changes in hearing function or balance. Kidney function as measured by mean serum creatinine values remained generally stable over the trial. Two patients treated with 15 mg/kg plazomicin had adverse events associated with renal function. Both events were assessed as mild in severity and involved increases in serum creatinine of 0.5 mg/dL and 0.7 mg/dL respectively, which returned to near-baseline values by the last follow-up visit. Two additional patients treated with 15 mg/kg plazomicin experienced serum creatinine abnormalities (an increase from 1.2 to 2.0 mg/dL and an increase from 0.8 to 1.5 mg/dL), neither of which were classified as adverse events, and that returned towards baseline at the last follow-up visit.

The results of this Phase 2 trial demonstrated the efficacy of plazomicin in patients with cUTI that was similar to the efficacy of levofloxacin in terms of achieving both microbiological eradication of the causative pathogen of the infection and clinical cure. Furthermore, plazomicin was generally well tolerated in this patient population.

Research Discovery and Development Programs

Beyond our plazomicin program, our research teams are focused on discovering medicines with novel mechanisms of action for serious infections caused by MDR pathogens including Acinetobacter baumannii and Pseudomonas aeruginosa. The CDC has categorized these pathogens as "serious" threats requiring prompt and sustained action. Our goal is to nominate a clinical candidate from our research programs in 2015 and to file an IND in 2016. Clinical trials for products from our research programs will require additional funding.

Small Molecule Drug Discovery Program

In 2006, we initiated a program to identify inhibitors of LpxC. LpxC is an essential enzyme for the formation of bacterial membranes in gram-negative bacteria that is highly conserved among gram-negative species. Inhibition of LpxC disrupts the structural integrity of the outer bacterial membrane, reducing its capacity to protect the cell and retain vital molecules in the space between the outer and inner membrane, leading to bacterial cell death.

Using our discovery engine, we made improvements to known LpxC inhibitors to generate a series of promising molecules that showed greater activity against gram-negative pathogens, improved safety in preclinical models, and better pharmaceutical properties. Given their novel mechanism of action, compounds generated in this program demonstrate no cross-resistance with current antibiotics and therefore retain activity against strains harboring resistance mechanisms that inactivate many other marketed antibiotics. This is illustrated in the figure below with

respect to ACHN-975 (a compound we are no longer pursuing in clinical trials), which demonstrates potent activity against a large set of almost 1,000 P. aeruginosa clinical isolates. The figure also shows the potency of other antibiotics commonly used to treat infections caused by P. aeruginosa infections. For these drugs, the dotted lines begin at the MIC value considered non-susceptible, according to 2012 CLSI criteria, demonstrating the current scarcity of effective therapeutic options for P. aeruginosa infections. None of the other drugs had a susceptible MIC90 against the test set.

In 2012, we conducted a first-in-human Phase 1 clinical trial of ACHN-975, which demonstrated linear, dose-dependent PK and good tolerability when administered intravenously in single doses at levels predicted to be effective in treating P. aeruginosa infections. In a subsequent multiple-dose Phase 1 trial in 2013, the first three subjects that received multiple doses of ACHN-975 developed inflammation at the infusion site, with venous thrombosis at the infusion site in one of these subjects, and the trial was terminated early. No subjects had signs or symptoms of a systemic inflammatory reaction and no other safety findings were observed. All three subjects were discharged from the Phase 1 unit after demonstrating resolution or substantial improvement of the infusion site reactions. The IND was withdrawn in May 2014. We are currently pursuing an extensive series of backup compounds with the goal of identifying those with potent antibacterial activity and an improved safety profile for selection of a candidate for IND-enabling studies in 2015. If we identify viable product candidates, we would have to submit a new IND application for any compound we seek to advance to clinical trials.

Therapeutic Antibody Discovery Program

Therapeutic monoclonal antibodies ("mAbs"), have several distinguishing features that make them attractive as antibacterial agents. First, we believe they will not be impacted by resistance mechanisms that inactivate existing small molecule-based antibiotics. Second, they are highly specific to their target, greatly reducing the potential for toxicity due to off-target binding. Third, humanized or fully human mAbs are well tolerated with low immunogenicity in patients. Finally, mAb therapeutics can achieve sustained exposure with a typical half-life of around 3 weeks, potentially enabling an antibacterial antibody to prevent or cure an infection following a single intramuscular or intravenous dose.

Our goal is to generate mAbs that can be deployed as a monotherapy to treat infections caused by MDR Acinetobacter baumannii and other gram-negative pathogens. Many of the antibacterial antibodies currently in development by others will likely be limited to prophylactic use for preventing infections or require adjunctive therapy with an effective antibiotic. Based on our experience developing agents for gram-negative pathogens, we have identified a set of targets and a corresponding screening funnel for each target that we believe to be well suited for therapeutic mAb discovery. Our unique approach has the potential to transform the way gram-negative infections are treated by enabling a safe, single-dose primary cure of infection or long-lasting step-down therapy upon discharge from the hospital.

Government Contracts

BARDA

Our program to develop plazomicin for the treatment of CRE infections of the bloodstream and lung, as well as for disease caused by certain bacterial biothreat pathogens, is partially funded under a contract with BARDA, an agency of the U.S. Department of Health and Human Services. This contract was awarded in August 2010 and consists of a base amount as well as three options, two of which have been exercised. The base amount and the two exercised options total $103.8 million of committed funding, of which $59.5 million has been recorded as revenues as of December 31, 2014, with $44.3 million remaining available. The potential funding amount under the unexercised option has not yet been determined. The unexercised option relates to the conduct of a clinical trial, certain nonclinical studies to support an NDA and certain nonclinical biodefense studies.

Overall, the contract calls for the development, manufacturing, nonclinical and clinical evaluation of, and regulatory filings for, plazomicin as a countermeasure for diseases caused by antibiotic-resistant pathogens. These pathogens include bacteria associated

with serious hospital-acquired infections, such as CRE, as well as biothreats, such as F. tularensis, which causes tularemia, and Y. pestis, which causes plague. As the prime contractor, we are responsible for all technical and regulatory activities under a research plan proposed by us and accepted by BARDA. From time to time, we may propose a change to the research plan to BARDA, and BARDA may or may not choose to accept the change to the research plan, along with any associated additional costs, subject to the availability of funding, as well as other factors. We are also obligated under the contract to satisfy various federal reporting requirements, including technical reporting with respect to our plazomicin development activities, reporting with respect to intellectual property and financial reporting. In addition, technical documents and regulatory filings may be reviewed by BARDA prior to their finalization and/or submission.

Payments under the contract with BARDA are made in installments as activities are conducted in accordance with the research plan. Payments to us are based on direct costs incurred and allowances for overhead, plus a fee, where applicable. In November 2013, we modified the most recent awarded option such that payments under this option would not exceed $60.4 million, even though the cost of the Phase 3 CARE trial and related expenses are expected to exceed the amount available to us under our BARDA contract for direct costs incurred. Under standard government contracting terms, the government receives only limited rights for government use of certain of our pre-existing data and certain data produced with non-federal funding, to the extent such data are required for delivery to BARDA under the project. The U.S. government receives unlimited rights to use and disclose new data first produced under the project with BARDA funding. The U.S. government is entitled to a nonexclusive, worldwide, royalty-free license to practice or have practiced any patent on an invention that is conceived or first reduced to practice under the project, and may obtain additional rights if we do not elect to retain ownership of a subject invention or if we do not satisfy certain disclosure and patent prosecution obligations with respect to a subject invention. The government’s rights do not include the composition of matter patents related to plazomicin, as these were developed and prosecuted prior to our entry into the BARDA contract and without government funding. The BARDA contract does not entitle the government to any sales royalties or other post-commercialization financial rights.

BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current year amounts allotted from Congressionally approved annual appropriations.

DTRA

In June 2007, we entered into a contract with DTRA to develop novel antibacterials for the treatment of biodefense pathogens. To date, we have received $33.5 million out of $35.4 million that was available for drawdown under this contract. In November 2012, DTRA terminated this contract for convenience. We are seeking payment from DTRA for additional expenses we have incurred in connection with this contract. We have not recognized any revenue with respect to these additional amounts. The payments we have received under the DTRA contract and the payments we are requesting are subject to an ongoing audit by the Defense Contract Audit Agency.

The DTRA contract related to the funding of our LpxC program, including ACHN-975. Under the contract’s terms, the U.S. government received rights to use and disclose new data first produced under the project with DTRA funding only to the extent they are related to government applications connected with certain select pathogens. In addition, the U.S. government is entitled to a nonexclusive, worldwide, royalty-free license to practice or have practiced any patent on an invention that was conceived or first reduced to practice under the project, including the composition of matter patent related to ACHN-975, and may obtain additional rights if we do not elect to retain ownership of a subject invention or if we do not satisfy certain disclosure and patent prosecution obligations with respect to a subject invention.

NIAID

In September 2008, we entered into a five-year contract with the U.S. National Institute of Allergy and Infectious Diseases ("NIAID"), to develop novel antibacterials for the treatment of biodefense pathogens. We received over $21.0 million under this contract, which supported a previous research and development program that we currently do not intend to advance. Our NIAID contract expired in August 2013. The U.S. government retains certain rights to data and intellectual property generated under the contract.

USAMRAA

In May 2012, we entered into a one-year contract with the U.S. Army Medical Research Acquisition Authority ("USAMRAA"). Under the contract we conducted the first-in-human single ascending dose study of ACHN-975. The total amount of the contract was $2.5 million, and the contract expired in May 2013. The U.S. government retains certain rights to data generated under the contract.

For more information regarding the government contracts referred to above see "Risk Factors—Risks Related to Our United States Government Contracts" and "Risk Factors—Risks Related to Intellectual Property—Provisions in our U.S. government contracts, including our contract with BARDA, may affect our intellectual property rights."

Commercial Agreements

ARK Diagnostics, Inc. Development Services Agreement

In August 2013, we entered into a development services agreement with ARK Diagnostics, Inc. ("ARK"). Under this agreement, we and ARK are co-developing an in vitro assay to measure levels of plazomicin in the blood to enable patients to receive safe and efficacious doses of plazomicin. Such an assay would be used to provide therapeutic drug management. ARK is responsible for the manufacture and supply of the developed assay for our plazomicin Phase 3 CARE trial program. Depending on the mutually agreed regulatory approval pathway and commercialization strategy for the assay, we will be required to pay ARK up to an aggregate amount of between $1.0 million and $1.6 million in milestone payments for the achievement of certain development, manufacturing and regulatory milestones, $1.0 million of which have been achieved and paid as of December 31, 2014. Intellectual property rights relating to the assays developed under the contract are jointly owned by us and ARK, but each party retains ownership of its background intellectual property and improvements thereto.

In addition to the co-development activities performed under the agreement, we are required to negotiate in good faith the terms of an agreement for the commercialization of the assay based upon certain core terms outlined in the development services agreement to be included in such a commercialization agreement. Such core terms include that ARK would have the first right to commercialize the assay in the United States and the EU and to manufacture and supply the assay worldwide for commercialization, while we would have the first right to commercialize the assay in any other country or territory, in addition to step-in rights to commercialize the assay in the United States and the EU if ARK elects not to do so. The development services agreement provides that if, by January 2016, we have still not agreed the terms of a commercialization agreement with ARK, ARK will provide us with an interim supply of the finished assay for at least two years following the approval of the NDA for plazomicin and interim supply of components to the assay to have the assay made for us by a third party for a further three years, until five years following the approval of the NDA, at a price that is comparable with the pricing offered by ARK to other distributors. If we still have not agreed with ARK on the terms of a commercialization agreement by January 1, 2018, then at our request, we, ARK and a third-party supplier reasonably acceptable to ARK shall enter into a technology transfer and license agreement, whereby on commercially reasonable terms, ARK would grant to the third-party supplier a license under ARK’s applicable intellectual property and perform a transfer of know-how to such third-party supplier, solely to the extent necessary for the purpose of manufacturing and supplying the assay to us for use or commercialization by us and our designees.

The development services agreement will expire upon the later of the completion of the development services and January 1, 2020. Either we or ARK may terminate for the other party’s uncured material breach, and we may terminate without cause upon 60 days written notice to ARK.

License Agreement with Isis Pharmaceuticals, Inc.

On January 25, 2006, we entered into a license agreement with Isis Pharmaceuticals, Inc. ("Isis"), pursuant to which Isis granted us an exclusive license under certain patents relating to aminoglycoside antibacterial compounds and related know-how to develop and commercialize certain novel aminoglycoside antibacterial compounds. We are required to use commercially reasonable efforts to develop and commercialize licensed compounds under the agreement. In consideration for the rights granted to us by Isis under the license agreement, we issued $1.5 million of our Series A convertible preferred stock to Isis in 2006. In addition, we are required to make payments to Isis upon the achievement of specified development and regulatory milestones totaling up to $19.5 million for the first aminoglycoside product developed under the agreement, including $4.0 million that was paid to Isis in the fourth quarter of 2014 following dosing the first patient in our Phase 3 CARE trial of plazomicin in September 2014, and up to $9.75 million for the second aminoglycoside product developed under this agreement, and to pay Isis a low double-digit share of non-royalty sublicensing revenues that we receive from sublicensees for the grant of sublicenses under our agreement with Isis, provided that the maximum amount we are required to pay Isis with respect to the sum of all development and regulatory milestones and non-royalty sublicensing revenue payment obligations for plazomicin, as the first aminoglycoside product under the agreement, is $19.5 million. Likewise, our cumulative development and regulatory milestone payment and non-royalty sublicensing revenues payment obligations for a second aminoglycoside product under the agreement with Isis will not exceed $9.75 million. To date, we have made

development milestone payments of $7.0 million to Isis with respect to plazomicin, $6.5 million of which was paid in cash and $0.5 million of which was paid in the form of our Series B convertible preferred stock. We are also required to pay additional milestone payments of up to $20.0 million in the aggregate upon the first achievement of specified threshold levels of annual net sales of all aminoglycoside products in a calendar year. If any aminoglycoside product, including plazomicin, is successfully commercialized, we will be required to pay royalties to Isis in the low single digits on worldwide net sales of licensed products by us, our affiliates and sublicensees.

Our license agreement with Isis will continue for as long as we are obligated to pay royalties to Isis, which will be on a product-by-product basis until the later of (a) ten years from the date of first commercial sale of an aminoglycoside product covered by the agreement in the United States, Japan or Europe; and (b) the abandonment, revocation, invalidation or expiration of the last valid claim of a patent covered under the agreement which covers such product, not to exceed twenty years after the first commercial sale in the United States, Japan or Europe. Either party may terminate the agreement for the uncured material breach of the other party, and

Isis may terminate the agreement if we fail to make timely payments, subject to a specified cure period. We may also terminate the agreement or the license with respect to a particular product without cause upon 60 days' notice.

License Agreement with the University of Washington

On December 1, 2006, we entered into a license agreement with the University of Washington ("UW"), pursuant to which UW granted us an exclusive license under UW's rights to certain patents and technology covering novel LpxC inhibitor antibacterial compounds, subject to UW's retained right to use such patents and technology for research and academic purposes. UW also granted us a non-exclusive license in related know-how. Certain of the patents and technology licensed under our agreement with UW were originally claimed to be co-owned or solely owned by Novartis. Subsequently, we, Novartis and UW acknowledged and agreed that such patents and technology are co-owned by Novartis and UW. Therefore, the exclusivity of our license is subject to Novartis' rights to use the licensed patents and technology and to grant licenses to others to do so. This agreement was amended in March 2009 to modify the timing of our reimbursement of certain patent prosecution expenses, and in January 2011 to amend the timing of certain milestone events. We are required to use commercially reasonable efforts to commercialize the licensed technology and to manufacture and maximize the sales of licensed products. In consideration for the rights granted to us by UW under the license agreement, we paid an up-front cash payment to UW upon execution of the agreement. In addition, if we achieve specified development and regulatory milestones, we will be required to make payments to UW totaling up to $2.15 million for the first product under the agreement to achieve the specified milestone, $150,000 of which has already been paid with respect to ACHN-975, and up to $1.075 million for each of the second and third products to achieve the specified milestone. In addition, if ACHN-975 or any other LpxC inhibitor covered under the agreement is successfully commercialized, we will owe UW a royalty in the low single digits based on worldwide net sales, if any, of licensed products by us and our sublicensees, subject to a requirement to pay to UW a minimum annual royalty following regulatory approval, and, beginning in 2009, a nominal annual license maintenance fee prior to regulatory approval. We are also obligated to pay UW a share of non-royalty sublicensing revenues that we receive from sublicensees for the grant of sublicenses under this agreement, ranging from the mid-single digit to very-low-double digit percentages of such revenues, based on timing of the execution of the sublicense.

The UW Agreement will continue until expiration of the last valid claim of a patent covered under the agreement, which we expect to occur no later than January 2024. However, UW has the right to terminate the agreement if we breach it and fail to cure such breach within a specified cure period or upon our insolvency. We may terminate this agreement for any reason upon 30 days' notice to UW.

Competition

The pharmaceutical industry is very competitive and subject to rapid and significant innovation. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical and generic drug companies, universities, and other research institutions. Many of our competitors have greater financial resources, as well as larger research and development staff and more experienced marketing and manufacturing organizations. As a result, these companies may obtain regulatory approval more rapidly than we are able to and may be more effective in selling and marketing their products. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are superior to, or more effectively marketed than, plazomicin or any other drug candidate that we are currently developing or that we may develop, which could render our products obsolete and noncompetitive.

The competition in the antibiotics market is intense. We are initially developing plazomicin as a treatment for presumed or confirmed bloodstream or pneumonia CRE infections, and if approved, plazomicin will face competition from commercially available antibiotics such as tigecycline, which is marketed by Pfizer as Tygacil, other aminoglycosides that are generically available (e.g., gentamicin, amikacin, tobramycin), and polymyxins that are generically available (colistin and polymyxin B).

In addition, if approved, plazomicin may face additional competition from antibiotics currently in clinical development. We are aware of other antibiotics currently in development. Actavis plc and AstraZeneca PLC are developing ceftazidime/avibactam and ceftaroline/avibactam for pneumonia and complicated urinary and

intra-abdominal infections. Tetraphase Pharmaceuticals is developing eravacycline for cUTI and intra-abdominal infections. The Medicines Company is developing Carbavance™ for cUTIs and MDR gram-negative infections, including CRE. Merck is developing relebactam for complicated urinary and intra-abdominal infections, and potentially for pneumonia.

If approved, we believe that plazomicin would compete effectively against both marketed and known pipeline competitors based on the following:

- Potent in vitro and in vivo activity against CRE, including strains bearing all classes of carbapenemases;
- Activity in the presence of a range of resistance mechanisms, including most aminoglycoside modifying enzymes, fluoroquinolone target site mutations, extended-spectrum beta-lactamases, and carbapenemases;

- Registrational program focused on bloodstream and pneumonia infections due to CRE;
- Superiority trial design with all-cause mortality endpoint; and
- Acceptable safety and tolerability profile.

If we are unable to demonstrate these or other advantages of plazomicin over competing drugs and drug candidates, we may not be able to successfully commercialize plazomicin and our results of operations may suffer. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make plazomicin or any other product candidates that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or regulatory approval or discovering, developing and commercializing antibiotics before we do.

Intellectual Property

The proprietary nature of, and protection for, our product candidates and our discovery programs, processes and know-how are important to our business. We have sought patent protection in the United States and certain other jurisdictions for plazomicin, ACHN-975, and certain other inventions to which we have rights, where available and when appropriate. Our policy is to pursue, maintain and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions and improvements that are commercially important to the development of our business. We also rely on trade secrets relating to our proprietary technology platform that may be important to the development of our business.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for our current and future product candidates and the methods used to develop and manufacture them, as well as successfully defending these patents against third-party challenges. Our ability to stop third parties from making, using, selling, offering to sell, or importing our products depends on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our product candidates, discovery programs and processes. For this and more comprehensive risks related to our intellectual property, see "Risk Factors—Risks Related to Intellectual Property."

Plazomicin (Aminoglycoside)

The patent portfolio for plazomicin is based upon an Achaogen-owned patent family that includes patents and patent applications directed to plazomicin and structural analogs thereof, pharmaceutical compositions containing plazomicin or analogs thereof, and methods of using plazomicin or analogs thereof in the treatment of bacterial infections. As of January 31, 2015, this patent family included two U.S. patents (U.S. Patent No. 8,383,596, issued February 26, 2013, and U.S. Patent No. 8,822,424, issued September 2, 2014, which we refer to herein as the ‘596 and ‘424 patents, respectively), one pending U.S. patent application (Application Serial No. 14/334,511, filed July 17, 2014) and fourteen corresponding foreign patents and patent applications. As of January 31, 2015, we had corresponding granted patents in Australia, Canada, China, Eurasia, Israel, Japan, Korea and Taiwan. In addition, as of January 31, 2015, we had corresponding patent applications pending in Brazil, China, Europe, Hong Kong, India and Mexico. With the exception of the ‘596 patent, which the USPTO has determined is entitled to 923 days of patent term adjustment, we expect any U.S. and foreign patents in this patent family to expire in November 2028. In view of the USPTO determination that the ‘596 patent is entitled to 923 days of patent term adjustment, we expect the ‘596 patent to expire in June 2031.

It is possible, assuming that plazomicin achieves regulatory approval and depending upon the date of any such approval, that the term of the ‘596 patent may be extended up to a maximum of five additional years under the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984, also referred to as the Hatch-Waxman Act. Patent term extension also may be available in certain foreign countries upon regulatory approval.

Antipseudomonal LpxC Inhibitor

Our patent portfolio for antipseudomonal LpxC inhibitor compounds is comprised of seven distinct patent families. Six of these patent families are Achaogen-owned, and one is in-licensed from UW and co-owned by UW with Novartis Corp.

The first of these Achaogen-owned patent families is directed to a chemical genus that encompasses LpxC inhibitor compounds, including ACHN-975, pharmaceutical compositions containing a compound encompassed within the chemical genus and methods of using a compound encompassed within the chemical genus in the treatment of bacterial infections. As of January 31, 2015, this patent family included patent applications pending in the United States (Application Serial No. 14/223,971, filed March 24, 2014), Canada, China, Europe, Hong Kong, India, Japan, and Taiwan. In addition, as of January 31, 2015, we had corresponding granted patents in Japan and Taiwan. We expect any U.S. and foreign patents granted in this patent family to expire in June 2028.

The second of these Achaogen-owned patent families is directed to ACHN-975 as a composition of matter and structural analogs thereof, pharmaceutical compositions containing ACHN-975 or analogs thereof, and methods of using ACHN-975 or analogs thereof in the treatment of bacterial infections. As of January 31, 2014, this patent family included applications pending in the United States (Application Serial No. 13/289,209, filed November 4, 2011), Australia, Canada, China, Europe, Israel, India, Japan, Korea, New Zealand, Singapore, South Africa and Venezuela. We expect any U.S. and foreign patents granted in this patent family to expire in November 2031.

The third of these Achaogen-owned patent families also is directed to a chemical genus that encompasses LpxC inhibitor compounds, but not ACHN-975. As of January 31, 2015, this patent family included applications pending in the United States (Application Serial No. 14/536,286, filed November 7, 2014) and Europe. We expect any U.S. and foreign patents granted in this patent family to expire in May 2033.

The fourth of these Achaogen-owned patent families also is directed to a chemical genus that encompasses LpxC inhibitor compounds, but not ACHN-975. As of January 31, 2015, this patent family included applications pending in the United States (Application Serial No. 14/537,048, filed November 10, 2014) and Europe. We expect any U.S. and foreign patents granted in this patent family to expire in May 2033.

The fifth and sixth of these Achaogen-owned patent families each is directed to a chemical genus that encompasses LpxC inhibitor compounds, but not ACHN-975. As of January 31, 2015, the first of these two patent families was comprised of International Patent Application No. PCT/US2014/024304, filed March 12, 2014 and the second was comprised of a pending U.S. provisional patent application. We expect any U.S. and foreign patents granted in the first of these two patent families to expire in 2034, and any U.S. and foreign patents granted in the second of these two patent families to expire in 2035.

As of January 31, 2015, the patent family in-licensed from UW included five issued U.S. patents, two of which (U.S. Patent Nos. 7,989,660 and 8,153,843) we believe may cover ACHN-975 and analogs thereof as a composition of matter. In addition, this patent family includes corresponding foreign patents and patent applications in Australia, Canada, China, Europe, Hong Kong, Indonesia, Israel, India, Japan, Korea, Mexico, the Philippines, Singapore, and South Africa. We believe that certain of these corresponding foreign patents and patent applications may cover ACHN-975 as a composition of matter and that certain of them do not. We expect any U.S. and foreign patents granted in this patent family to expire in January 2024.

If we are successful in developing and obtaining regulatory approval of an antipseudomonal LpxC inhibitor, the term of one U.S. patent issuing from one of our Achaogen-owned patent application families that covers such approved product may be eligible for up to five years of patent term extension under the provisions of the Hatch-Waxman Act. Patent term extension also may be available in certain foreign jurisdictions upon regulatory approval.

Trade Secrets

In addition to patents, we rely on trade secrets and know-how to develop and maintain our competitive position. We seek to protect our proprietary data and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors, and partners. These agreements are designed to protect our proprietary information. We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Trade secrets and know-how can be difficult to protect. Consequently, we anticipate that trade secrets and know-how will, over time, be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from academic to industry scientific positions.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with appropriate federal, state, local and foreign statutes and regulations, require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA"), and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA’s refusal to approve pending NDAs, withdrawal of an

approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin;
- approval by an independent institutional review board ("IRB"), at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice ("GCP"), requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice ("cGMP"), requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. In 2008, we submitted our first IND to the FDA for plazomicin. We also previously submitted an IND to the FDA for ACHN-975 in 2012; however, as described above this IND was withdrawn in May 2014 following termination of the clinical program for this compound.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health ("NIH"), for public dissemination on their www.clinicaltrials.gov website.

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

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- 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: 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, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

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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. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution 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.

Special Protocol Assessment

The SPA process is designed to facilitate the FDA's review and approval of drugs by allowing the FDA to evaluate the proposed design and size of Phase 3 clinical trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and data analysis, within 45 days of receipt of the request.

The FDA ultimately assesses whether the protocol design and planned analysis of the trial are acceptable to support regulatory approval of the product candidate with respect to effectiveness of the indication studied. All agreements and disagreements between the FDA and the sponsor regarding an SPA must be clearly documented in an SPA letter or the minutes of a meeting between the sponsor and the FDA.

Even if the FDA agrees to the design, execution and analyses proposed in protocols reviewed under the SPA process, the FDA may revoke or alter its agreement under the following circumstances:

- public health concerns emerge that were unrecognized at the time of the protocol assessment, or the director of the review division determines that a substantial scientific issue essential to determining safety or efficacy has been identified after testing has begun;
- a sponsor fails to follow a protocol that was agreed upon with the FDA; or
- the relevant data, assumptions, or information provided by the sponsor in a request for SPA change, are found to be false statements or misstatements, or are found to omit relevant facts.

A documented SPA may be modified, and such modification will be deemed binding on the FDA review division, except under the circumstances described above, if FDA and the sponsor agree in writing to modify the protocol and such modification is intended to improve the study.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act ("PDUFA"), guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug 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. 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.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are 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 reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. 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.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. 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 may inspect one or more clinical trial sites to assure compliance with GCP requirements.

The FDA generally accepts data from foreign clinical trials in support of an NDA if the trials were conducted under an IND. If a foreign clinical trial is not conducted under an IND, the FDA nevertheless may accept the data in support of an NDA if the study was conducted in accordance with GCP requirements and the FDA is able to validate the data through an on-site inspection, if deemed necessary. Although the FDA generally requests that marketing applications be supported by some data from domestic clinical studies, the FDA may accept foreign data as the sole basis for marketing approval if (1) the foreign data are applicable to the U.S. population and U.S. medical practice, (2) the studies were performed by clinical investigators with recognized competence, and (3) the data may be considered valid without the need for an on-site inspection or, if the FDA considers the inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA’s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of 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 a drug’s safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a 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-marketing studies or surveillance programs. After approval, some 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.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need, or that the drug qualifies as a QIDP under the recently enacted GAIN Act. The FDA will

determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the new PDUFA agreement, these six and ten month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds

approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, 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. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Moreover, under the provisions of the FDASIA, passed in July 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug that is intended, 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 drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We received fast track designation from the FDA for plazomicin in August 2012. More recently in December 2014, plazomicin was designated a QIDP by the FDA under the recently enacted GAIN Act.

Post-Approval Requirements

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.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product’s safety and effectiveness after commercialization.

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 requirements 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 mandatory 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, 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, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that our product candidates are new chemical entities. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application ("ANDA"), or a 505(b)(2) NDA submitted by another company that references the previously approved drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. For drug products that contain an "antibiotic" ingredient approved prior to 1997, the statute imposes certain limitations on the award of non-patent exclusivity. However, we do not believe these limitations would apply to any of our investigational antibiotics.

Qualified Infectious Disease Product Exclusivity

Under the GAIN Act provisions of FDASIA, which was signed into law in July 2012, the FDA may designate a product as a "qualified infectious disease product." In order to receive this designation, a drug must qualify as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by either (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens, or (2) a so-called "qualifying pathogen" found on a list of potentially dangerous, drug-resistant organisms to be established and maintained by the FDA under the new law. A sponsor must request such designation before submitting a marketing application. We expect to request qualified infectious disease product designations for our product candidates prior to submitting a marketing application for such product candidates, as appropriate.

Upon approving an application for a qualified infectious disease product, the FDA will extend by an additional five years any non-patent marketing exclusivity period awarded, such as a five-year exclusivity period awarded for a new molecular entity. This extension is in addition to any pediatric exclusivity extension awarded, and the extension will be awarded only to a drug first approved on or after the date of enactment.

The GAIN Act provisions prohibit the grant of an exclusivity extension where the application is a supplement to an application for which an extension is in effect or has expired, is a subsequent application for a specified change to an approved product, or is an application for a product that does not meet the definition of qualified infectious disease product based on the uses for which it is ultimately approved.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. For example, in the European Union, we must obtain authorization of

a clinical trial application, in each member state in which we intend to conduct a clinical trial. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

To obtain a marketing authorization of a drug in the European Union, we may submit marketing authorization applications ("MAAs"), either under the so-called centralized or national authorization procedures.

Centralized Procedure

The centralized procedure provides for the grant of a single marketing authorization following a favorable opinion by the EMA that is valid in all European Union member states, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions. The centralized procedure is optional for products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA 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 of Medicinal Products for Human Use ("the CHMP"). Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks.

National Authorization Procedures

There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.
- Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In the European Union, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Regulation of In Vitro Diagnostic Assays

In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and

distribution, export and import, and post-market surveillance. Diagnostic tests are classified as medical devices under the FDCA. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and approval of a premarket approval application ("PMA"). The FDA classifies all medical devices into one of three classes. Devices deemed to pose lower risk are categorized as either Class I or II, which requires the manufacturer to submit to the FDA a 510(k) pre-market notification requesting clearance of the device for commercial distribution in the United States, unless an exemption applies. Devices

deemed by the FDA to pose the greatest risk, such as life sustaining, life-supporting or implantable devices, or devices deemed not substantially equivalent to a previously 510(k)-cleared device are categorized as Class III, requiring a PMA.

To obtain 510(k) clearance for a medical device, a pre-market notification must be submitted to the FDA demonstrating that the proposed device is substantially equivalent to a previously 510(k)-cleared device or a device that was in commercial distribution before May 28, 1976 for which the FDA has not yet called for the submission of a PMA, or the device must be one that has been reclassified from Class III to either Class II or I. The 510(k) clearance process usually takes from three to twelve months from the date the application is submitted and filed with the FDA, but may take significantly longer and clearance is never assured. Although many 510(k) pre-market notifications are cleared without clinical data, in some cases, the FDA requires significant clinical data to support substantial equivalence. In reviewing a pre-market notification, the FDA may request additional information, including clinical data, which may significantly prolong the review process. After a device receives 510(k) clearance, any subsequent modification of the device that could significantly affect its safety or effectiveness, or that would constitute a major change in its intended use, will require a new 510(k) clearance or could require pre-market approval. The FDA requires each manufacturer to make this determination initially, but the FDA may review any such decision and may disagree with a manufacturer’s determination. If the FDA disagrees with a manufacturer’s determination, the FDA may require the manufacturer to cease marketing and/or recall the modified device until 510(k) clearance or a PMA is obtained.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA’s satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation ("QSR"), which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. FDA review of an initial PMA application is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA’s evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

We and our partner, ARK, are developing a companion diagnostic assay for plazomicin and will work together to generate the data required for submission of either a 510(k) submission or a PMA application. We will remain in close contact with the Center for Devices and Radiological Health ("CDRH"), at the FDA to ensure that any changes in requirements are incorporated into the development plans. We anticipate that meetings with the FDA with regard to plazomicin as well as the companion diagnostic assay will include representatives from the Center for Drug Evaluation and Research, and CDRH to ensure that the drug and device submissions are coordinated to enable the FDA to conduct a parallel review of both submissions. On July 14, 2011, the FDA issued for comment a draft guidance document addressing the development and clearance or approval process for "In vitro Companion Diagnostic Devices." According to the draft guidance, for novel therapeutic products such as plazomicin, the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic. While this draft guidance is not yet finalized, we believe our programs for the development of our companion diagnostic are consistent with the draft guidance as proposed.

In the European Economic Area ("EEA"), in vitro medical devices are required to conform with the essential requirements of the EU Directive on in vitro diagnostic medical devices (Directive No 98/79/EC, as amended). To

demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of medical device and its classification. For low-risk devices, the conformity assessment can be carried out internally, but for higher risk devices it requires the intervention of an accredited EEA Notified Body. If successful, the conformity assessment concludes with the drawing up by the manufacturer of an EC Declaration of Conformity entitling the manufacturer to affix the CE mark to its products and to sell them throughout the EEA. The data generated for the U.S. registration will be sufficient to satisfy the regulatory requirements for the European Union and other countries.

Fraud and Abuse and Data Privacy and Security Laws and Regulations.

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state fraud and abuse laws restrict business practices in the biopharmaceutical industry. These laws include anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not meet the requirements of a statutory or regulatory exception or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-covered, uses. In addition, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), also created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ("PPACA"), signed into law on March 2010, broadened the reach of both the Anti-Kickback Statute and the criminal healthcare fraud statute by amending the intent requirement such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. PPACA created new federal requirements for reporting, by applicable manufacturers of covered drugs, payments and other transfers of value to physicians and teaching hospitals. Applicable manufacturers are also required to report annually to the government certain ownership and investment interests held by physicians and their immediate family members, and payments or other transfers of value to such physician owners and their immediate family members. In addition, certain states require implementation of commercial compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices, and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act ("HITECH"), and its implementing regulations, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of

covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts.

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products or companion diagnostic assay for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. By way of example, in the United States, the PPACA contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, addressed new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extension products, mandatory discounts for certain Medicare Part D beneficiaries, and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

Manufacturing

We do not own or operate manufacturing facilities for the production of any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely on a limited number of third-party contract manufacturers for all of our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. We expect that our in vitro assay will be manufactured by ARK or another third-party supplier. For plazomicin, we source raw materials from various commercial suppliers, primarily located in the People's Republic of China, including sisomicin, the aminoglycoside precursor for plazomicin. Our drug substance is currently manufactured by Hovione Inter Limited and the finished drug product by a U.S. based contract manufacturer. We do not have long-term agreements with these third parties. We do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates after they are approved. We currently employ internal resources to manage our manufacturing. If any of our products are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products.

Plazomicin is an organic compound of low molecular weight, commonly referred to as a small molecule. Plazomicin is also considered a semi-synthetic molecule since it is derived from a primary starting material that is a natural product, sisomicin, produced by microbial fermentation. Sisomicin is combined with other starting materials over a series of chemical steps to produce plazomicin. We believe that our use of a synthetic process will enable us to have a cost of manufacturing for plazomicin that is similar to other small molecule antibiotics.

Research and Development Expenses

We devote a substantial portion of our resources to developing new product candidates. Please see "Management's Discussion and Analysis of Financial Condition and Results of Operations-Financial Overview and Results of Operations-Research and Development Expenses" for the amounts spent on company-sponsored research and development for the past three fiscal years.

Customer Concentration and Geographic Information

For the years ended December 31, 2014, 2013 and 2012, all of the Company's revenue has been generated solely from funding pursuant to U.S. government contracts, and accordingly all contracts receivable relate to funding from U.S. government. See Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

All of our revenues for the years ended December 31, 2014, 2013, and 2012 were earned in the United States. All of our long-lived assets are located in the United States.

Employees

As of December 31, 2014, we had 44 full-time employees, 33 of whom were primarily engaged in research and development activities and 11 of whom were primarily engaged in business development, finance, legal, human resources, facilities, information technology administration and general management. None of our employees is represented by a labor union and we consider our employee relations to be good.

Additional Information

We view our operations and measure our business as one reportable segment operating primarily in the United States. See Note 2 to our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information. Additional information required by this item is incorporated herein by reference to Part I, Item 6, "Selected Consolidated Financial Data."

We were originally incorporated in Delaware in June 2002 and commenced operations in 2004. We completed our initial public offering of our common stock in March 2014. Our mailing address and executive offices are located at 7000 Shoreline Court, Suite 371, South San Francisco, CA 94080 and our telephone number at that address is (650) 800-3636. We maintain an Internet website at the following address: www.achaogen.com. The information on our website is not incorporated by reference in this annual report on Form 10-K or in any other filings we make with the SEC.

We make available on or through our website certain reports and amendments to those reports that we file with or furnish to the SEC in accordance with the Exchange Act. These include our annual reports on Form 10-K, our quarterly reports on Form 10-Q, and our current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC.

Item 1A. Risk Factors.

Risks Related to Our Business and Capital Requirements

We have a limited operating history, have incurred net losses in each year since our inception and anticipate that we will continue to incur significant losses for the foreseeable future, and if we are unable to achieve and sustain profitability, the market value of our common stock will likely decline.

We are a clinical-stage biopharmaceutical company with a limited operating history. We have not generated any revenue from the sale of products and have incurred losses in each year since we commenced operations in 2004. All of our product candidates are in development, and none has been approved for sale. In the years ended December 31, 2014, 2013 and 2012, we derived all of our revenue from government contracts for research and development. Our net losses for the years ended December 31, 2014, 2013 and 2012 were $20.2 million, $13.1 million and $18.4 million, respectively. As of December 31, 2014, we had an accumulated deficit of $148.9 million.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we continue to conduct our Phase 3 CARE (Combating Antibiotic Resistant Enterobacteriaceae) trial of our lead product candidate, plazomicin, seek marketing approval for plazomicin, and continue the development of our other product candidates. Our expenses will also increase substantially if and as we:

- conduct additional clinical trials for our product candidates;
- continue to discover and develop additional product candidates;
- establish a sales, marketing and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;
- establish a manufacturing and supply chain sufficient for commercial quantities of any product candidates for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, scientific and commercial personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts, as well as to support our transition to a public reporting company; and
- acquire or in-license other product candidates and technologies.

If our product candidates fail to demonstrate safety and efficacy in clinical trials, do not gain regulatory approval, or do not achieve market acceptance following regulatory approval and commercialization, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. If we are unable to achieve and sustain profitability, the market value of our common stock will likely decline. Because of the numerous risks and uncertainties associated with developing biopharmaceutical products, we are unable to predict the extent of any future losses or when, if ever, we will become profitable.

We are substantially dependent on the success of our lead product candidate, plazomicin, which is in Phase 3 clinical development. If we are unable to develop, obtain marketing approval for and successfully commercialize plazomicin, or experience significant delays in doing so, our business could be materially harmed.

We currently have no products approved for sale, and since 2007, we have invested a significant portion of our efforts and financial resources in the development of plazomicin. Our future success is substantially dependent on our ability to successfully develop, obtain regulatory approval for and, ultimately, successfully commercialize plazomicin. In September 2014, we dosed our first patients in our Phase 3 CARE trial. We have not conducted a clinical trial of plazomicin in patients with CRE infections, and we have no direct clinical evidence that plazomicin is effective in treating CRE infections in humans. Our Phase 2 trial evaluated the efficacy of plazomicin compared with levofloxacin in patients with complicated urinary tract infections ("cUTI"). Our ability to develop, obtain regulatory approval for, and successfully commercialize plazomicin effectively will depend on several factors, including the following:

- successful completion of our Phase 3 CARE trial or other clinical trials, which will depend substantially upon the satisfactory performance of third-party contractors;

- successful demonstration of a mortality benefit, pharmacoeconomic benefits and/or a favorable risk-benefit outcome of plazomicin in a pivotal clinical trial;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States;
- establishing commercial manufacturing and supply arrangements;
- establishing a commercial infrastructure;
- identifying and successfully establishing one or more collaborations to commercialize plazomicin;
- acceptance of the product by patients, the medical community and third-party payors;
- establishing market share while competing with other therapies;
- successfully executing our pricing and reimbursement strategy;
- a continued acceptable safety and adverse event profile of the product following regulatory approval; and
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering the product.

In addition, our product development program includes the development of an in vitro diagnostic ("IVD") assay which must successfully complete a clinical performance study, conducted concurrently with and utilizing patient samples from the Phase 3 CARE trial of plazomicin, and be approved or cleared for marketing by the FDA and certain other foreign regulatory agencies, contemporaneously with the marketing approval for plazomicin, and then be commercialized concurrently with plazomicin in the associated markets. If we are unable to develop, receive marketing approval for plazomicin or the IVD assay in a timely manner or at all, we could experience significant delays or an inability to commercialize plazomicin, which would materially and adversely affect our business, financial condition, and results of operations.

Clinical drug development involves a lengthy and expensive process with uncertain outcomes that may lead to delayed timelines and increased cost, and may prevent us from being able to complete clinical trials.

Clinical testing is expensive, can take many years to complete, and its outcome and timeline is inherently uncertain. The results of preclinical and clinical studies of our product candidates may not be predictive of the results of later-stage clinical trials. For example, the positive results generated to date in nonclinical and clinical studies for plazomicin do not ensure that our Phase 3 CARE trial will demonstrate similar results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks.

The first patient in our Phase 3 CARE trial for plazomicin was enrolled in September 2014. Enrollment continues at a rate that has been slower than anticipated and we have been exploring strategies to improve patient recruitment and remain in discussions with the FDA regarding potential modifications to the study design as well as additional clinical trials that could support and, possibly, facilitate regulatory filings for plazomicin. We cannot be certain that the trial, or any other future clinical trials for plazomicin, or other product candidates, will begin on time, not need to be redesigned, enroll an adequate number of patients on time or be completed on schedule, if at all, or that any interim analyses with respect to such trials will be completed on schedule or support continued clinical development of the associated product candidate.

Clinical trials can be delayed or aborted for a variety of reasons, including delay or failure:

- to obtain regulatory approval to commence a trial;
- to recruit and enroll suitable patients to participate in a trial;
- to reach agreement on acceptable terms with prospective contract research organizations ("CROs"), clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- to obtain institutional review board ("IRB") approval at each site;
- to have patients complete a trial or return for post-treatment follow-up;
- of clinical sites to adhere to trial protocols or continue to participate in a trial;
- to address any patient safety concerns that arise during the course of a trial;
- to address any conflicts with new or existing laws or regulations;

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- to add a sufficient number of clinical trial sites; or
- to manufacture sufficient quantities of product candidate for use in clinical trials.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, slow down or halt our product development and approval processes, and jeopardize our ability to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain additional financing if needed. Patient enrollment in clinical trials is a function of many factors, including: the nature of clinical trial protocols, existence of competing protocols or treatments (if any), the size and longevity of the target patient population, proximity of patients to clinical sites and eligibility criteria for the clinical trials. Although we will continue to look for opportunities for faster regulatory approval of plazomicin or our other product candidates, including potential additional clinical trials, we cannot guarantee that such opportunities will arise, that the FDA or other regulatory authorities will agree with any proposals we make or that such proposals, even if approved, will be successful.

We could also encounter delays if a clinical trial is suspended or terminated by us upon recommendation of the data monitoring committee for such trial, by the IRBs of the institutions in which such trials are being conducted, or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate revenue from the sale of any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval processes, and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may significantly harm our business, financial condition and prospects significantly.

Our Phase 3 CARE trial for plazomicin is subject to a number of specific risks that may affect the outcome of the trial, including the lack of a prior clinical trial in patients with CRE infections and challenges in enrolling an adequate number of patients with rare infections.

Our Phase 3 CARE trial for plazomicin is subject to a number of specific risks arising from our clinical program and the design of the trial. We have not conducted a clinical trial of plazomicin in patients with CRE infections or with bloodstream infections or pneumonia, who are the subjects of our Phase 3 CARE trial, and we have no direct clinical evidence that plazomicin is effective in treating CRE infections in humans. Our Phase 2 trial demonstrated that plazomicin was as effective as the comparator drug in treating cUTI arising from non-CRE bacteria. Although we believe that plazomicin will be effective in treating CRE infections in humans based upon our nonclinical in vitro and in vivo animal model study results, together with our Phase 2 trial results, these results are not necessarily predictive of the results in humans and we cannot guarantee that plazomicin will demonstrate the expected efficacy in our Phase 3 CARE trial in patients. We also cannot guarantee that the projections made from our pharmacokinetic and pharmacodynamic models we developed from our nonclinical and clinical plazomicin studies will be validated in our Phase 3 CARE trial.

Because our Phase 3 CARE trial for plazomicin is enrolling patients with rare infections, finding a sufficient number of suitable patients with CRE infections to enroll in the trial is a significant challenge. Enrollment of patients in this trial continues at a rate that has been slower than we anticipated and we have been exploring strategies to improve patient recruitment and remain in discussions with the FDA regarding potential modifications to the study design as well as additional clinical trials that could support and, possibly, facilitate regulatory filings for plazomicin. In addition, we may face competition in enrolling suitable patients as a result of other companies conducting clinical trials for antibiotic product candidates treating similar infections, resulting in slower than anticipated enrollment in our trial. Enrollment delays in this trial may result in increased development costs for plazomicin, or slow down or halt our product development and approval process for plazomicin. We may choose to revise the enrollment protocol, commence a new trial in a different patient population, or take other actions that may result in a substantial change in

the clinical development program of plazomicin.

Our Phase 3 CARE trial also involves dosing of patients with plazomicin for longer durations (7–14 days) than in our Phase 1 and 2 trials at the comparable dosage (up to five days), which may lead to additional or more severe adverse events than were reported in our Phase 1 and 2 trials, including as a result of toxicity in the kidneys, inner ear, or hypotension.

See the risk factor entitled “Serious adverse events or undesirable side effects or other unexpected properties of plazomicin or any other product candidate may be identified during development or after approval that could delay, prevent or cause the

withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval."

Our Phase 3 CARE trial is using a superiority design rather than a non-inferiority design. In order to meet our primary endpoint, we must show that plazomicin is superior to the comparator therapy with respect to all-cause mortality at 28 days. This is a different standard than most other antibiotic clinical trials, which are designed to show that the antibiotic is not inferior to the comparator therapy. We may be unable to demonstrate superiority or the anticipated pharmacoeconomic benefits of plazomicin therapy in our Phase 3 CARE trial. Our choice of a mortality endpoint means that success will depend to a significant degree on the accuracy of our assumptions about mortality rates in the comparator and plazomicin arms of our Phase 3 CARE trial. Although we believe we have been conservative in our assumptions, if, for example, patients in the comparator arm of our trial have significantly lower mortality than we expect, we may find that our trial is unfeasible or may have to enroll more patients at additional cost and delay. Further, if we choose to revise our current trial protocol or complete an alternative pivotal trial for plazomicin, we may not be able to claim certain of the market and label benefits that a successful superiority trial could provide. Any failure to meet our endpoints in the Phase 3 CARE trial or adequately address safety concerns would jeopardize our ability to obtain regulatory approval for and commercialize plazomicin and significantly harm our business, financial condition, and prospects.

See also the risk factor entitled "Clinical drug development involves a lengthy and expensive process with uncertain outcomes that may lead to delayed timelines and increased cost, and may prevent us from being able to complete clinical trials."

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate our product development, other operations or commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is an expensive and highly uncertain process that takes years to complete. We expect our expenses to increase substantially as we continue the clinical development of our lead product candidate, plazomicin, seek marketing approval for plazomicin and continue the development of our other product candidates. If we obtain marketing approval of plazomicin, we also expect to incur significant sales, marketing, manufacturing and supply expenses.

As of December 31, 2014, we had working capital of $63.9 million and cash, cash equivalents and short-term investments of $63.7 million. We believe we have sufficient capital resources to fund our operations through at least the next 12 months. However, enrollment in our Phase 3 CARE trial of plazomicin has been slower than anticipated and if this continues, we may decide to change our clinical development plan for plazomicin, in which case, we will need to seek additional funds sooner than planned. In addition, other factors may arise causing us to need additional capital resources sooner than anticipated. We anticipate that we will need to raise substantial additional financing in the future to fund our operations, including for obtaining marketing approval for plazomicin.

We may obtain additional financing through public or private equity offerings, debt financings, a credit facility, government contracts and/or strategic collaborations. Additional financing may not be available to us when we need it or it may not be available to us on acceptable terms, if at all. In addition, although we currently anticipate being able to generate additional financing through non-dilutive means, we may be unable to do so. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. The amount and timing of our future financing requirements will depend on many factors, including:

- continued funding under our contract with BARDA;
- whether or not we decide to pursue additional or alternative pivotal trials for plazomicin;
- the size and type of the nonclinical and clinical trials that we decide to pursue in the development of our product candidates, including plazomicin;
- the type, number, costs and results of the product candidate development programs which we are pursuing or may choose to pursue in the future;
- the rate of progress and cost of our clinical trials, preclinical studies and other discovery and research and development activities;
- the timing of, and costs involved in, seeking and obtaining FDA and other regulatory approvals;
- our ability to enter into additional collaboration, licensing or other arrangements and the terms and timing of such arrangements;

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- the costs of preparing, filing, prosecuting, maintaining and enforcing any patent claims and other intellectual property rights, including litigation costs and the results of such litigation;
- the emergence of competing technologies and other adverse market developments;
- the resources we devote to marketing, and, if approved, commercializing our product candidates;
- the scope, progress, expansion, and costs of manufacturing our product candidates;
- our ability to enter into additional government contracts, or other collaborative agreements, to support the development of our product candidates and development efforts; and
- the costs associated with being a public company.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. We currently have no understandings, commitments or agreements relating to any of these types of transactions.

If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license to others technologies or clinical product candidates or programs that we would prefer to develop and commercialize ourselves.

Failure to successfully validate, develop and obtain regulatory clearance or approval for our IVD assay could harm our product development strategy.

An important element of our clinical development strategy for plazomicin is the development of an IVD assay to measure levels of plazomicin in the blood, which will enable patients to receive safe and efficacious doses of plazomicin. In collaboration with ARK Diagnostics, Inc. (“ARK”), we are co-developing such an assay for our Phase 3 CARE program, which will be commercialized concurrently with plazomicin, if approved.

IVD assays are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and therefore require separate regulatory clearance or approval prior to commercialization. An IVD assay that is required for safe and effective use of a drug is referred to as a companion diagnostic. The clinical development of novel therapeutics with a companion diagnostic is complex from an operational and regulatory perspective because of the need for both the drug and the diagnostic to receive regulatory clearance or approval. Specifically, on July 14, 2011, the FDA issued for comment a draft guidance document addressing the development and approval processes for “In Vitro Companion Diagnostic Devices.” According to the draft guidance, for novel therapeutic products such as plazomicin, a companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic. If the regulatory clearance or approval process for our IVD assay is delayed, our ability to commercialize plazomicin could be delayed until we receive regulatory clearance or approval for the companion diagnostic assay.

It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of our assay during the development and regulatory approval process. We also expect to develop the assay for use on additional analyzers beyond the current Roche Modular P. We, ARK or our future collaborators may encounter difficulties in developing, obtaining regulatory clearance or approval for and manufacturing of the assay with appropriate quality standards, similar to those we face with respect to our drug product candidates themselves. Failure to overcome these hurdles could have an adverse effect on our ability to obtain regulatory approval for or to obtain market acceptance for and to commercialize our assay or plazomicin.

If we fail to demonstrate the safety and efficacy of plazomicin or any other product candidate that we develop to the satisfaction of the FDA or comparable foreign regulatory authorities we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of plazomicin or such other product candidate. This would adversely impact our ability to generate revenue, our business and our results of operations.

We are not permitted to commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the EMA, and we may never receive such approvals. To gain approval to market a drug product, we must complete extensive preclinical development and clinical trials that demonstrate the safety and efficacy of the product for the intended indication to the satisfaction of the FDA or other regulatory authority.

We have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that plazomicin will be successful in clinical trials or

receive regulatory approval. Further, plazomicin may not receive regulatory approval even if it is successful in clinical trials. If we do not receive

regulatory approval for plazomicin, we may not be able to continue our operations. Even if we successfully obtain regulatory approval to market plazomicin, our revenue will be dependent, in part, upon our or a commercial partner's ability to obtain regulatory approval of an IVD assay to be used with plazomicin, as well as upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights.

The FDA or any foreign regulatory agencies can delay, limit, or deny approval of plazomicin for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory agency that plazomicin is safe and effective for the requested indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate that the clinical and other benefits of plazomicin outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional preclinical or clinical studies;
- the FDA's or the applicable foreign regulatory agency's non-approval of the formulation, labeling or the specifications of plazomicin;
- the FDA's or the applicable foreign regulatory agency's failure to approve the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Even if we eventually complete clinical testing and receive approval of an NDA or foreign regulatory filing for plazomicin, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. The FDA or the applicable foreign regulatory agency also may approve plazomicin for a more limited indication or a narrower patient population than we originally requested, and the FDA, or applicable foreign regulatory agency, may not approve the labeling that we believe is necessary or desirable for the successful commercialization of plazomicin. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of plazomicin and would materially adversely impact our business and prospects. Any other product candidate we advanced to the marketing approval stage would also be subject to the risks delineated above.

Although we have entered into a Special Protocol Assessment agreement with the FDA relating to our Phase 3 CARE trial of plazomicin, and have obtained feedback from the EMA through their scientific advice procedure, this agreement and feedback do not guarantee any particular outcome with respect to regulatory review of the pivotal trial or with respect to regulatory approval of plazomicin.

In September 2013, the protocol for our Phase 3 CARE trial of plazomicin was reviewed and agreed upon by the FDA under a Special Protocol Assessment agreement ("SPA"), which creates a written agreement between the sponsoring company and the FDA regarding clinical trial design and other clinical trial issues, such as the trial endpoints, that can be used to support approval of a product candidate. The SPA is intended to provide assurance that if the agreed upon clinical trial protocols are followed and the clinical trial endpoints are achieved, the data may serve as the primary basis for an efficacy claim in support of an NDA. Agreement on an SPA is not a guarantee of approval, and there is no assurance that the design of, or data collected from, the trial will be adequate to obtain the requisite regulatory approval. The SPA is not binding on the FDA if public health concerns unrecognized at the time the SPA was entered into become evident, if other new scientific concerns regarding product safety or efficacy arise, if the information provided by the sponsoring company in the SPA request changes or is found to be false or misleading or omit relevant facts, or if the sponsoring company fails to comply with the agreed upon clinical trial protocols. Moreover, SPA agreements do not address all of the variables and details that may go into planning for or conducting a clinical trial, and any change in the protocol for a clinical trial can invalidate the SPA agreement. In addition, upon written agreement of both parties, the SPA may be changed, and the FDA retains significant latitude and discretion in interpreting the terms of an SPA and any resulting trial data. As a result, we do not know how the FDA will interpret the parties' respective commitments under the SPA, how it will interpret the data and results from the Phase 3 CARE trial, whether the FDA will require that we conduct or complete one or more additional clinical trials to support potential approval, including the completion of our ongoing clinical trial of plazomicin, or whether plazomicin will

receive any regulatory approvals.

Similarly, we have solicited feedback on our planned Phase 3 CARE trial for plazomicin through the EMA's scientific advice procedure and believe that this trial, if successful, will be acceptable to support a marketing application in the European Union ("EU"). However, this feedback is not a guarantee of approval, and we do not know how the EMA will interpret the data and results from our Phase 3 CARE trial and other elements of our development program, whether they will require that we

conduct one or more additional clinical trials or nonclinical studies to support potential approval, or whether plazomicin will receive any regulatory approvals in the EU. We have initiated discussions with the FDA and the EMA regarding additional clinical trials that could support regulatory filings for plazomicin. We currently expect to be in a position to provide an update on the development of plazomicin by early in the second quarter of 2015.

Serious adverse events or undesirable side effects or other unexpected properties of plazomicin or any other product candidate may be identified during development or after approval that could delay, prevent or cause the withdrawal of regulatory approval, limit the commercial potential, or result in significant negative consequences following marketing approval.

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an IRB, or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. If plazomicin or any of our other product candidates are associated with serious adverse events or undesirable side effects or have properties that are unexpected, we may need to abandon their development or limit development 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.

To date, plazomicin has generally been well tolerated in clinical trials conducted in healthy subjects, subjects with renal impairment, and in patients with complicated urinary tract infections, and there have been no reports of serious adverse events related to plazomicin in our completed clinical trials. However, our Phase 3 CARE trial for plazomicin involves more extended dosing (7–14 days) than our Phase 1 and 2 trials at the comparable dosage (up to five days), which may lead to additional or more severe adverse events than were reported in our Phase 1 and 2 trials. Toxicity in the kidneys and inner ear are the most significant identified risks for plazomicin, which are well-known risks for the aminoglycoside class of antibiotics. Hypotension is also a potential risk for plazomicin.

Undesirable side effects or other unexpected adverse events or properties of plazomicin or any of our other product candidates could arise or become known either during clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, plazomicin or our other product candidates. If such an event occurs after plazomicin or such other product candidates are approved, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such product;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more post-market studies;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating revenue from the sale of our products and harm our business and results of operations.

We cannot predict when bacteria may evolve resistance to plazomicin, which could affect the revenue potential for plazomicin.

We are developing plazomicin to treat multi-drug resistant infections. The bacteria responsible for these infections evolve quickly and readily transfer their resistance mechanisms within and between species. We cannot predict when bacterial resistance to plazomicin may become prevalent.

As with some other commercially available aminoglycosides, plazomicin is not active against organisms expressing a resistance mechanism known as ribosomal methyltransferase. Although occurrence of this resistance mechanism among CRE is currently rare outside of certain countries in Asia, there have been isolated cases of infections by bacteria carrying ribosomal methyltransferase elsewhere, including in the United States. We cannot predict whether ribosomal methyltransferase will become widespread in regions where we intend to market plazomicin if it is

approved. The growth of MDR infections in community settings or in countries with poor public health infrastructures, or the potential use of plazomicin outside of controlled hospital

settings, could contribute to the rise of plazomicin resistance. If resistance to plazomicin becomes prevalent, our ability to generate revenue from plazomicin could suffer.

We will be dependent on ARK to develop and manufacture our IVD assay for our Phase 3 CARE trial for plazomicin, and may become dependent on ARK to commercialize such IVD assay.

We will be dependent on the sustained cooperation and effort of ARK in the development and manufacture of our IVD assay for plazomicin for our Phase 3 CARE trial, including in the generation of analytical data for regulatory approval of such assay. We have also agreed to negotiate with ARK for a commercialization agreement for the IVD assay, and have agreed that any such commercialization agreement would provide ARK with the first right to commercialize the assay in the United States and the EU, and to manufacture and supply the assay worldwide for commercialization, while we would have the first right to commercialize the assay in any other country or territory, in addition to rights to commercialize the assay in the United States and the EU if ARK elects not to do so. Should we enter into such an agreement with ARK, we will be dependent on ARK with respect to such manufacturing and supply and with respect to commercialization in the United States and the EU. This will reduce our control over these activities but does not relieve us of our responsibility to ensure compliance with all required legal, regulatory and scientific standards with respect to the assay.

If ARK does not successfully carry out its contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we may not be able to complete, or may be delayed in completing, clinical trials required to support approval of our product candidates and clearance or approval of the assay. We or ARK may encounter difficulties in developing the assay for commercial application in one or more countries, including issues in relation to automation, selectivity/specificity, analytical validation, reproducibility, or clinical validation of such assay. If we do not enter into such a commercialization agreement with ARK, and ARK elects not to participate in the commercialization of the assay in the United States and/or the EU, we would have to find an alternative collaborator, which we may not be able to do on commercially reasonable terms, or at all. If ARK or any such alternative collaborator does not perform its contractual duties or obligations, experiences work stoppages, does not meet expected deadlines, terminates its agreements with us or needs to be replaced, or if they otherwise do not meet our expectations for development, manufacture or commercialization of the assay, we may need to enter into new arrangements with one or more alternative third parties for development, manufacture or commercialization of the assay or an alternative assay. We may not be able to do so on commercially reasonably terms, or within the terms of the commercialization agreement without amending such terms, or at all, which could adversely impact our business and results of operations.

If we are not successful in discovering, developing and commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our efforts is focused, and will continue to be focused, on our Phase 3 CARE trial and potential approval of our lead product candidate, plazomicin, a key element of our strategy is to discover, develop and commercialize a portfolio of therapeutics to treat multi-drug resistant bacterial infections. We are seeking to do so through our internal research programs and are exploring, and intend to explore in the future, strategic partnerships for the development of new products. Other than plazomicin, all of our other potential product candidates remain in the discovery and preclinical stages.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- we may be unable to successfully modify candidate compounds to be active in gram-negative bacteria or defeat bacterial resistance mechanisms or identify viable product candidates in our screening campaigns;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;

- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors; and

- the development of bacterial resistance to potential product candidates may render them ineffective against target infections.

We withdrew ACHN-975, one of the product candidates from our LpxC inhibitor development program, from clinical trials due to inflammation at the infusion site in some of our Phase 1 subjects and withdrew the IND application for this compound in May 2014. We are actively assessing alternative backup compounds in order to identify candidates that preclinical lab tests will show are effective and likely to exhibit a superior clinical safety profile. We cannot guarantee that these efforts will be successful. If we identify viable product candidates, we would have to submit a new IND application for any compound we seek to advance to clinical trials.

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth may be impaired.

Even if a product candidate does obtain regulatory approval it may never achieve market acceptance by physicians, patients, hospitals, third-party payors and others in the medical community necessary for commercial success and the market opportunity may be smaller than we estimate.

Even if we obtain FDA or other regulatory approvals, and are able to launch plazomicin or any other product candidate commercially, the product candidate may not achieve market acceptance among physicians, patients, hospitals (including pharmacy directors) and third-party payors and, ultimately, may not be commercially successful. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

- the efficacy and safety of the product candidate as demonstrated in clinical trials;
- relative convenience and ease of administration;
- the clinical indications for which the product candidate is approved;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- the willingness of physicians to prescribe the product;
- the willingness of hospital pharmacy directors to purchase our products for their formularies;
- acceptance by physicians, operators of hospitals and treatment facilities and parties responsible for reimbursement of the product;
- the availability of adequate coverage and reimbursement by third-party payors and government authorities;
- the effectiveness of our sales and marketing efforts;
- the strength of marketing and distribution support;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved risk evaluation and mitigation strategy;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- the emergence of bacterial resistance to the product candidate; and
- the rate at which resistance to other drugs in the target infections grow.

Any failure by plazomicin or any other product candidate that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

The availability of adequate third-party coverage and reimbursement for newly approved products is uncertain, and failure to obtain adequate coverage and reimbursement from government and other third-party payors could impede our ability to market any future products we may develop and could limit our ability to generate revenue.

There is significant uncertainty related to the third-party payor coverage and reimbursement of newly approved medical products. The commercial success of our future products in both domestic and international markets depends on whether third-

party coverage and reimbursement is available for our future products. Governmental payors, including Medicare and Medicaid, health maintenance organizations and other third-party payors are increasingly attempting to manage their healthcare expenditures by limiting both coverage and the level of reimbursement of new drugs and biologics and, as a result, they may not cover or provide adequate reimbursement for our future products. These payors may not view our future products as cost-effective, and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our future products to be marketed on a competitive basis.

Third-party payors are exerting increasing influence on decisions regarding the use of, and coverage and reimbursement levels for, particular treatments. Such third-party payors, including Medicare, are challenging the prices charged for medical products and services, and many third-party payors limit or delay coverage and reimbursement for newly approved healthcare products. In particular, third-party payors may limit the covered indications. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated revenue from the sale of our product candidates. If we decrease the prices for our product candidates because of competitive pressures or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our prospects for revenue and profitability will suffer.

In addition, to the extent that our product candidates will be used in a hospital inpatient setting, hospitals often receive fixed reimbursement for all of a patient's care, including the cost of our drug products and IVD assay, based on the patient's diagnosis. For example, Medicare reimbursement for hospital inpatient stays is generally made under a prospective payment system that is determined by a classification system known as the Medicare severity diagnosis-related groups. Our patients' access to adequate coverage and reimbursement by government and private insurance plans is central to the acceptance of our future products. We may be unable to sell our products on a profitable basis if third-party payors reduce their current levels of payment, or if our costs of production increase faster than increases in reimbursement levels.

We are developing our lead product candidate plazomicin for the treatment of serious CRE infections, which constitute a growing but relatively small patient population. Antibiotics have historically been marketed towards broad patient populations at relatively low prices. We currently intend to seek pricing and reimbursement for plazomicin based on the superior mortality benefit and pharmacoeconomic advantages over existing treatments we are seeking to demonstrate in our Phase 3 CARE trial. If we are unable to demonstrate such benefits, or if governmental or other third-party payors do not view the benefits as worth the cost, we will be unable to achieve our pricing and reimbursement objectives and our prospects for revenue and profitability will suffer.

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

We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct our preclinical studies and clinical trials on our product candidates in compliance with applicable regulatory requirements. These third parties are not our employees and, except for restrictions imposed by our contracts with such third parties, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our preclinical studies and clinical trials, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and the applicable legal, regulatory, and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. The FDA and regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as current good clinical practices ("cGCPs"), for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. If we or any of our third party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, we are required to report certain financial interests of our third party investigators if these relationships exceed certain financial thresholds and meet other criteria. The FDA or comparable foreign regulatory authorities may question the integrity of the data from those clinical trials conducted by principal investigators who previously served or currently serve as scientific advisors or consultants to us from time to time and

receive cash compensation in connection with such services. Our clinical trials must also generally be conducted with products produced under current good manufacturing practice ("cGMP") regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Many of the third parties with whom we contract may also have relationships with other commercial entities, some of which may compete with us. If the third parties conducting our preclinical studies or our clinical trials do not perform their contractual duties or obligations or comply with regulatory requirements we may need to enter into new arrangements with alternative third parties. This could be costly, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated, and we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable product candidate, or to commercialize such product candidate being tested in such studies or trials. If any of our relationships with these third parties

terminate, we may not be able to enter into arrangements with alternative third party contractors or to do so on commercially reasonable terms. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We rely on third-party contract manufacturing organizations to manufacture and supply plazomicin and other product candidates for us, as well as certain raw materials used in the production thereof. If one of our suppliers or manufacturers fails to perform adequately we may be required to incur significant delays and costs to find new suppliers or manufacturers.

We currently have limited experience in, and we do not own facilities for, manufacturing our product candidates, including plazomicin. We rely upon third-party manufacturing organizations to manufacture and supply our product candidates and certain raw materials used in the production thereof. Some of our key components for the production of plazomicin have a limited number of suppliers. In particular, sisomicin, the aminoglycoside precursor for plazomicin, is supplied by a single manufacturer in China for which we do not have a commercial supply agreement. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacture of our drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We do not have commercial supply agreements with our suppliers. In the event that we and our suppliers cannot agree to the terms and conditions for them to provide clinical and commercial supply needs, we would not be able to manufacture our product or candidates until a qualified alternative supplier is identified, which could also delay the development of, and impair our ability to commercialize, our product candidates.

Our third party suppliers may not be able to meet our supply needs or timelines and this may negatively affect our business. A majority of the manufacturing process is operated internationally, and therefore may be subject to similar risks of the sort described by the risk factor entitled “A variety of risks associated with international operations could materially adversely affect our business.”

The failure of third-party manufacturers or suppliers to perform adequately or the termination of our arrangements with any of them may adversely affect our business.

We may be subject to costly product liability claims related to our clinical trials and product candidates and, if we are unable to obtain adequate insurance or are required to pay for liabilities resulting from a claim excluded from, or beyond the limits of our insurance coverage, a material liability claim could adversely affect our financial condition.

Because we conduct clinical trials with human patients, we face the risk that the use of our product candidates may result in adverse side effects to patients in our clinical trials. We face even greater risks upon any commercialization of our product candidates. Although we have product liability insurance, which covers our clinical trials for up to $5.0 million, our insurance may be insufficient to reimburse us for any expenses or losses we may suffer, and we will be required to increase our product liability insurance coverage for our advanced clinical trials that we plan to initiate. We do not know whether we will be able to continue to obtain product liability coverage and obtain expanded coverage if we require it, on acceptable terms, if at all. We may not have sufficient resources to pay for any liabilities resulting from a claim excluded from, or beyond the limits of, our insurance coverage. Where we have provided indemnities in favor of third parties under our agreements with them, there is also a risk that these third parties could incur liability and bring a claim under such indemnities. An individual may bring a product liability claim against us alleging that one of our product candidates or products causes, or is claimed to have caused, an injury or is found to be unsuitable for consumer use. Any product liability claim brought against us, with or without merit, could result in:

- withdrawal of clinical trial volunteers, investigators, patients or trial sites;

- the inability to commercialize our product candidates;
- decreased demand for our product candidates;
- regulatory investigations that could require costly recalls or product modifications;

- loss of revenue;
- substantial costs of litigation;
- liabilities that substantially exceed our product liability insurance, which we would then be required to pay ourselves;
- an increase in our product liability insurance rates or the inability to maintain insurance coverage in the future on acceptable terms, if at all;
- the diversion of management's attention from our business; and
- damage to our reputation and the reputation of our products.

Product liability claims may subject us to the foregoing and other risks, which could have a material adverse effect on our business, results of operations, financial condition and prospects.

If we fail to establish an effective distribution process, which includes utilizing cold chain logistics for plazomicin and the associated IVD assay, our business may be adversely affected.

We do not currently have the infrastructure necessary for distributing pharmaceutical products to patients. We intend to contract with a third-party logistics company to warehouse these products and distribute them, and we will require plazomicin and the associated IVD assay to be maintained at a controlled temperature for some of the distribution chain. Failure to secure contracts with a logistics company could negatively impact the distribution of plazomicin or the IVD assay. If we are unable to effectively establish and manage the distribution process, the commercial launch and sales of plazomicin and the associated IVD assay will be delayed or severely compromised and our results of operations may be harmed.

In addition, the use of third party distributors, including with respect to cold chain logistics for plazomicin and the associated IVD assay, involves certain risks, including, but not limited to, risks that distributors or pharmacies will:

- not provide us with accurate or timely information regarding their inventories, the number of patients who are using plazomicin or the IVD assay, or complaints regarding them;
- not effectively sell or support plazomicin or the associated IVD assay with sufficient cold storage;
- reduce their efforts or discontinue to sell or support plazomicin or the IVD assay;
- not devote the resources necessary to sell plazomicin or the IVD assay in the volumes and within the time frames that we expect;
- be unable to satisfy financial obligations to us or others; or
- cease operations.

Plazomicin is still undergoing evaluation for, and we expect our IVD assay will have, a room temperature shelf life. Currently cold chain is required and if we do not effectively maintain our cold chain supply logistics, then we may experience an unusual number of product returns or out of date product. Any such failure may result in decreased product sales and lower product revenue, which would harm our business.

We currently have no sales and marketing staff or distribution organization. If we are unable to develop a sales and marketing and distribution capability on our own or through third parties, we will not be successful in commercializing our future products.

We currently have no sales, marketing or distribution organization or history. To achieve commercial success for any approved product candidate, we must either develop a sales, marketing and distribution organization or outsource these functions to third parties. If we rely on third parties for marketing and distributing our approved products, any revenue we receive will depend upon the efforts of third parties, which may not be successful and are only partially within our control, and our product revenue may be lower than if we directly marketed or sold our products. If we are unable to enter into arrangements with third parties to sell, market and distribute product candidates for which we have received regulatory approval on acceptable terms or at all, we will need to market these products ourselves. This is likely to be expensive and logistically difficult, as it would require us to build our own sales, marketing and distribution capacity. We have no historical operations in this area, and if such efforts were necessary, we may not be able to successfully commercialize our future products. If we are not successful in commercializing our future products, either on our own or through third parties, any future product revenue will be materially and adversely affected.

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

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The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to plazomicin and other product candidates that we may seek to develop or commercialize in the future. There are a number of pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of multi-drug resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, safer or less costly than plazomicin or any other product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

There are a variety of available therapies marketed for the treatment of MDR infections that we would expect would compete with plazomicin, including tigecycline, which is marketed by Pfizer as Tygacil, other aminoglycosides that are generically available (such as gentamicin, amikacin, tobramycin), and polymixins that are generically available (colistin and polymixin B). Many of the available therapies are well-established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. If plazomicin is approved, it may be priced at a premium over other competitive products. This may limit plazomicin's adoption for MDR gram-negative infections.

There are also a number of products in late-stage clinical development by third parties to treat MDR gram-negative infections. Actavis plc and AstraZeneca PLC are developing ceftazidime/avibactam and ceftaroline/avibactam for pneumonia and complicated urinary and intra-abdominal infections. Tetraphase Pharmaceuticals is developing eravacycline for complicated urinary and intra-abdominal infections, as well as pneumonia. The Medicines Company is developing Carbavance™ for complicated urinary tract infections and various infection types due to CRE. Merck is developing relebactam for complicated urinary and intra-abdominal infections, and potentially for pneumonia. We may also eventually face competition from products in earlier development stage. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than us, it could result in our competitors establishing a strong market position before we are able to enter the market.

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the Generating Antibiotics Incentives Now Act (the "GAIN Act"). The GAIN Act provides incentives for the development of new, qualified infectious disease products, including adding five years to the otherwise applicable regulatory exclusivity period. These incentives, along with government contract funding and other incentives for antibiotic research, may result in more competition in the market for new antibiotics.

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

Finally, the success of any product that is successfully commercialized will depend in large part on our ability to prevent competitors from launching a generic version that would compete with such product. If such competitors are able to establish that our patents are invalid or not infringed by the generic version of our product, they may be able to launch a generic product prior to the expected expiration of our relevant patents, and any generic competition could have a material adverse effect on our business, results of operations, financial condition and prospects.

We may attempt to form collaborations in the future with respect to our product candidates, but we may not be able to do so, which may cause us to alter our development and commercialization plans.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties with respect to our programs that we believe will complement or augment our existing business. For example, we currently intend to identify one or more strategic partners for the commercialization of plazomicin, and we may also attempt to find one or more strategic partners for the development or commercialization of one or more of our other product candidates. We face significant competition in seeking appropriate strategic partners, and the

negotiation process to secure appropriate terms is time-consuming and complex. We may not be successful in our efforts to establish such a strategic partnership for any product candidates and programs on terms that are acceptable to us, or at all.

Any delays in identifying suitable collaborators and entering into agreements to develop or commercialize our product candidates could negatively impact the development or commercialization of our product candidates in geographic regions where we do not have development and commercialization infrastructure. Absent a collaboration partner, we would need to undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or

commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we are unable to do so, we may not be able to develop our product candidates or bring them to market and our business may be materially and adversely affected.

We may be unable to realize the potential benefits of any collaboration.

Even if we are successful in entering into a collaboration with respect to the development or commercialization of one or more product candidates, there is no guarantee that the collaboration will be successful. Collaborations may pose a number of risks, including:

- collaborators often have significant discretion in determining the efforts and resources that they will apply to the collaboration, and may not commit sufficient resources to the development, marketing or commercialization of the product or products that are subject to the collaboration;
- collaborators may not perform their obligations as expected;
- collaborators may cease to devote resources to the development or commercialization of our product candidates if the collaborators view our product candidates as competitive with their own products or product candidates;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the course of development, might cause delays or termination of the development or commercialization of product candidates, and might result in legal proceedings, which would be time-consuming, distracting and expensive;
- collaborators may be impacted by changes in their strategic focus or available funding, or business combinations involving them, which could cause them to divert resources away from the collaboration;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the collaborations may not result in us achieving revenue to justify such transactions; and
- collaborations may be terminated and, if terminated, may result in a need for us to raise additional capital to pursue further development or commercialization of the applicable product candidate.

As a result, a collaboration may not result in the successful development or commercialization of our product candidates.

We may need to grow our organization, and we may experience difficulties in managing growth.

As of December 31, 2014, we had 44 employees. We will need to expand our managerial, operational, financial and other resources in order to manage our operations and clinical trials, continue our development activities, commercialize plazomicin or other product candidates and transition to becoming a public reporting company. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our business strategy requires that we:

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

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

We are highly dependent on the services of our Chief Executive Officer, Kenneth J. Hillan, M.B., Ch.B. and our ability to attract and retain qualified personnel.

We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. We are highly dependent on the principal members of our management and scientific staff, particularly our Chief Executive Officer, Dr. Hillan. If we are not able to retain Dr. Hillan or are not able to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including

Dr. Hillan, we may not be able to retain their services as expected. In addition to the competition for personnel, the San Francisco Bay Area in particular is characterized by a high cost of living. Although we historically have not had any material difficulty attracting experienced personnel to our company, we could in the future have such difficulties and may be required to expend significant financial resources in our employee recruitment and retention efforts.

In addition, we have scientific and clinical advisors who assist us in formulating our product development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us, or may have arrangements with other companies to assist in the development of products that may compete with ours.

If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Recent changes in our executive leadership and any similar changes in the future may serve as a significant distraction for our management and employees.

Since the beginning of 2014, there have been a number of changes to our executive leadership team. In February 2014, we hired our Senior Vice President, Chief Financial Officer, Derek Bertocci and in July 2014, we hired our Chief Medical Officer, Ian Friedland, M.D. In November 2014, our former Senior Vice President, Development Operations and Portfolio Management, Becki Filice, resigned from her employment with us for personal reasons. Such changes, or any other future changes in our executive leadership, may disrupt our operations as we adjust to the reallocation of responsibilities and assimilate new leadership and, potentially, differing perspectives on our strategic direction. If the transition in executive leadership is not smooth, the resulting disruption could negatively affect our operations and impede our ability to execute our strategic plan.

Our business involves the use of hazardous materials and we and our third-party manufacturers must comply with environmental laws and regulations, which may be expensive and restrict how we do business.

Our third-party manufacturers' activities and our own activities involve the controlled storage, use and disposal of hazardous materials, including the components of our pharmaceutical product candidates, test samples and reagents, biological materials and other hazardous compounds. We and our manufacturers are subject to federal, state, local and foreign laws and regulations governing the use, generation, manufacture, storage, handling and disposal of these hazardous materials. We currently carry no insurance specifically covering environmental claims relating to the use of hazardous materials. Although we believe that our safety procedures for handling and disposing of these materials and waste products comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental injury or contamination from the use, storage, handling or disposal of hazardous materials. In the event of an accident, state or federal or other applicable authorities may curtail our use of these materials and/or interrupt our business operations. In addition, if an accident or environmental discharge occurs, or if we discover contamination caused by prior operations, including by prior owners and operators of properties we acquire, we could be liable for cleanup obligations, damages and fines. If such unexpected costs are substantial, this could significantly harm our financial condition and results of operations.

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

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

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.
We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or

negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA; (2) manufacturing standards; (3) federal and state healthcare fraud and abuse laws and regulations; or (4) laws that require the true, complete and accurate reporting of financial information or data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws 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 misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We incur significant costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives.

Prior to our IPO in March 2014, we had not been subject to the reporting requirements of the Exchange Act or the other rules and regulations of the SEC or any securities exchange relating to public companies. We continue to identify those areas in which changes should be made to our financial and management control systems to manage our growth and our obligations as a public company. These areas include corporate governance, corporate control, disclosure controls and procedures and financial reporting and accounting systems. We have made, and will continue to make, changes in these and other areas. However, the expenses associated with being a public company could be material, particularly after we cease to be an “emerging growth company.” Compliance with the various reporting and other requirements applicable to public companies require considerable time and attention of management. In addition, the changes we make may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis.

In addition, certain types of insurance, including directors’ and officers’ liability insurance are more expensive as a public company. Being a public company could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If we are not able to implement the requirements of Section 404 of the Sarbanes-Oxley Act of 2002 in a timely manner or with adequate compliance, we may be subject to sanctions by regulatory authorities.

Section 404 of the Sarbanes-Oxley Act of 2002 requires that we evaluate and determine the effectiveness of our internal controls over financial reporting and, beginning with our annual report for the year ending December 31, 2015, provide a management report on the internal control over financial reporting. If we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We will be evaluating our internal controls systems to allow management to report on, and eventually our independent auditors will attest to, the effectiveness of the operation of our internal controls. We will be performing the system and process evaluation and testing (and any necessary remediation) required to comply with the management certification and eventual auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002. The aforementioned auditor attestation requirements will not apply to us until we are no longer an “emerging growth company.”

To date, we have not conducted a review of our internal controls for the purpose of providing a management report on the internal control over financial reporting. We cannot be certain as to the timing of completion of our evaluation, testing and remediation action or the impact of the same on our operations. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm

identifies deficiencies in our internal controls that are deemed to be material weaknesses, we could be subject to sanctions or investigations by The NASDAQ Stock Market LLC ("NASDAQ"), the SEC or other regulatory authorities, which would entail expenditure of additional financial and management resources and could materially adversely affect our stock price. Deficient internal controls could also cause us to fail to meet our reporting obligations or cause investors to lose confidence in our reported financial information, which could have a negative effect on our stock price.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We have designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple errors or mistakes. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

A variety of risks associated with international operations could materially adversely affect our business.

Certain of our existing suppliers are located outside of the United States, including our sole source supplier for sisomicin, a key raw material for the production of plazomicin, which is located in China, and for which we do not have a commercial supply agreement. Additionally, if plazomicin is approved for commercialization outside the United States we will likely seek to enter into agreements with third parties to market plazomicin outside the United States. We are, or we expect that we will be, subject to additional risks related to these international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- potential liability resulting from development work conducted by these third parties; and
- business interruptions resulting from geopolitical events, including war and terrorism, or natural disasters.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters is located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our information technology systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are geographically concentrated and operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our U.S. Government Contracts

Our use of government funding for certain of our programs adds uncertainty to our research and commercialization efforts with respect to those programs and may impose requirements that increase the costs of commercialization and production of product candidates developed under those government-funded programs.

Our development of plazomicin as a countermeasure for diseases caused by antibiotic-resistant pathogens and biothreats is currently being funded in significant part through a contract with BARDA. We have also received funding in the past for other programs from DTRA and from the NIH's National Institute of Allergy and Infectious Diseases division. Contracts funded by the U.S. government and its agencies, including our contract with BARDA, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason;
- reduce or modify the government's obligations under such agreements without the consent of the other party;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;
- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- suspend or debar the contractor from doing future business with the government;
- control and potentially prohibit the export of products; and
- pursue criminal or civil remedies under the False Claims Act ("FCA"), the False Statements Act and similar remedy provisions specific to government agreements.

We may not have the right to prohibit the U.S. government from using or allowing others to use certain technologies developed by us, and we may not be able to prohibit third-party companies, including our competitors, from using those technologies in providing products and services to the U.S. government. The U.S. government generally obtains the right to royalty-free use of technologies that are developed under U.S. government contracts.

For further information, see "Risks Related to Intellectual Property—Provisions in our U.S. government contracts, including our contract with BARDA, may affect our intellectual property rights."

In addition, government contracts normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These requirements include, for example:

- specialized accounting systems unique to government contracts;
- mandatory financial audits and potential liability for price adjustments or recoupment of government funds after such funds have been spent;
- public disclosures of certain contract information, which may enable competitors to gain insights into our research program; and
- mandatory socioeconomic compliance requirements, including labor standards, anti-human-trafficking, non-discrimination, and affirmative action programs and environmental compliance requirements.

If we fail to maintain compliance with these requirements, we may be subject to potential contract or FCA liability and to termination of our contracts.

We are dependent on our BARDA contract to fund our Phase 3 CARE trial of plazomicin, and if we do not receive all of the funds under this contract, we may be forced to suspend or terminate this program or obtain alternative sources of funding.

We expect a significant portion of the funding for our Phase 3 CARE trial of plazomicin will continue to come from our BARDA contract. BARDA may terminate our contract at any time for convenience and there can be no assurances that this contract will not be terminated. Changes in government budgets and agendas may result in a decreased and de-prioritized emphasis on supporting the development of antibacterial products such as plazomicin. Although we are using a portion of the net proceeds from our IPO to fund our plazomicin development program, any reduction or delay in BARDA funding may force us to suspend or terminate the program or seek alternative funding, which may not be available on non-dilutive terms, terms favorable to us or at all. Further, although our BARDA contract contains an unexercised option for additional funding to support the plazomicin development program, we have not determined the dollar amount of this option and cannot make any assurances as to when or whether the option will be exercised.

U.S. government agencies have special contracting requirements that give them the ability to unilaterally control our contracts.

U.S. government contracts typically contain unfavorable termination provisions and are subject to audit and modification by the government at its sole discretion, which will subject us to additional risks. These risks include the ability of the U.S. government to unilaterally:

- audit and object to our BARDA contract-related costs and fees, and require us to reimburse all such costs and fees;
- suspend or prevent us for a set period of time from receiving new contracts or extending our existing contracts based on violations or suspected violations of laws or regulations;
- cancel, terminate or suspend our contracts based on violations or suspected violations of laws or regulations;
- terminate our contracts if in the government's interest, including if funds become unavailable to the applicable governmental agency;
- reduce the scope and value of our contract; and
- change certain terms and conditions in our contract.

The U.S. government will be able to terminate any of its contracts with us, either for convenience or if we default by failing to perform in accordance with or to achieve the milestones set forth in the contract schedules and terms. Termination-for-convenience provisions generally enable us to recover only our costs incurred or committed and settlement expenses on the work completed prior to termination. Except for the amount of services received by the government, termination-for-default provisions do not permit these recoveries and would make us liable for excess costs incurred by the U.S. government in procuring undelivered items from another source.

The U.S. government's determination to award a future contract or contract option may be challenged by an interested party, such as another bidder, at the U.S. Government Accountability Office (the "GAO"), or in federal court. If such a challenge is successful, our BARDA contract or any future contract we may be awarded may be terminated.

The laws and regulations governing the procurement of goods and services by the U.S. government provide procedures by which other bidders and interested parties may challenge the award of a government contract. If we are awarded a government contract, such challenges or protests could be filed even if there are not any valid legal grounds on which to base the protest. If any such protests are filed, the government agency may decide to suspend our performance under the contract while such protests are being considered by the GAO or the applicable federal court, thus potentially delaying delivery of payment. In addition, we could be forced to expend considerable funds to defend any potential award. If a protest is successful, the government may be ordered to terminate any one or more of our contracts and reselect bids. The government agencies with which we have contracts could even be directed to award a potential contract to one of the other bidders.

Our business is subject to audit by the U.S. government, including under our contracts with BARDA and DTRA, and a negative outcome in an audit could adversely affect our business.

U.S. government agencies such as the Department of Health and Human Services ("DHHS") and DCAA routinely audit and investigate government contractors. These agencies review a contractor's performance under its contracts, cost structure and compliance with applicable laws, regulations and standards.

The DHHS and the DCAA also review the adequacy of, and a contractor's compliance with, its internal control systems and policies, including the contractor's purchasing, property, estimating, compensation and management information systems. Any costs found to be improperly allocated to a specific contract will not be paid, while such costs already paid must be refunded. If an audit uncovers improper or illegal activities, we may be subject to civil and criminal penalties and administrative sanctions, including:

- termination of contracts;
- forfeiture of profits;
- suspension of payments;
- fines; and
- suspension or prohibition from conducting business with the U.S. government.

In addition, we could suffer serious reputational harm if allegations of impropriety were made against us, which could cause our stock price to decrease.

There is no assurance that we will receive payment from DTRA for additional expenses related to our LpxC inhibitor program, and the final settlement we may agree to with DTRA may require us to refund a portion of past payments received by us.

In November 2012, DTRA terminated for convenience a contract with us that provided funding for our LpxC inhibitor program. In connection with the termination, we are seeking payment from DTRA for additional expenses we have incurred. We cannot be certain that we will be able to prevail upon DTRA to make such payments or that we would be successful in any subsequent legal proceeding to challenge DTRA's decision.

In connection with our claim for payment from DTRA, the DCAA has audited the expenses for which we are seeking payment, as well as the $33.5 million previously paid to us under the DTRA contract. The audit findings provided to us by DCAA have indicated no net repayment due from us. DTRA has indicated that they will consider DCAA's audit findings, along with other internal information, in developing a recommendation for a settlement. The terms of a final settlement with DTRA may result in a payment to us or may require us to refund some of the amounts we previously received from DTRA.

Laws and regulations affecting government contracts make it more costly and difficult for us to successfully conduct our business.

We must comply with numerous laws and regulations relating to the formation, administration and performance of government contracts, which can make it more difficult for us to retain our rights under our BARDA contract. These laws and regulations affect how we conduct business with government agencies. Among the most significant government contracting regulations that affect our business are:

- the Federal Acquisition Regulations ("FAR") and agency-specific regulations supplemental to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts;
- business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and include other requirements such as the Anti-Kickback Statute and Foreign Corrupt Practices Act;
- export and import control laws and regulations; and
- laws, regulations and executive orders restricting the use and dissemination of information classified for national security purposes and the exportation of certain products and technical data.

Any changes in applicable laws and regulations could restrict our ability to maintain our existing BARDA contract and obtain new contracts, which could limit our ability to conduct our business and materially adversely affect our results of operations.

Risks Related to Intellectual Property

If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. In particular, our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. However, we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

Further, the patentability of inventions, and the validity, enforceability and scope of patents in the biotechnology and pharmaceutical field involve complex legal and scientific questions and can be uncertain. As a result, patent applications that we own or license may fail to result in issued patents in the United States or in other foreign countries for many reasons. For example, there is no assurance that we were the first to invent or the first to file patent applications in respect of the inventions claimed in our patent applications. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. We may also be unaware of certain prior art

relating to our patent applications and patents, which could prevent a patent from issuing from a pending patent application, or result in an issued patent being invalidated. Even if patents have issued, or do successfully issue, from patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications

may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold, license or pursue with respect to our product candidates is threatened, it could threaten our ability to commercialize our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market any of our product candidates under patent protection, if approved, would be reduced. Changes to the patent laws in the United States and other jurisdictions could also diminish the value of our patents and patent applications or narrow the scope of our patent protection.

Furthermore, certain of the patents that we license from the University of Washington are co-owned by Novartis AG. The exclusivity of our license from the University of Washington is therefore subject to Novartis' rights to use the licensed patents and technology for its own purposes, and to grant licenses to others to do so. We therefore rely primarily on our owned patent rights to provide patent protection for our LpxC inhibitor compounds. However, none of these owned patent rights have yet issued, and if these fail to result in issued patents, our competitive position could be adversely affected.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

In addition to the protection afforded by patents, we rely on confidential proprietary information, including trade secrets, and know-how to develop and maintain our competitive position. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. We seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Further, the laws of some foreign countries, including China, where we currently source raw materials for plazomicin, do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including interference or derivation proceedings before the U.S. Patent and Trademark Office ("USPTO"). Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant

patent or that the patent claims are invalid, and we may not be able to do this. Proving that a patent is invalid is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially

reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. We may also elect to enter into license agreements in order to settle patent infringement claims or to resolve disputes prior to litigation, and any such license agreements may require us to pay royalties and other fees that could be significant. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be involved in lawsuits to protect or enforce our intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, the patents of our licensors, or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, in whole or in part, or may refuse to stop the other party in such infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent.

Interference or derivation proceedings provoked by third parties or brought by the USPTO or any foreign patent authority may be necessary to determine the priority of inventions or other matters of inventorship with respect to our patents or patent applications. We may also become involved in other proceedings, such as re-examination or opposition proceedings, before the USPTO or its foreign counterparts relating to our intellectual property or the intellectual property rights of others. An unfavorable outcome in any such proceedings could require us to cease using the related technology or to attempt to license rights to it from the prevailing party, or could cause us to lose valuable intellectual property rights. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. Litigation or other proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may also become involved in disputes with others regarding the ownership of intellectual property rights. For example, we jointly develop intellectual property with certain parties, and disagreements may therefore arise as to the ownership of the intellectual property developed pursuant to these relationships. If we are unable to resolve these disputes, we could lose valuable intellectual property rights.

We may not be able to prevent misappropriation of our trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. 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, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and/or management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. 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 but where enforcement is not as strong as in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions, including China, where we currently source raw materials for plazomicin. The legal systems of

certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates from third parties, we could lose license rights that are important to our business.

While the primary patent family covering plazomicin is Achaogen-owned, our development and commercialization of plazomicin is subject to our license agreement with Isis Pharmaceuticals, Inc., and a portion of the patent portfolio for our LpxC inhibitor program is in-licensed from the University of Washington. Under our existing license agreements, we are subject to various obligations, including diligence obligations with respect to development and commercialization activities, payment obligations for achievement of certain milestones and royalties on product sales, as well as other material obligations. If we fail to comply with any of these obligations or otherwise breach our license agreements, our licensing collaborators may have the right to terminate the applicable license in whole or in part. The loss of our license agreement with Isis Pharmaceuticals, Inc. could materially adversely affect our ability to proceed with the development or potential commercialization of plazomicin as currently planned, while the loss of our license agreement with the University of Washington could materially adversely affect our ability to proceed with any development or potential commercialization of our LpxC inhibitor program.

The risks described elsewhere pertaining to our patents and other intellectual property rights also apply to the intellectual property rights that we license, and any failure by us or our licensors to obtain, maintain and enforce these rights could have a material adverse effect on our business. In some cases we do not have control over the prosecution, maintenance or enforcement of the patents that we license, and may not have sufficient ability to consult and input into the patent prosecution and maintenance process with respect to such patents, and our licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain and enforce the licensed patents.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors or collaborators might not have been the first to make the inventions covered by an issued patent or pending patent application that we own or license;
- we or our licensors or collaborators might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. The USPTO and various non-U.S.

governmental patent agencies require compliance

with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to use our technologies and this circumstance would have a material adverse effect on our business.

Provisions in our U.S. government contracts, including our contract with BARDA, may affect our intellectual property rights.

Certain of our activities have been funded, and may in the future be funded, by the U.S. government. When new technologies are developed with U.S. government funding, the government obtains certain rights in any resulting patents, including the right to a nonexclusive license authorizing the government to use the invention. These rights may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government, U.S. government funding must be disclosed in any resulting patent applications, and our rights in such inventions may be subject to certain requirements to manufacture products in the United States.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (the "Leahy-Smith Act") was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO has promulgated regulations and developed procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not come into effect until March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

We may be subject to claims that our employees or consultants have wrongfully used or disclosed alleged trade secrets of former or other employers.

Many of our employees and consultants, including our senior management, have been employed or retained by other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or consultants have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or consultant's former or other employer. We are not aware of any material threatened or pending claims related to these matters, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

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

of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request.

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

Risks Related to Government Regulation

The regulatory approval process is expensive, time consuming and uncertain and may prevent us from obtaining, or cause delays in obtaining, approvals for the commercialization of some or all of our product candidates, which will materially impair our ability to generate revenue.

The design, development, research, testing, manufacturing, labeling, storage, recordkeeping, approval, selling, import, export, advertising, promotion, and distribution of drug products are subject to extensive and evolving regulation by federal, state and local governmental authorities in the United States, principally by the FDA, and foreign regulatory authorities, with regulations differing from country to country. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. Neither we nor any future collaboration partner is permitted to market plazomicin or any other product candidate in the United States until we receive regulatory approval of an NDA from the FDA.

We have not submitted an application or obtained marketing approval for plazomicin or any other product candidate anywhere in the world. An NDA must include extensive preclinical and clinical data and supporting information to establish to the FDA's satisfaction the product candidate's safety and efficacy for each desired indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product candidate. Obtaining regulatory approval of an NDA can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable U.S. and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of approved products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending NDAs or supplements to approved NDAs.

Prior to receiving approval to commercialize any of our product candidates in the United States or abroad, we and any applicable collaboration partners must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA and other regulatory authorities abroad, that such product candidates are safe and effective for their intended uses. Preclinical testing and clinical trials are long, expensive and uncertain processes. We may spend several years completing our testing for any particular product candidate, and failure can occur at any stage. Negative or inconclusive results or adverse medical events during a clinical trial could also cause the FDA or us to terminate a clinical trial or require that we repeat it or conduct additional clinical trials. Additionally, data obtained from preclinical studies and clinical trials can be interpreted in different ways and the FDA or other regulatory authorities may interpret the results of our studies and trials less favorably than we do. Even if we believe the preclinical or clinical data for a product candidate is promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. Administering any product candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials of such product candidates and result in the FDA or other regulatory authorities denying approval of such product candidates for any or all targeted indications. The FDA or other regulatory authorities may determine that plazomicin or any other product candidate that we develop is not effective, or is only moderately effective, or has undesirable or unintended side effects, toxicities, safety profile or other characteristics that preclude marketing approval or prevent or limit commercial use. In addition, any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

The regulatory approval process is expensive and may take several years to complete. The FDA and foreign regulatory entities have substantial discretion in the approval process. Despite the time and expense exerted, failure can occur at any stage, and we could encounter problems that cause us to abandon or repeat clinical trials, or perform additional preclinical studies and clinical trials. The number of preclinical studies and clinical trials that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. The FDA can delay, limit or deny approval

of a product candidate for many reasons, including, but not limited to, the following:

- product candidate may not be deemed safe or effective;
- FDA officials may not find the data from preclinical studies and clinical trials sufficient;

- the FDA may request additional analyses, reports, data and studies;
- the FDA may ask questions regarding, or adopt different interpretations of, data and results;
- the FDA might not approve our or our third-party manufacturer's processes or facilities; or
- the FDA may change its approval policies or adopt new regulations.

Although we have received FDA fast track designation for our development of plazomicin to treat serious CRE infections, we cannot guarantee that we will experience a faster review or approval process compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

If any of our product candidates fails to demonstrate safety and efficacy in clinical trials or does not gain regulatory approval, or if we experience delays in obtaining regulatory approval, our business and results of operations will be materially and adversely harmed.

Even if we receive regulatory approval for a product candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to restrictions, withdrawal from the market, or penalties if we fail to comply with applicable regulatory requirements or if we experience unanticipated problems with our product candidates, when and if approved.

Once regulatory approval has been granted, the approved product and its manufacturer are subject to continual review by the FDA and/or non-U.S. regulatory authorities. Any regulatory approval that we receive for our product candidates may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for potentially costly post-marketing follow-up studies or surveillance to monitor the safety and efficacy of the product. In addition, if the FDA and/or non-U.S. regulatory authorities approve any of our product candidates, we will be subject to extensive and ongoing regulatory requirements by the FDA and other regulatory authorities with regard to labeling, packaging, adverse event reporting, storage, distribution, advertising, promotion, recordkeeping and submission of safety and other post-market information. Manufacturers of our products and manufacturers' facilities are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must approve these manufacturing facilities before they can be used to manufacture our products, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products. If we, any future collaboration partner or a regulatory authority discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, the collaboration partner, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing.

The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA also imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with regulatory requirements of the FDA and/or other non-U.S. regulatory authorities, we could be subject to administrative or judicially imposed sanctions, including:

- warning letters or untitled letters;
- mandated modifications to promotional materials or the required provision of corrective information to healthcare practitioners;
- restrictions imposed on the product or its manufacturers or manufacturing processes;
- restrictions imposed on the labeling or marketing of the product;
- restrictions imposed on product distribution or use;
- requirements for post-marketing clinical trials;

- suspension of any ongoing clinical trials;
- suspension of or withdrawal of regulatory approval;
- voluntary or mandatory product recalls and publicity requirements;

- refusal to approve pending applications for marketing approval of new products or supplements to approved applications filed by us;
- restrictions on operations, including costly new manufacturing requirements;
- seizure or detention of our products;
- refusal to permit the import or export of our products;
- required entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- civil or criminal penalties; or
- injunctions.

Widely publicized events concerning the safety risk of certain drug products have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and the imposition by the FDA of risk evaluation and mitigation strategies ("REMS") to ensure that the benefits of the drug outweigh its risks. In addition, because of the serious public health risks of high profile adverse safety events with certain products, the FDA may require, as a condition of approval, costly REMS programs.

The regulatory requirements and policies may change and additional government regulations may be enacted for which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we or any future collaboration partner are not able to maintain regulatory compliance, we or such collaboration partner, as applicable, will not be permitted to market our future products and our business will suffer. Failure to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our product candidates internationally.

We may seek a distribution and marketing collaborator for plazomicin or other product candidates commercialized outside of the United States. In order to market our product candidates in the European Economic Area (the "EEA"), which is comprised of the 28 Member States of the EU, plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, we or our collaboration partners must obtain separate regulatory approvals. More concretely, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization ("MA"). There are two types of marketing authorizations:

- the Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use of the EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as for drugs produced through certain specified biotechnological processes (such as recombinant DNA technology, controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells, and hybridoma and monoclonal antibody methods), advanced therapy medicinal products, orphan medicinal products, and medicinal products indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.
- national MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member State through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

We have had limited interactions with foreign regulatory authorities, and approval procedures vary among countries and can involve additional clinical testing. In addition, the time required to obtain approval from foreign regulatory

authorities may differ from that required to obtain FDA approval. Clinical trials conducted in one country may not be accepted by regulatory authorities

in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on our ability to obtain approval in other countries. The foreign regulatory approval process generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may or may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and even if we file, we may not receive necessary approvals to commercialize our product candidates in any market.

Our product development program for plazomicin is dependent, in part, upon our or a commercial partner's ability to obtain regulatory clearance or approval of an IVD assay to be used with plazomicin.

Our product development program for plazomicin includes the development of an IVD assay, which must itself successfully complete a clinical performance study conducted concurrently with and utilizing patient samples from the Phase 3 CARE trial of plazomicin, be approved or cleared for marketing by the FDA and certain other foreign regulatory agencies, and then be commercialized concurrently with plazomicin in the associated markets.

Before marketing or selling a new medical device, we or our commercial partner must obtain either clearance from the FDA under Section 510(k) of the Federal Food, Drug and Cosmetic Act (the "FDCA") or approval of a pre-market approval ("PMA") application from the FDA, unless an exemption from pre-market review applies. In the 510(k) clearance process, the FDA must determine that a proposed device is "substantially equivalent" to a device legally on the market, known as a "predicate" device, with respect to intended use, technology and safety and effectiveness, in order to clear the proposed device for marketing. The PMA pathway requires an applicant to demonstrate the safety and effectiveness of the device based, in part, on extensive data, including, but not limited to, technical, preclinical, clinical trial, manufacturing and labeling data. The PMA process is typically required for devices that are deemed to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices. Both the 510(k) and PMA processes can be expensive and lengthy and require the payment of significant fees, unless an exemption applies. The FDA's 510(k) clearance process usually takes from three to 12 months, but may take longer. The process of obtaining a PMA is much more costly and uncertain than the 510(k) clearance process and generally takes at least one year or longer, from the time the application is submitted to the FDA until an approval is obtained. We do not know at present whether the 510(k) clearance process will be available for our IVD assay. If not, we will need to undertake the more costly and more uncertain PMA process.

If the FDA requires us or our commercial partner to go through the PMA process, the introduction of our IVD and plazomicin could be delayed or canceled.

In addition, the FDA may change its clearance and approval policies, adopt additional regulations or revise existing regulations, or take other actions which may prevent or delay approval or clearance of the IVD assay or impact our ability to modify the IVD assay on a timely basis after it has been approved or cleared. Any delay in, or failure to receive or maintain, clearance or approval for our IVD assay could prevent us from generating revenue from plazomicin and the IVD assay and adversely affect our business operations and financial results. Additionally, the FDA and other regulatory authorities have broad enforcement powers. Regulatory enforcement or inquiries, or other increased scrutiny on us, could affect the perceived safety and efficacy of our products and dissuade our customers from using our products.

Sales of medical devices outside the United States are subject to foreign regulatory requirements that vary widely from country to country. The foreign regulatory approval or certification process may include all of the risks associated with obtaining FDA clearance or approval. If we fail to receive necessary approvals or certifications to commercialize our products in foreign jurisdictions on a timely basis, or at all, our business, results of operations and financial condition could be adversely affected. Moreover, foreign regulatory requirements have become increasingly stringent in recent years, and we may become subject to more rigorous regulation by foreign regulatory authorities in the future. Penalties for a company's noncompliance with foreign governmental regulation could be severe, including revocation or suspension of a company's business license and criminal sanctions. In addition, the costs associated with compliance with any domestic or foreign governmental law or regulation imposed in the future may have a material adverse effect on us.

Healthcare reform measures could hinder or prevent our product candidates' commercial success.

In the United States, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future revenue and profitability and the future revenue and profitability of our potential customers. Federal and state lawmakers regularly propose and, at times, enact legislation that results in significant changes to the healthcare system, some of which is intended to contain or reduce the costs of medical products and services. For example, in March 2010, the President signed one of the most significant healthcare reform measures in decades, the Affordable

Care Act. It contains a number of provisions, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse measures, all of which will impact existing government healthcare programs and will result in the development of new programs. The Affordable Care Act, among other things:

- imposes a non-deductible annual fee on pharmaceutical manufacturers or importers who sell "branded prescription drugs";
- increases the minimum level of Medicaid rebates payable by manufacturers of brand-name drugs from 15.1% to 23.1%;
- imposes a 2.3% medical device excise tax that manufacturers and importers will be required to pay on their sales of certain medical devices;
- requires collection of rebates for drugs paid by Medicaid managed care organizations;
- addresses new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extension products;
- requires manufacturers to participate in a coverage gap discount program, under which they 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; and
- mandates a further shift in the burden of Medicaid payments to the states.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 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. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures.

We are subject to healthcare laws, regulation and enforcement and our failure to comply with those laws could adversely affect our business, operations and financial condition.

Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The regulations that may affect our ability to operate include, without limitation:

- the federal Anti-Kickback Statute, which prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- the federal False Claims Act, which prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, false claims, or knowingly using false statements, to obtain payment from the federal government, and which may apply to entities that provide coding and billing advice to customers;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- the federal physician sunshine requirements under the Affordable Care Act, which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching

hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and

state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent healthcare reform legislation has strengthened these laws. For example, the recently enacted Affordable Care Act, among other things, amends the intent requirement of the Federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the Federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

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

Risks Related to Our Common Stock

The price of our common stock may be volatile.

There was no public market for our common stock prior to our IPO in March 2014, the trading volume of our common stock on The NASDAQ Global Market has been limited since then, and there can be no assurance that an active and liquid trading market for our common stock will be sustained. We cannot predict the extent to which investor interest in our company will lead to the development of or sustain an active trading market on The NASDAQ Global Market or otherwise or how liquid that market might become. If an active public market does not develop or is not sustained, it may be difficult for stockholders to sell their shares of common stock at prices that are attractive to them, or at all. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products, product candidates or technologies by using our shares of common stock as consideration. Stockholders may also be unable to sell their shares of common stock at prices that are attractive to them due to fluctuations in the market price of our common stock. Factors that could cause volatility in the market price of our common stock include, but are not limited to:

- announcements relating to our current development program for plazomicin, including any periodic updates relating to timing or rate of enrollment of trial subjects in our Phase 3 CARE trial, adverse events, site initiation, and timing of release of interim analyses and final trial results or revisions, modifications to our clinical development plan for plazomicin, including changes to enrollment protocols or additional clinical trials;
- results from, or any delays in, clinical trial programs relating to our product candidates, including our Phase 3 CARE trial for plazomicin;
- ability to commercialize or obtain regulatory approval for our product candidates, or delays in commercializing or obtaining regulatory approval;
- any need to suspend or discontinue clinical trials due to side effects or other safety risks, or any need to conduct studies on the long-term effects associated with the use of our product candidates;
- manufacturing issues related to our product candidates for clinical trials or future products for commercialization;
- commercial success and market acceptance of our product candidates following regulatory approval;

- undesirable side effects caused by product candidates after they have entered the market;
- spread of bacterial resistance to our product candidates;
- ability to discover, develop and commercialize additional product candidates;

- announcements relating to collaborations that we may enter into with respect to the development or commercialization of our product candidates, or the timing of payments we may make or receive under these arrangements;
- announcements relating to the receipt, modification or termination of government contracts or grants, or the timing of payments we may receive under these arrangements;
- success of our competitors in discovering, developing or commercializing products;
- strategic transactions undertaken by us;
- additions or departures of key personnel;
- product liability claims related to our clinical trials or product candidates;
- prevailing economic conditions;
- business disruptions caused by earthquakes or other natural disasters;
- disputes concerning our intellectual property or other proprietary rights;
- FDA or other U.S. or foreign regulatory actions affecting us or our industry;
- healthcare reform measures in the United States;
- sales of our common stock by our officers, directors or significant stockholders;
- future sales or issuances of equity or debt securities by us;
- fluctuations in our quarterly operating results; and
- the issuance of new or changed securities analysts' reports or recommendations regarding us.

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

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

Based on the beneficial ownership of our common stock as of December 31, 2014 (including options exercisable within 60 days of December 31, 2014), our officers and directors, together with holders of 5% or more of our then outstanding common stock and their respective affiliates, beneficially owned approximately 47% of our common stock. Accordingly, these stockholders will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

We are an "emerging growth company" and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including not being required to comply with the auditor attestation requirements of section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common

stock and our stock price may be more volatile.

In addition, Section 102 of the JOBS Act also provides that an “emerging growth company” can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. An “emerging growth company” can therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. However, we have chosen to “opt out” of such extended transition period, and as a result, we will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies. Section 107 of the JOBS Act provides that our decision to opt out of the extended transition period for complying with new or revised accounting standards is irrevocable.

Future sales of our common stock or securities convertible or exchangeable for our common stock may depress our stock price.

If our existing stockholders or holders of our options or warrants sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. The perception in the market that these sales may occur could also cause the trading price of our common stock to decline. As of December 31, 2014, we have outstanding a total of 17,907,135 shares of common stock.

In addition, based on the number of shares subject to outstanding awards under our Amended and Restated 2003 Stock Plan or subject to outstanding awards or available for issuance under our 2014 Equity Incentive Award Plan (our "2014 Plan"), our 2014 Employment Commencement Incentive Plan (our "Inducement Plan") and our 2014 Employee Stock Purchase Plan (our "ESPP"), in each case, as of December 31, 2014, 3,292,701 shares of common stock that are either subject to outstanding awards, outstanding but subject to vesting, or reserved for future issuance under our 2003 Plan, 2014 Plan, Inducement Plan or ESPP will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules. We have filed a registration statement permitting shares of common stock issued in the future pursuant to the 2003 Plan, 2014 Plan, or ESPP to be freely resold by plan participants in the public market, applicable vesting schedules and, for shares held by directors, executive officers and other affiliates, volume limitations under Rule 144 for shares. The 2014 Plan and ESPP also contain a provision for the annual increase of the number of shares reserved for issuance under such plan, which shares we also intend to register in the future as such annual increase occurs. If the shares we may issue from time to time under the 2003 Plan, 2014 Plan, the Inducement Plan or ESPP are sold, or if it is perceived that they will be sold, by the award recipient in the public market, the trading price of our common stock could decline.

As of March 1, 2015, certain holders of 1,746,461 shares of our common stock and warrants exercisable for 40,454 shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Sales of such shares could also cause the trading price of our common stock to decline.

Provisions of our charter documents or Delaware law could delay or prevent an acquisition of our company, even if the acquisition would be beneficial to our stockholders, and could make it more difficult for you to change management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. In addition, these provisions may frustrate or prevent any attempt by our stockholders to replace or remove our current management by making it more difficult to replace or remove our board of directors. These provisions include:

- a classified board of directors so that not all directors are elected at one time;
- a prohibition on stockholder action through written consent;
- no cumulative voting in the election of directors;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director;
- a requirement that special meetings of stockholders be called only by the board of directors, the chairman of the board of directors, the chief executive officer or, in the absence of a chief executive officer, the president;
- an advance notice requirement for stockholder proposals and nominations;
-

directors may not be removed without cause and may only be removed with cause by the affirmative vote of 66 2/3% of all outstanding shares of our capital stock with the power to vote in the election of directors;

- the authority of our board of directors to issue preferred stock with such terms as our board of directors may determine; and

- a requirement of approval of not less than 66 2/3% of all outstanding shares of our capital stock with the power to vote to amend any bylaws by stockholder action, or to amend specific provisions of our certificate of incorporation.

In addition, Delaware law prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder, generally a person who, together with its affiliates, owns or within the last three years has owned 15% or more of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. Accordingly, Delaware law may discourage, delay or prevent a change in control of our company. Furthermore, our amended and restated certificate of incorporation will specify that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving actions brought against us by stockholders. We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action.

Provisions in our charter and other provisions of Delaware law could limit the price that investors are willing to pay in the future for shares of our common stock.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future; therefore capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We have never declared or paid cash dividends on our capital stock. We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. We currently intend to retain all available funds and any future earnings to fund the development and growth of our business. In addition, the terms of any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. In addition, if our operating results fail to meet the forecast of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease our principal facilities, which consist of approximately 16,000 square feet of office, research and laboratory space located in South San Francisco, California. The leases covering this space expire on April 14, 2017, with options to further extend the lease for an additional three years.

Item 3. Legal Proceedings.

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

Part II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity.

Our common stock has been listed on The NASDAQ Global Market under the symbol "AKAO" since March 12, 2014. Prior to that date, there was no public trading market for our common stock. The following table details the quarterly high and low sales prices for our common stock as reported by The NASDAQ Global Market for AKAO from March 12, 2014 through December 31, 2014.

	Price Range	
Fiscal year ended December 31, 2014	High	Low
1st Quarter (from March 12, 2014)	$19.69	$12.81
2nd Quarter	$17.44	$11.66
3rd Quarter	$14.44	$7.72
4th Quarter	$14.19	$7.80

On March 13, 2015, the last trading day prior to March 16, 2015, the closing price for our common stock as reported by the NASDAQ Global Market was $10.27.

Performance Graph

This graph is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any filing of Achaogen, Inc. under the Securities Act or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

The graph below matches Achaogen, Inc.'s cumulative 9-Month total stockholder return on common stock with the cumulative total returns of the NASDAQ Composite index and the NASDAQ Biotechnology index. The graph shows the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) at market close on March 12, 2014 (the first day of trading of our common stock) through December 31, 2014. Pursuant to applicable Securities and Exchange Commission rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods and we do not make or endorse any predictions as to future stockholder returns.

	Ticker	3/12/2014	3/31/2014	6/30/2014	9/30/2014	12/31/2014
Achaogen, Inc.	AKAO	$100	$108	$98	$63	$91
Nasdaq Composite Index	IXIC	100	97	102	105	111
Nasdaq Biotechnology Index	NBI	100	90	98	105	117

Holders of Common Stock

As of March 2, 2015, there were approximately 30 holders of record of our common stock.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Securities Authorized for Issuance under Equity Compensation Plans

The information required under this item is incorporated herein by reference to our definitive proxy statement pursuant to regulation 14A, which proxy statement is expected to be filed with Securities and Exchange Commission not later than 120 days after the close of our fiscal year ended December 31, 2014.

Recent Sales of Unregistered Securities

From January 1, 2014 through December 31, 2014, we sold and issued the following unregistered securities, which share numbers have been adjusted, as appropriate, for the 11-to-1 reverse stock split that occurred on March 10, 2014:

1. Prior to filing our registration statement on Form S-8 in 2014, we granted stock options to purchase an aggregate of 232,994 shares of common stock, at a weighted-average exercise price of $9.24 per share, to employees pursuant to our 2003 Plan. Of these, 31,932 shares were canceled without being exercised.
2. Prior to filing our registration statement on Form S-8 in 2014, we granted stock options to purchase an aggregate of 207,909 shares of common stock, at a weighted-average exercise price of $12.58 per share, to employees and directors pursuant to our 2014 Plan.
3. In January 2014, we sold 909 shares of common stock to an accredited investor for cash consideration of $1,400 upon the exercise of a warrant to purchase common stock.
4. In March 2014, upon the closing of our IPO, all 9,796,342 shares of our then-outstanding convertible preferred stock automatically converted into 10,386,894 shares of common stock.

We claimed exemption from registration under the Securities Act for the sales and issuances of securities in the transactions described in paragraphs (1) and (2) above under Section 4(a)(2) of the Securities Act in that such sales and issuances did not involve a public offering, or under Rule 701 promulgated under the Securities Act, in that they were offered and sold either pursuant to written compensatory plans or pursuant to a written contract relating to compensation, as provided by Rule 701.

We claimed exemption from registration under the Securities Act for the sales and issuances of securities in the transaction described in paragraphs (3) through (4) above under Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder, as transactions by an issuer not involving any public offering, or under Section 3(a)(9) of the Securities Act. The purchasers of the securities in these transactions represented that they were accredited investors and that they were acquiring the securities for investment only and not with a view toward the public sale or distribution thereof. Such purchasers received written disclosures that the securities had not been registered under the Securities Act of 1933, as amended, and that any resale must be made pursuant to a registration statement or an available exemption from registration. All purchasers either received adequate financial statement or non-financial statement information about the Registrant or had adequate access, through their relationship with the Registrant, to financial statement or non-financial statement information about the Registrant. The sale of these securities was made without general solicitation or advertising.

Use of Proceeds from Registered Securities

On March 17, 2014, we closed our IPO and issued 6,900,000 shares of our common stock at an initial offering price of $12.00 per share. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-193559), which was declared effective by the SEC on March 11, 2014, and a registration statement on Form S-1 (File No. 333-194494), which was effective immediately upon filing on March 11, 2014 . No additional shares were registered. The joint book-running managers for the IPO were Credit Suisse Securities (USA) LLC and Cowen and Company, LLC. The aggregate offering price to the public for the shares sold in the IPO was $82.8 million. We received net proceeds from the IPO of approximately $73.9 million, after deducting underwriting discounts and commissions of approximately $5.8 million and expenses of approximately $3.1 million payable by us. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates.

In June 2014, we repaid our loans with Oxford and Silicon Valley Bank. None of such payments were direct or indirect payments to any of our directors or officers or their associates, to persons owning 10% or more of our capital stock, or to any of our affiliates.

Other than as described above, there have been no material changes in the planned use of proceeds from our IPO as described in the Prospectus.

Issuer Purchases of Equity Securities

Not applicable.

Item 6. Selected Consolidated Financial Data

You should read the following selected consolidated financial data together with the section of this report entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our consolidated financial statements and the related notes included in this report. The selected consolidated statement of operations data for the years ended December 31, 2014, 2013 and 2012 and the selected consolidated balance sheet data as of December 31, 2014 and 2013 are derived from our audited consolidated financial statements included elsewhere in

this Annual Report on Form 10-K. The selected consolidated balance sheet data as of December 31, 2012 are derived from our audited consolidated financial statements not included in this Annual Report on Form 10-K. Our historical results are not necessarily indicative of the results that may be expected in the future and interim results are

not necessarily indicative of results to be expected for the full year.

	Year Ended December 31,		
	2014	2013	2012
	(in thousands, except share and per share data)		
Consolidated Statement of Operations Data:			
Revenue:			
Contract revenue	$19,970	$18,512	$17,941
Operating expenses:			
Research and development	30,110	23,484	26,581
General and administrative	9,646	6,992	7,349
Total operating expenses	39,756	30,476	33,930
Loss from operations	(19,786)	(11,964)	(15,989)
Interest expense	(397)	(1,331)	(2,427)
Other income and expenses, net	7	183	51
Net loss	$(20,176)	$(13,112)	$(18,365)
Net loss per share—basic and diluted	$(1.42)	$(33.83)	$(52.77)
Shares used to compute net loss per share—basic and diluted	14,210,098	387,547	347,993

	December 31,		
	2014	2013	2012
		(in thousands)	
Consolidated Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$63,679	$10,738	$7,073
Working capital (deficit)	63,917	8,852	(306)
Total assets	70,322	20,758	13,266
Notes payable	—	6,687	10,847
Related party convertible notes and loan payable	—	—	8,128
Convertible preferred stock	—	132,278	100,354
Accumulated deficit	(148,900)	(128,724)	(115,612)
Total stockholders' equity (deficit)	64,613	(124,576)	(112,578)

Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this report entitled “Selected Consolidated Financial Data” and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this report contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations, and intentions. As a result of many factors, including those factors set forth in the “Risk Factors” section of this Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by these forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company passionately committed to the discovery, development, and commercialization of novel antibacterials to treat multi-drug resistant (“MDR”) gram-negative infections. We are developing plazomicin, our lead product candidate, for the treatment of serious bacterial infections due to MDR Enterobacteriaceae, including carbapenem-resistant Enterobacteriaceae (“CRE”). In 2013, the Centers for Disease Control and Prevention identified CRE as a “nightmare bacteria” and an immediate public health threat that requires “urgent and aggressive action.” Through the Special Protocol Assessment procedure, the U.S. Food and Drug Administration (“FDA”) has agreed that the design and planned analyses of our Phase 3 CARE (Combating Antibiotic Resistant Enterobacteriaceae) trial adequately address objectives in support of a New Drug Application (“NDA”). In 2012, the FDA granted fast track designation for the development and regulatory review of plazomicin to treat serious

and life-threatening CRE infections. In 2014, plazomicin received Qualified Infectious Disease Product ("QIDP") designation from the FDA. The QIDP designation was created by the Generating Antibiotic Incentives Now Act, which was part of the FDA Safety and Innovation Act and provides certain incentives for the development of new antibiotics, including priority review and an additional five years of market exclusivity. Our plazomicin program is funded in part with a contract from the Biomedical

Advanced Research and Development Authority ("BARDA"), an agency of the Department of Health and Human Services, for up to $103.8 million. We have global commercialization rights to plazomicin, which has patent protection in the United States extending through 2031. Plazomicin is the first clinical candidate from our gram-negative antibiotic discovery engine, and we have other programs in early and late preclinical stages focused on other MDR gram-negative infections.

The first patients enrolled in the Phase 3 CARE trial of plazomicin in September 2014. Enrollment continues at a rate that has been slower than anticipated. We have been exploring strategies to improve patient recruitment and remain in discussions with the FDA regarding potential modifications to the study design as well as additional clinical trials that could support and, possibly, facilitate regulatory filings for plazomicin. We currently expect to provide an update on our development plans for plazomicin by early in the second quarter of 2015.

Since commencing operations in 2004, we have devoted substantially all of our resources to identifying and developing our product candidates, including conducting preclinical studies and clinical trials and providing general and administrative support for these functions. In addition to plazomicin, our research team is focused on discovering medicines with novel mechanisms of action for serious infections caused by gram-negative bacteria, including MDR Pseudomonas aeruginosa and MDR Acinetobacter baumannii. We are taking a multifaceted approach to identify new anti-bacterial agents through our research. Our goal is to nominate a clinical candidate from our small molecule or therapeutic antibody research programs in 2015 and to file an investigational new drug application in 2016.

Since our inception through December 31, 2014, we have financed our operations with the proceeds of our IPO of common stock, funding under our contracts with government agencies, private placements of our equity securities and certain debt related financing arrangements. Currently, our plazomicin program is funded in part with a contract from BARDA. Our other programs are currently funded primarily with company funds, although we also received a relatively small grant in 2014 from the U.S. National Institutes of Health (the “NIH”). Historically, our preclinical programs have received funding support from organizations in addition to the NIH, such as the U.S. Department of Defense and The Wellcome Trust, a global charitable foundation. We intend to continue to seek further collaborations with government agencies, non-profit foundations, and other research and development funding organizations to support our discovery efforts and advance the product candidates in our pipeline.

On March 17, 2014, we completed our IPO of common stock. We sold 6,900,000 shares of our common stock, which included 900,000 shares issued as a result of the underwriters exercising their over-allotment option in full. We received cash proceeds of approximately $73.9 million from the IPO, net of underwriting commissions and related expenses.

We have never been profitable and have incurred net losses in each year since the commencement of our operations. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and associated general and administrative costs. We expect to incur substantial losses from operations in the foreseeable future as we advance plazomicin and other product candidates through preclinical and clinical development, seek regulatory approval, and prepare for, and, if approved, proceed to commercialization. We will be required to obtain further funding through public or private equity offerings, debt financings, collaboration and licensing arrangements or other sources. 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.

Critical Accounting Policies and Use of Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the respective reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are most critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management’s judgments and

estimates.

Revenue Recognition

We recognize revenue when: (i) evidence of an arrangement exists, (ii) fees are fixed or determinable, (iii) services have been delivered, and (iv) collectability is reasonably assured. We currently generate revenue solely from funding pursuant to government contracts. Our government contracts provide us with payments for certain types of expenditures in return for research and development activities over a contractually defined period. Revenue from these government contracts are recognized in the period during which the related costs are incurred and the related services are rendered, provided that the applicable conditions under the government contracts have been met.

Funds received from third parties under contract arrangements are recorded as revenue if we are deemed to be the principal participant in the contract arrangements because the activities under the contracts are part of our development programs. If we are not the principal participant, the funds from contracts are recorded as a reduction to research and development expense. Contracts funds received are not refundable and are recognized when the related qualified research and development costs are incurred and when there is reasonable assurance that the funds will be received. Funds received in advance are recorded as deferred revenue. Management has determined that we are the principal participant under our government contract arrangements, and accordingly, we record amounts earned under the arrangements as revenue.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include certain payroll and personnel expenses, laboratory supplies, consulting costs, external contract research and development expenses, and allocated overhead, including rent, equipment depreciation, and utilities and relate to both programs sponsored by us as well as costs incurred pursuant to collaboration agreements and government contracts. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities on our behalf are deferred and expensed as the goods are delivered or the related services are performed.

For certain research and development services where we have not yet been invoiced or otherwise notified of actual cost from the third-party contracted service providers, we are required to estimate the extent of the services that have been performed on our behalf and the associated costs incurred at each reporting period. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include services from:

- contract research organizations and other service providers in connection with clinical studies;
- contract manufacturers in connection with the production of clinical trial materials; and
- vendors in connection with preclinical development activities.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage such studies and trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows and expense recognition. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which these services will be performed and the level of effort to be expended and costs to be incurred during each reporting period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual accordingly. Our estimation of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in our reporting changes in estimates in any particular period. To date, there have been no material adjustments from our estimates to the amount actually incurred.

Stock-Based Compensation

Stock-based compensation expense for all stock-based compensation awards is based on the grant date fair value. Grant date fair value of time based stock options is estimated using the Black-Scholes option pricing model and the Monte-Carlo simulation model for stock options with a market condition. The grant date fair value of restricted stock units is based on the closing price of our stock on the date of grant. We have limited historical information available to support the underlying estimates of certain assumptions required to value stock options. The expected term of options is estimated based on the simplified method. We do not have sufficient trading history to solely rely on the volatility of our own common stock for establishing expected volatility. Therefore, we based our expected volatility on the historical stock volatilities of our common stock as well as several comparable publicly listed companies over a period equal to the expected term of the options. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant for the expected term of the stock option. We estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The impact from a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from that

estimated, we may be required to record adjustments to stock-based compensation expense in future periods. We recognize compensation expense on a straight-line basis over the requisite service period.

The assumptions used in calculating the fair value of share-based payment awards represent management's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation expense could be materially different in the future. In addition, if our actual

forfeiture rate is materially different from our estimate, the stock-based compensation expense could be significantly different from what we have recorded in the current period.

Common Stock Valuations

Prior to our IPO, we were required to periodically estimate the fair value of our common stock when issuing stock options and computing our estimated stock-based compensation expense. The fair value of our common stock was determined on a periodic basis by our board of directors, with the assistance of an independent third-party valuation expert. The assumptions underlying these valuations represented management's best estimates, which involved inherent uncertainties and the application of significant levels of management judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation could be materially different. In determining the fair value of our common stock, our board of directors considered valuation methods intended to comply with Section 409A of the Internal Revenue Code that create a presumption that the resulting valuation is reasonable for federal tax purposes.

The fair value of the common stock underlying our stock options was estimated at each grant date by our board of directors. Our board of directors intended all options granted to be exercisable at a price per share not less than the estimated per share fair value of our common stock underlying those options on the date of grant. The valuations of our common stock were determined in accordance with the guidelines outlined in the American Institute of Certified Public Accountants Practice Aid, Valuation of Privately-Held-Company Equity Securities Issued as Compensation.

Income Taxes

We are subject to income tax in the United States. We use the asset and liability method of accounting for income taxes in which deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the consolidated financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be reversed. The effect on deferred tax assets and liabilities of a change in tax rates is recognized as income in the period that includes the enactment date. A valuation allowance is established if it is more likely than not that all or a portion of the deferred tax asset will not be realized.

Our tax positions are subject to income tax audits by multiple tax jurisdictions. We recognize the tax benefit of an uncertain tax position only if it is more likely than not that the position is sustainable upon examination by the taxing authority, based on the technical merits. The tax benefit recognized is measured as the largest amount of benefit which is more likely than not (greater than 50% likely) to be realized upon settlement with the taxing authority. We recognize interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

We calculate the current and deferred income tax provision based on estimates and assumptions that could differ from the actual results reflected in income tax returns filed in subsequent years. Adjustments based on filed income tax returns are recorded when identified. The amount of income taxes paid is subject to examination by U.S. federal and state tax authorities. The estimate of the potential outcome of any uncertain tax issue is subject to management's assessment of relevant risks, facts, and circumstances existing at that time. To the extent the assessment of such tax position changes, the change in estimate is recorded in the period in which the determination is made.

Financial Overview and Results of Operations

General

We have not generated net income from operations and, at December 31, 2014, we had an accumulated deficit of $148.9 million, primarily as a result of research and development and general and administrative expenses. While we may in the future generate revenue from a variety of sources, including product sales, license fees, milestone payments and research and development payments in connection with strategic partnerships, our current revenue is generated solely from research and development funding pursuant to government contracts. Our product candidates are still in clinical development and may never be successfully developed or commercialized. Other than the government funding described below, we do not expect to derive any revenue from any product candidates that we develop until we obtain regulatory approval and commercialize such products, which we do not expect will occur before 2017, if at all, or until such time that we potentially enter into collaboration agreements with third parties for the development and commercialization of such product candidates. Accordingly, we expect to continue to incur substantial losses from operations for the foreseeable future, and there can be no assurance that we will ever generate significant revenue or

profits.

Contract Revenue

Our contract revenue represents services performed for the development of our product candidates under government contracts. For the years ended December 31, 2014, 2013 and 2012, contract revenue was $20.0 million, $18.5 million and $17.9 million,

respectively. We have derived all of our revenue to date from funding provided under U.S. government contracts in connection with the development of our product candidates.

Biomedical Advanced Research and Development Authority ("BARDA")

We have received funding for our lead product candidate, plazomicin, under a contract with BARDA, an agency of the U.S. Department of Health and Human Services for the development, manufacturing, nonclinical and clinical evaluation of, and regulatory filings for, plazomicin as a countermeasure for disease caused by antibiotic-resistant pathogens and biothreats. In August 2010, BARDA awarded us a contract (the "BARDA Contract"), which provides for payments to us based on direct costs incurred and allowances for overhead, plus a fee, where applicable. In November 2013, we modified the most recent awarded option such that payments under this option would not exceed $60.4 million, even though the cost of the Phase 3 CARE trial and related expenses are expected to exceed the amount available to us under our BARDA contract for direct costs incurred. The total committed funding under our BARDA contract is $103.8 million. The contract also currently includes an option for additional work that has not yet been exercised by BARDA. The unexercised option relates to the conduct of an open-label safety trial, certain nonclinical studies to support an NDA and certain nonclinical biodefense studies. Potential funding under the unexercised option has not yet been determined, and we anticipate that BARDA will evaluate award of this option in 2015.

For the years ended December 31, 2014, 2013 and 2012, total revenue recognized under the BARDA Contract was $20.0 million, $18.1 million and $11.6 million, respectively, of which $5.2 million and $7.2 million were included in contracts receivable at December 31, 2014 and 2013, respectively. As of December 31, 2014, a total of $59.5 million under the BARDA Contract has been recorded as revenue, with $44.3 million remaining available under the contract.

National Institute of Allergy and Infectious Diseases ("NIAID")

We received funding for a previous research and development program that we currently do not intend to advance, under a contract with NIAID, a division of the National Institutes of Health, or NIH. In September 2008, NIAID awarded us a contract, which we refer to as the NIAID Contract, which as amended in September 2011 provided up to a total of $22.2 million in funding over five years through August 2013. In July 2014, the Company was awarded a one-year, $407,000 grant by NIAID to conduct discovery research on novel antibiotics targeting gram-negative bacteria.

For the years ended December 31, 2014, 2013 and 2012, we recognized revenue under the NIAID Contract of zero, $0.2 million and $2.6 million, respectively, of which zero and $42,000 were included in contracts receivable at December 31, 2014 and 2013, respectively.

Defense Threat Reduction Agency ("DTRA")

We received funding from DTRA, a division of the Department of Defense, to develop novel antibacterials for the treatment of biodefense pathogens. In June 2007, DTRA awarded us a contract, which we refer to as the DTRA Contract, that provided up to a total of $18.8 million in funding over two years. The DTRA Contract was subsequently modified to extend through the end of November 2012 and to provide for a total of $35.4 million of funding for drawdown. In November 2012, DTRA terminated the contract for convenience. In connection with the termination, we are seeking payment from DTRA for additional expenses we have incurred. The Company cannot be certain that it will be able to prevail upon DTRA to make such payments or that the Company would be successful in any subsequent legal proceeding to challenge DTRA’s decision. We have not recognized any revenue with respect to these additional amounts.

In connection with the Company’s claim for payment from DTRA, the Defense Contract Audit Agency (“DCAA”) has audited the expenses for which the Company is seeking payment, as well as the $33.5 million previously paid to the Company under the DTRA contract. The audit findings provided to the Company by DCAA have indicated no net repayment due from the Company. DTRA has indicated that they will consider DCAA’s audit findings, along with other internal information, in developing a recommendation for a settlement. The terms of a final settlement with DTRA may result in a payment to the Company or may require the Company to refund some of the amounts the Company previously received from DTRA.

For the year ended December 31, 2012, we recognized revenue under the DTRA Contract of $1.5 million. No revenues were recognized during the years ended December 31, 2014 and 2013.

U.S. Army Medical Research Acquisition Authority (USAMRAA)

In May 2012, we were awarded a one-year $2.5 million contract from the U.S. Army Medical Research Acquisition Authority to support our Phase 1 clinical trial of ACHN-975. Total revenue recognized was zero, $0.3 million and $2.2 million for the years ended December 31, 2014, 2013 and 2012, respectively. There were no contracts receivable outstanding under the USAMRAA contract at December 31, 2014 and 2013.

Research and Development Expenses

For the years ended December 31, 2014, 2013 and 2012, research and development expenses were $30.1 million, $23.5 million and $26.6 million, respectively. Research and development expenses consist primarily of costs associated with research, discovery and preclinical studies of potential new drug compounds, plus product development efforts related to clinical trials and materials manufacturing processes. Research and development costs are expensed as incurred and include the following:

- expenses incurred under agreements with contract research organizations, investigative sites, and consultants that conduct our clinical trials and a substantial portion of our preclinical activities;
- employee and consultant-related expenses, which include salaries, benefits, stock-based compensation and consulting fees;
- third-party supplier expenses including the cost of acquiring and manufacturing clinical trial and other materials; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, amortization or depreciation of leasehold improvements, equipment and laboratory supplies and other expenses.

We expect to continue to incur substantial expenses related to our development activities for the foreseeable future as we continue the development of our product candidates. In particular, we expect our research and development costs associated with our plazomicin program to increase significantly as our Phase 3 CARE trial progresses. As product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials, we expect that our research and development expenses will increase in the future.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, professional fees for legal, consulting, audit and tax services, rent and other general operating expenses not otherwise included in research and development. For the years ended December 31, 2014, 2013 and 2012, general and administrative expenses were $9.6 million, $7.0 million and $7.3 million, respectively. We anticipate general and administrative expenses may continue to increase in future periods, reflecting an expanding infrastructure and increased professional fees as we continue to operate as a public company.

Comparison of Years Ended December 31, 2014 and 2013

	Year Ended December 31,		Change
	2014	2013	
		(in thousands)	
Contract revenue	$19,970	$18,512	$1,458
Operating expenses:			
Research and development	30,110	23,484	6,626
General and administrative	9,646	6,992	2,654
Loss from operations	(19,786)	(11,964)	(7,822)
Interest expense	(397)	(1,331)	934
Other income and expense, net	7	183	(176)
Net loss	$(20,176)	$(13,112)	$(7,064)

Contract Revenue

Contract revenue in each period related solely to funding pursuant to our government contracts. Contract revenue increased $1.5 million to $20.0 million for the year ended December 31, 2014 from $18.5 million for the year ended December 31, 2013. This increase was mainly attributable to an increase in research and development services performed under our BARDA Contract during 2014.

Research and Development Expenses

Research and development ("R&D") expenses increased $6.6 million to $30.1 million for the year ended December 31, 2014 from $23.5 million for the comparable period in 2013. This increase was primarily due to payment of a $4.0 million milestone license fee to Isis Pharmaceuticals following dosing the first patient in our Phase 3 CARE trial of

plazomicin in September 2014, a $1.5 million increase in plazomicin program costs as we moved into our Phase 3 CARE clinical trial of plazomicin and a $2.2 million increase in headcount related costs, including $0.2 million stock-based compensation. Partially offsetting this increase was a decrease

of $1.1 million in expenses incurred for other research programs due to the discontinuation, during 2013, of our Phase 1 clinical trial of ACHN-975 from the LpxC inhibitor program.

We record R&D expenses by program where directly identifiable. In the table below, we have allocated indirect R&D costs based on time charged directly to programs by R&D employees. Indirect R&D costs include employee benefit expenses, employee time not charged directly to a program, laboratory supplies and expenses, and allocated facility expenses.

The following table illustrates the components of our research and development expenses during the periods indicated:

	Year Ended December 31,		Change
	2014	2013	
		(in thousands)	
Research and development expenses by program:			
Plazomicin	$24,114	$16,520	$7,594
Other research programs	5,996	6,964	(968)
Total research and development expenses	$30,110	$23,484	$6,626

General and Administrative Expenses

General and administrative expenses increased $2.6 million to $9.6 million for the year ended December 31, 2014 from $7.0 million for the comparable period in 2013. The increase in general and administrative expenses was due to increases of $1.3 million in personnel-related costs, including $0.8 million in stock-based compensation, an increase of $1.6 million of costs associated with being a public company including directors and officers liability insurance, directors fees, professional fees and franchise taxes. These increases were partially offset by a decrease in restructuring costs of $0.3 million.

Interest Expense

Interest expense decreased $0.9 million to $0.4 million from $1.3 million for the years ended December 31, 2014 and 2013, respectively. The decrease was primarily a result of the pay-off of our loans outstanding plus the full amortization, during 2013, of the beneficial conversion features of our convertible loans with The Wellcome Trust Limited.

Comparison of Years Ended December 31, 2013 and 2012

	Year Ended December 31,		Change
	2013	2012	
		(in thousands)	
Contract revenue	$18,512	$17,941	$571
Operating expenses:			
Research and development	23,484	26,581	(3,097)
General and administrative	6,992	7,349	(357)
Loss from operations	(11,964)	(15,989)	4,025
Interest expense	(1,331)	(2,427)	1,096
Other income and expense, net	183	51	132
Net loss	$(13,112)	$(18,365)	$5,253

Contract Revenue

Contract revenue in each period related solely to funding pursuant to our government contracts. Contract revenue increased $0.6 million to $18.5 million for the year ended December 31, 2013 from $17.9 million for the year ended December 31, 2012. This increase was mainly attributable to an increase in research and development services performed under our BARDA Contract during 2013.

Research and Development Expenses

Research and development expenses decreased $3.1 million to $23.5 million for the year ended December 31, 2013 from $26.6 million for the comparable period in 2012. This was primarily due to a $3.9 million decrease in clinical trial costs as a result of the completion of our Phase 2 clinical trial of plazomicin in the second quarter of 2012 and a Phase 1 clinical trial of ACHN-975 in the fourth quarter of 2012, a $1.6 million decrease in personnel-related costs as a result of a net headcount reduction of 15 employees in

our research and development organization since July 2012, and a $1.0 million decrease in nonclinical research and development costs, partially offset by a $3.5 million increase in the design and start-up expenses for our Phase 3 CARE clinical trial.

We record R&D expenses by program where directly identifiable. In the table below, we have allocated indirect R&D costs based on time charged directly to programs by R&D employees. Indirect R&D costs include employee benefit expenses, employee time not charged directly to a program, laboratory supplies and expenses, and allocated facility expenses.

The following table illustrates the components of our research and development expenses during the periods indicated:

	Year Ended December 31,		Change
	2013	2012	
		(in thousands)	
Research and development expenses by program:			
Plazomicin	$16,520	$14,265	$2,255
Other research programs	6,964	12,316	(5,352)
Total research and development expenses	$23,484	$26,581	$(3,097)

General and Administrative Expenses

General and administrative expenses decreased $0.3 million, to $7.0 million for the year ended December 31, 2013 from $7.3 million for the comparable period in 2012. The decrease in general and administrative expenses was primarily due to a decrease of $0.8 million in personnel-related costs from a net headcount reduction of nine employees in our general and administrative organization since July 2012, offset in part by increased consulting expenses from corporate development and finance support related activities.

Interest Expense

Interest expense decreased $1.1 million to $1.3 million from $2.4 million for the years ended December 31, 2013 and 2012, respectively. The decrease was primarily a result of the full amortization, during 2013, of the beneficial conversion features of our convertible loans with The Wellcome Trust Limited.

Liquidity and Capital Resources

Since our inception through December 31, 2014, we have financed our operations with the proceeds from our IPO of our common stock, funding under our contracts with U.S. government agencies, private placements of our equity securities and certain debt related financing arrangements. On March 17, 2014, we completed our IPO of common stock. We sold 6,900,000 shares of our common stock, which included 900,000 shares issued as a result of the underwriters exercising their over-allotment option in full. We received cash proceeds of approximately $73.9 million from the IPO, net of underwriting commissions and related expenses.

At December 31, 2014, we had working capital of $63.9 million and cash, cash equivalents and short-term investments of $63.7 million. In addition to our existing cash, cash equivalents and short-term investments, we have historically received funding provided under U.S. government contracts in connection with the development of our product candidates. In particular, we have received funding for our lead product candidate, plazomicin, under a contract with BARDA for the development, manufacturing, nonclinical and clinical evaluation of, and regulatory filings for, plazomicin as a countermeasure for disease caused by antibiotic-resistant pathogens and biothreats. In April 2013, we were awarded an additional $60.4 million under the BARDA contract to support our Phase 3 CARE trial of plazomicin, for total committed funding of $103.8 million.

Plan of Operations and Future Funding Requirements

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates. Specifically, we have incurred and we expect to continue to incur substantial expenses in connection with our clinical development of plazomicin. We believe we have sufficient capital resources to fund our operating plan through at least the next 12 months.

We do not expect that our current capital resources will be sufficient to enable us to seek marketing approval for plazomicin or commercially launch plazomicin. Additionally, enrollment in our Phase 3 CARE trial of plazomicin

continues at a rate that has been slower than we had anticipated and, as a result, we may change our operating plans if enrollment continues to be slower than expected or as a result of other factors. We have been exploring strategies to improve patient recruitment and remain in discussions with the FDA regarding potential modifications to the study design as well as additional clinical trials that could support and, possibly, facilitate regulatory filings for plazomicin. If we modify our development plans for plazomicin, or if our current operating plan were

to otherwise change, we will require additional funding earlier than previously planned. We currently expect to provide an update on our development plans for plazomicin by early in the second quarter of 2015.

We anticipate that we will need to raise substantial additional financing in the future to fund our operations, including for obtaining marketing approval for plazomicin. We may obtain additional financing through public or private equity offerings, debt financings, a credit facility, government contracts and/or strategic collaborations. Additional financing may not be available to us when we need it or it may not be available to us on acceptable terms, if at all. In addition, although we currently anticipate being able to generate additional financing through non-dilutive means, we may be unable to do so. Our failure to raise capital as and when needed could have a negative impact on our financial condition and our ability to pursue our business strategies. The amount and timing of our future financing requirements will depend on many factors, including:

- continued funding under our contract with BARDA;
- whether or not we decide to pursue additional or alternative pivotal trials for plazomicin;
- the size and type of the nonclinical and clinical trials that we decide to pursue in the development of our product candidates, including plazomicin;
- the type, number, costs and results of the product candidate development programs which we are pursuing or may choose to pursue in the future;
- the rate of progress and cost of our clinical trials, preclinical studies and other discovery and research and development activities;
- the timing of, and costs involved in, seeking and obtaining FDA and other regulatory approvals;
- our ability to enter into additional collaboration, licensing or other arrangements and the terms and timing of such arrangements;
- the costs of preparing, filing, prosecuting, maintaining and enforcing any patent claims and other intellectual property rights, including litigation costs and the results of such litigation;
- the emergence of competing technologies and other adverse market developments;
- the resources we devote to marketing, and, if approved, commercializing our product candidates;
- the scope, progress, expansion, and costs of manufacturing our product candidates;
- our ability to enter into additional government contracts, or other collaborative agreements, to support the development of our product candidates and development efforts; and
- the costs associated with being a public company.

Cash Flows

The following table sets forth the primary sources and uses of cash and cash equivalents for each of the periods presented below:

	Year Ended December 31,		
	2014	2013	2012
		(in thousands)	
Net cash (used in) provided by:			
Operating activities	$(14,283)	$(13,854)	$(16,762)
Investing activities	(45,427)	(110)	(533)
Financing activities	67,853	17,629	11,840
Net increase (decrease) in cash and cash equivalents	$8,143	$3,665	$(5,455)

Operating Activities

Net cash used in operating activities was $14.3 million, $13.9 million and $16.8 million for the years ended December 31, 2014, 2013 and 2012, respectively. The primary use of cash in these periods was to fund our operations related to the development of our product candidates. Cash used for the year ended December 31, 2014 is primarily comprised of our net loss of $20.2 million,

partially offset by non-cash charges for stock-based compensation expense, depreciation and amortization expense, amortization of premium on short-term investments and non-cash interest expense of $2.9 million and a net change in operating assets and liabilities of $3.0 million. Cash used for the year ended December 31, 2013 is primarily comprised of our net loss of $13.1 million and a net change in operating assets and liabilities of $3.2 million, partially offset by non-cash charges for stock-based compensation expense, depreciation and amortization expense, non-cash interest expense and non-cash restructuring charges of $2.4 million. Cash used for the year ended December 31, 2012 is primarily comprised of our net loss of $18.4 million and a net change in operating assets and liabilities of $1.6 million, partially offset by non-cash charges for stock-based compensation expense, depreciation and amortization expense and non-cash interest expense of $3.2 million.

Investing Activities

Cash used in investing activities was $45.4 million, $0.1 million and $0.5 million for the years ended December 31, 2014, 2013 and 2012, respectively. Cash used for the year ended December 31, 2014 consisted of purchases of short-term investments of $45.1 million and purchases of property and equipment of $0.3 million. Cash used for the years ended December 31, 2013 and 2012 consisted of purchases of property and equipment.

Financing Activities

Cash provided by financing activities amounted to $67.9 million for the year ended December 31, 2014. The net cash provided by financing activities for the year ended December 31, 2014 consisted primarily of $73.9 million of net proceeds from our initial public offering of our common stock and $0.8 million of proceeds from issuance of common stock in connection with our equity incentive plans, partially offset by repayment of our notes payable to Oxford Finance LLC and Silicon Valley Bank of $6.9 million.

Cash provided by financing activities amounted to $17.6 million for the year ended December 31, 2013. The net cash provided by financing activities for the year ended December 31, 2013 consisted primarily of the $22.2 million of net proceeds from the issuance of convertible preferred stock in our Series D convertible preferred stock financing during the year, partially offset by $4.6 million for the repayment of our notes payable to Oxford Finance LLC and Silicon Valley Bank.

Cash provided by financing activities amounted to $11.8 million for the year ended December 31, 2012. The net cash provided by financing activities in 2012 consisted primarily of the net proceeds from the issuance of $2.7 million of convertible notes issued to a group of existing investors in November 2012 as part of a bridge financing, $8.0 million in notes payable issued in April 2012 to Oxford Finance LLC and Silicon Valley Bank under the Loan Agreement, and $2.4 million received from our funding agreement with The Wellcome Trust, partially offset by $1.5 million for the repayment of our notes payable to Oxford Finance LLC and Silicon Valley Bank.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2014 (in thousands):

	Payments due by period				
	Total	Less than 1 year	1 to 3 years	4 to 5 years	After 5 years
Lease obligations	$1,352	$578	$774	$—	$—

Lease Obligations

We lease our principal facilities, which consist of approximately 16,000 square feet of office, research and laboratory space located in South San Francisco, California. The leases covering this space expire on April 14, 2017, with options to further extend the lease for an additional three years.

Other Commitments

We have obligations to make future payments to third parties under license agreements, including sublicense fees, royalties, and payments that become due and payable on the achievement of certain development, regulatory and commercialization milestones. However, because the achievement of these milestones is not fixed and determinable, such commitments have not been included on our balance sheet or in the Contractual Obligations and Commitments table above.

Indemnification

In the normal course of business, we enter into contracts and agreements that contain a variety of representations and warranties and provide for general indemnifications. Our exposure under these agreements is unknown because it involves claims that may be made against us in the future, but have not yet been made. To date, we have not paid any claims or been required to defend any action

related to our indemnification obligations. However, we may record charges in the future as a result of these indemnification obligations.

In accordance with our amended and restated certificate of incorporation and our amended and restated bylaws, we have indemnification obligations to our officers and directors for specified events or occurrences, subject to some limits, while they are serving at our request in such capacities. We have also entered into indemnification agreements with our directors and executive officers. There have been no claims to date, and we have director and officer insurance that may enable us to recover a portion of any amounts paid for future potential claims.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Recent Accounting Pronouncements

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 the revenue recognition requirements in ASC 605, Revenue Recognition. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. The ASU's effective date is for interim and annual periods beginning after December 15, 2016. Adoption of the ASU is either retrospective to each prior period presented or retrospective with a cumulative adjustment to retained earnings or accumulated deficit as of the adoption date. Early adoption is not permitted. The Company is assessing the potential effects of this ASU on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Topic 205-40), Going Concern. This ASU introduces an explicit requirement for management to assess if there is substantial doubt about an entity's ability to continue as a going concern, and to provide related footnote disclosures in certain circumstances. In connection with each annual and interim period, management must assess if there is substantial doubt about an entity's ability to continue as a going concern within one year after the issuance date. Disclosures are required if conditions give rise to substantial doubt. ASU 2014-15 is effective for all entities in the first annual period ending after December 15, 2016. The Company is currently assessing the potential effects of this ASU on its consolidated financial statements.

JOBS Act Accounting Election

The Jumpstart our Business Startups Act of 2012 ("JOBS Act"), permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We are choosing to “opt out” of this provision and, as a result, we will comply with new or revised accounting standards as required when they are adopted. This decision to opt out of the extended transition period under the JOBS Act is irrevocable.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to limited market risk related to fluctuations in interest rates and market prices. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. The primary objective of our investment activities is to preserve our capital to fund our operations.

We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and investments in a variety of securities of high credit quality. As of December 31, 2014, we had cash and cash equivalents of $63.7 million consisting of cash and money market funds deposited in highly rated financial institutions in the United States and corporate debt securities of institutions with investment grade credit ratings. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our investments are primarily short-term in duration, we believe that our exposure to interest rate risk is not significant. We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed nor do we anticipate being exposed to material risks due to changes in interest rates. Assuming a hypothetical increase in interest rates of one percentage point, the fair value of our total investment

portfolio as of December 31, 2014, would have potentially declined by approximately $0.2 million. We actively monitor changes in interest rates.

We contract for the conduct of certain clinical development and manufacturing activities with vendors outside the United States. We are subject to exposure due to fluctuations in foreign exchange rates in connection with these agreements. For the year ended December 31, 2014, a 1% movement in foreign exchange rates would not be material to us.

We do not believe that inflation or fluctuations in foreign exchange rates had a significant impact on our results of operations for any periods presented in our financial statements.

Item 8. Financial Statements and Supplementary Data.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of
Achaogen, Inc.

We have audited the accompanying consolidated balance sheets of Achaogen, Inc. as of December 31, 2014 and 2013, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our 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 audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes 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. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Achaogen, Inc. at December 31, 2014 and 2013, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP
Redwood City, California
March 16, 2015

Achaogen, Inc.
Consolidated Balance Sheets
(in thousands except for share and per share amounts)

	December 31, 2014	December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$18,881	$10,738
Short-term investments	44,798	—
Contracts receivable	5,234	7,230
Prepaids and other current assets	520	1,873
Total current assets	69,433	19,841
Property and equipment, net	725	743
Restricted cash	127	127
Deposit and other assets	37	47
Total assets	$70,322	$20,758
Liabilities, Convertible Preferred Stock, and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$2,122	$2,923
Accrued liabilities	3,266	3,004
Notes payable, current portion	—	4,989
Other current liabilities	128	73
Total current liabilities	5,516	10,989
Deferred rent	193	125
Notes payable, noncurrent portion	—	1,698
Other long-term liabilities	—	244
Total liabilities	5,709	13,056
Commitments and contingencies (Note 7)		
Convertible preferred stock, $0.001 par value, zero shares and 132,202,910 shares authorized at December 31, 2014 and 2013, respectively; zero shares and 9,796,342 shares issued and outstanding at December 31, 2014 and 2013, respectively; liquidation value of $132,809 at December 31, 2013	—	132,278
Stockholders' equity (deficit):		
Common stock, $0.001 par value, 290,000,000 and 163,000,000 shares authorized at December 31, 2014 and 2013, respectively; 17,907,135 and 392,844 shares issued and outstanding at December 31, 2014 and 2013, respectively	18	—
Preferred stock, $0.001 par value, 10,000,000 shares and zero shares authorized at December 31, 2014 and December 31, 2013, respectively; zero shares issued and outstanding at December 31, 2014 and December 31, 2013	—	—
Additional paid-in capital	213,527	4,148
Accumulated deficit	(148,900)	(128,724)
Accumulated other comprehensive loss	(32)	—
Total stockholders' equity (deficit)	64,613	(124,576)
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	$70,322	$20,758

See accompanying notes to consolidated financial statements.

Achaogen, Inc.
Consolidated Statements of Operations
(in thousands except for share and per share amounts)

	Year Ended December 31,		
	2014	2013	2012
Contract revenue	$19,970	$18,512	$17,941
Operating expenses:			
Research and development	30,110	23,484	26,581
General and administrative	9,646	6,992	7,349
Total operating expenses	39,756	30,476	33,930
Loss from operations	(19,786)	(11,964)	(15,989)
Interest expense	(397)	(1,331)	(2,427)
Other income and expense, net	7	183	51
Net loss	$(20,176)	$(13,112)	$(18,365)
Basic and diluted net loss per common share	$(1.42)	$(33.83)	$(52.77)
Weighted-average common shares outstanding used to calculate basic and diluted net loss per common share	14,210,098	387,547	347,993

See accompanying notes to consolidated financial statements.

Achaogen, Inc.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,		
	2014	2013	2012
Net loss	$(20,176)	$(13,112)	$(18,365)
Other comprehensive loss:			
Net unrealized losses on available-for-sale securities	(32)	—	—
Total comprehensive loss	$(20,208)	$(13,112)	$(18,365)

See accompanying notes to consolidated financial statements.

Achaogen, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands except for share amounts)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance at January 1, 2012	7,120,608	$100,354	323,906	$—	$2,031	$(97,247)	$ —	$ (95,216)
Issuance of common stock under stock plan	—	—	49,934	—	174	—	—	174
Stock-based compensation expense	—	—	—	—	829	—	—	829
Net loss	—	—	—	—	—	(18,365)	—	(18,365)
Balance at December 31, 2012	7,120,608	100,354	373,840	—	3,034	(115,612)	—	(112,578)
Sale of shares of Series D convertible preferred stock, net of issuance costs	1,864,788	22,200	—	—	—	—	—	—
Issuance of shares of Series D convertible preferred stock in exchange for convertible notes and interest payable to related parties	227,784	2,732	—	—	—	—	—	—
Issuance of shares of Series D convertible preferred stock upon conversion of the related-party loan payable to The Wellcome Trust	583,162	6,992	—	—	—	—	—	—
Issuance of common stock under stock plan	—	—	19,004	—	61	—	—	61
Stock-based compensation expense	—	—	—	—	1,053	—	—	1,053
Net loss	—	—	—	—	—	(13,112)	—	(13,112)
Balance at December 31, 2013	9,796,342	132,278	392,844	—	4,148	(128,724)	—	(124,576)
Conversion of preferred stock to common stock upon initial public offering	(9,796,342)	(132,278)	10,386,894	11	132,267	—	—	132,278
Issuance of common stock upon initial public offering, net of issuance	—	—	6,900,000	7	73,929	—	—	73,936

costs								
Issuance of common stock upon exercise of warrant	—	—	909	—	2	—	—	2
Issuance of common stock under stock plans	—	—	208,693	—	706	—	—	706
Issuance of common stock under ESPP	—	—	17,795	—	139	—	—	139
Reclassification of warrant liability to additional paid-in capital	—	—	—	—	286	—	—	286
Stock-based compensation expense	—	—	—	—	2,050	—	—	2,050
Unrealized loss on available-for-sale securities, net of taxes	—	—	—	—	—	—	(32)	(32)
Net loss	—	—	—	—	—	(20,176)	—	(20,176)
Balance at December 31, 2014	—	$—	17,907,135	$18	$213,527	$(148,900)	$ (32)	$ 64,613

See accompanying notes to consolidated financial statements.

Achaogen, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2014	2013	2012
Cash flows from operating activities:			
Net loss	$(20,176)	$(13,112)	$(18,365)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	358	506	565
Amortization of premium on short-term investments	257	—	—
Stock-based compensation expense	2,050	1,053	829
Revaluation of convertible preferred stock warrant	42	—	—
Loss on asset disposition	—	10	—
Non-cash interest expense relating to notes payable	209	472	524
Non-cash interest expense relating to related-party convertible loan payable	—	197	1,246
Non-cash restructuring charges	—	196	—
Change in operating assets and liabilities:			
Contracts receivable	1,996	(2,972)	631
Prepaids and other assets	1,397	(1,456)	98
Accounts payable and accrued liabilities	(539)	1,450	(1,911)
Other liabilities	123	(198)	(379)
Net cash used in operating activities	(14,283)	(13,854)	(16,762)
Cash flows from investing activities:			
Purchase of property and equipment	(340)	(110)	(568)
Purchase of short-term investments	(45,087)	—	—
Change in restricted cash	—	—	35
Net cash used in investing activities	(45,427)	(110)	(533)
Cash flows from financing activities:			
Proceeds from initial public offering, net of issuance costs	73,936	—	—
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	22,200	—
Proceeds from issuance of related-party convertible notes payable	—	—	2,687
Proceeds from the issuance of common stock in connection with equity incentive plans	811	61	174
Proceeds from exercise of stock warrants	2	—	—
Proceeds from issuance of related-party convertible loan payable	—	—	2,445
Proceeds from issuance of notes payable	—	—	7,996
Repayment of notes payable	(6,896)	(4,632)	(1,462)
Net cash provided by financing activities	67,853	17,629	11,840
Net increase (decrease) in cash and cash equivalents	8,143	3,665	(5,455)
Cash and cash equivalents, beginning of year	10,738	7,073	12,528
Cash and cash equivalents, end of year	$18,881	$10,738	$7,073
Supplemental disclosures of cash flow information			
Interest paid	$221	$693	$699
Supplemental disclosures of noncash investing and financing information			
Conversion of related-party convertible loan and notes payable to convertible preferred stock	$—	$9,724	$—

Conversion of convertible preferred stock into common stock	$132,278	$—	$—
Reclassification of warrant liability to additional paid-in capital	$286	$—	$—

See accompanying notes to consolidated financial statements.

Achaogen, Inc.
Notes to Consolidated Financial Statements
1. Organization and Operations
Achaogen, Inc. (together with its consolidated subsidiary, the “Company”) is a clinical-stage biopharmaceutical company committed to the discovery, development, and commercialization of novel antibacterials to treat multi-drug resistant gram-negative infections. The Company is developing plazomicin, its lead product candidate, for the treatment of serious bacterial infections due to multi-drug resistant Enterobacteriaceae, including carbapenem-resistant Enterobacteriaceae. The Company is running an ongoing Phase 3 CARE (Combating Antibiotic Resistant Enterobacteriaceae) trial of plazomicin and the first patients were enrolled in the trial in the third quarter of 2014.
The Company was incorporated in Delaware in 2002 and commenced operations in 2004. Since commencing operations in 2004, the Company has devoted substantially all of its resources to identifying and developing its product candidates, including conducting preclinical studies and clinical trials and providing general and administrative support for these operations.
In March 2014, the Company completed its initial public offering ("IPO") of shares of its common stock, pursuant to which the Company issued 6,900,000 shares of common stock, which includes 900,000 shares issued pursuant to the over-allotment option granted to its underwriters, and received net proceeds of approximately $73.9 million, after deducting underwriting discounts, commissions and offering expenses. In connection with the completion of the Company's IPO, all shares of convertible preferred stock converted into 10,386,894 shares of common stock and all of the Company's convertible preferred stock warrants were converted into warrants to purchase common stock.
The Company has incurred losses and negative cash flows from operations every year since its inception. As of December 31, 2014, the Company had cash, cash equivalents and short-term investments of approximately $63.7 million and an accumulated deficit of approximately $148.9 million. Management expects to continue to incur additional substantial losses in the foreseeable future as a result of the Company’s research and development activities. Management plans to finance operations through equity or debt financing arrangements, government contracts, and/or third party collaboration funding; however, if the Company is unable to raise additional funding to meet its working capital needs, it will be forced to delay or reduce the scope of its research programs and/or limit or cease its operations.
Reclassifications
Certain prior period amounts in the consolidated statements of operations were reclassified to conform to the current year's presentation. Such reclassification did not impact our net loss or financial position.
2. Summary of Significant Accounting Policies
Basis of Presentation and Consolidation
The consolidated financial statements are prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) and include the consolidated accounts of the Company and its subsidiary. Intercompany accounts and transactions have been eliminated in consolidation. During 2012, the Company established a wholly owned foreign subsidiary in the United Kingdom. There have been no significant activities for this entity during the fiscal years ended December 31, 2014, 2013 and 2012.
Use of Estimates
The accompanying financial statements have been prepared in accordance with U.S. GAAP. The preparation of financial statements in conformity with U.S. GAAP requires management to make judgments, assumptions and estimates that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosures of contingent liabilities. On an ongoing basis, management evaluates its estimates, including those related to clinical trial accruals, fair value of liabilities, convertible preferred stock and related warrants, common stock and stock-based awards and income taxes. Management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ materially from those estimates.
Fair Value of Financial Instruments
The carrying amounts of the Company’s financial instruments, including cash and cash equivalents, contracts receivable, prepaid and other current assets, accounts payable, accrued liabilities, and other current liabilities

approximate fair value due to

their short-term maturities. Short-term investments consist of available-for-sale securities as of December 31, 2014 and are carried at fair value.

Cash and Cash Equivalents

Cash equivalents include only securities having an original maturity of three months or less at the time of purchase. As of December 31, 2014 and 2013, cash and cash equivalents consisted of bank deposits, cash, and investments in money market funds.

Short-term Investments

Short-term investments consist of debt securities with maturities greater than three months, but less than one year from the date of acquisition, and are classified as available for sale. Short-term investments are carried at fair value. Unrealized gains and losses on available-for-sale securities are excluded from earnings and were reported as a component of net unrealized losses on available-for-sale securities in the Company's consolidated statements of comprehensive loss. The amortized cost of debt securities reflects amortization of purchase premiums and accretion of purchase discounts to date, which is included in interest income.

The Company reviews all of its marketable securities on a regular basis to evaluate whether any security has experienced an other-than-temporary decline in fair value.

Restricted Cash

At December 31, 2014 and 2013, the Company had long-term restricted cash of $127,000. The restricted cash, which consists of a money market account with one of the Company’s financial institutions, serves as collateral for a letter of credit provided as a security deposit under the Company’s facility lease. The facility lease expires on April 14, 2017.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions regarding resource allocation and assessing performance. The Company has one operating segment.

Customer Concentration

For the years ended December 31, 2014, 2013 and 2012, all of the Company’s revenue has been generated solely from funding pursuant to U.S. government contracts, and accordingly all contracts receivable relate to funding from U.S. government contracts.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a significant concentration of credit risk consist of cash, cash equivalents and short-term investments. Cash and cash equivalents are deposited in checking and money market accounts at one financial institution, which at times, may exceed federally insured limits. Management believes that the financial institution is financially sound, and, accordingly, minimal credit risk exists with respect to this financial institution. Our investment policy limits investments to certain types of debt securities issued by the U.S. government, its agencies and institutions with investment-grade credit ratings and places restrictions on maturities and concentration by type and issuer. The Company is exposed to credit risk in the event of default by the institutions holding its cash and cash equivalents or issuing the debt securities. As of December 31, 2014, the Company has not experienced any credit losses in such accounts or investments.

Contracts Receivable

Contracts receivable represent amounts owed to the Company under certain government contracts. The Company had no amounts reserved for doubtful accounts as of December 31, 2014 and 2013, as the Company expects full collection of the receivable balances.

Property and Equipment, Net

Property and equipment consists of office equipment, laboratory equipment, and leasehold improvements and is stated at cost, less accumulated depreciation and amortization. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets, generally three to five years. Leasehold improvements are amortized over their estimated useful lives or the remaining lease term, whichever is shorter. Maintenance and repair costs are recorded as a component of operating expenses in the Company’s consolidated statement of operations when incurred.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. If indicators of impairment exist, an impairment loss would be recognized when the estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. The impairment charge is determined based upon the excess of the carrying value of the asset over its estimated fair value, with estimated fair value determined based upon an estimate of discounted future cash flows or other appropriate measures of estimated fair value. For the year ended December 31, 2013, the Company recorded impairment charges of $194,000 related to the cessation of use of leasehold improvements and property and equipment in certain areas of leased property. See Note 14 for further information regarding the restructuring activities and the impairment.

Convertible Preferred Stock Warrant Liabilities

The Company accounted for its Series A and Series C convertible preferred stock warrants as freestanding warrants for shares that are puttable or redeemable. At December 31, 2013, these warrants were classified as liabilities on the consolidated balance sheet at their estimated fair value. At the end of each reporting period, changes in estimated fair value during the period were recorded as a component of other income and expense, net. At the time of the IPO, the warrants to purchase preferred stock were converted into warrants to purchase common stock, which are no longer subject to remeasurement, and the preferred stock warrant liability was reclassified to additional paid-in capital at its then fair value.

Stock-Based Compensation

The Company measures and recognizes the compensation expense for all stock-based awards made to employees and directors, including employee stock options, stock grants and employee stock purchases related to the Employee Stock Purchase Plan (“ESPP”) based on estimated fair values. The Company uses the Black-Scholes option-pricing valuation model to estimate the grant-date fair value of stock option and ESPP awards with time-based vesting terms. The determination of fair value for stock-based awards on the date of grant using an option-pricing model requires management to make certain assumptions regarding a number of complex and subjective variables. The fair value of restricted stock unit (“RSU”) awards with time-based vesting terms is based on the grant date share price. The Company recognizes stock-based compensation cost over the award’s requisite service period on a straight-line basis for time-based awards and on a graded basis for awards that are contingent on the achievement of market-based conditions. The Company records stock-based compensation expense, net of the estimated impact of forfeited awards. As such, the Company recognizes stock-based compensation expense only for those stock-based awards that are expected to vest over their requisite service period, based on the vesting provisions of the individual underlying grants.

During 2014, 2013 and 2012, the Company issued stock-based option awards with market-based conditions that vest upon achievement of certain market price thresholds of the Company’s common stock. The estimated fair value for market-based stock option awards is determined using a lattice valuation model with a Monte-Carlo simulation. The model takes into consideration the historical volatility of the Company’s stock and the risk-free interest rate at the date of grant. In addition, the model is used to estimate the derived service period for the awards. The derived service period is the estimated period of time that would be required to satisfy the market condition, assuming the market condition will be satisfied. Stock-based compensation expense is recognized over the implicit service period derived from the Monte-Carlo simulation model, as applicable, but is accelerated if the market condition is achieved earlier than estimated.

For non-employee stock-based awards, the measurement date on which the estimated fair value of the stock-based award is calculated is equal to the earlier of (i) the date at which a commitment for performance by the counterparty to earn the equity instrument is reached or (ii) the date at which the counterparty’s performance is complete. The Company recognizes stock-based compensation expense for the estimated fair value of the vested portion of non-employee awards.

Revenue Recognition

The Company recognizes revenue when: (i) evidence of an arrangement exists, (ii) fees are fixed or determinable, (iii) services have been delivered, and (iv) collectability is reasonably assured. The Company currently generates revenue entirely from government contracts. Government contracts are agreements that provide the Company with payments for certain types of expenditures in return for research and development activities over a contractually

defined period. Revenue from government contracts is recognized in the period during which the related costs are incurred and the related services are rendered, provided that the applicable conditions under the government contracts have been met. Costs of contract revenue are recorded as a component of operating expenses in the Company's consolidated statements of operations.

Funds received from third parties under contract arrangements are recorded as revenue if the Company is deemed to be the principal participant in the contract arrangements because the activities under the contracts are part of the Company’s development programs. If the Company is not the principal participant, the funds from contracts are recorded as a reduction to research and development expense. Contracts funds received are not refundable and are recognized when the related qualified research and

development costs are incurred and when there is reasonable assurance that the funds will be received. Funds billed and received in advance are recorded as deferred revenue.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development expenses include certain payroll and personnel expenses; laboratory supplies; consulting costs; external contract research and development expenses; and allocated overhead, including rent, equipment depreciation and utilities, and relate to both Company-sponsored programs as well as costs incurred pursuant to collaboration agreements and government contracts. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized and recognized as an expense as the goods are delivered or the related services are performed.

The Company estimates preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on its behalf. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. Payments made to third parties under these arrangements in advance of the receipt of the related services are recorded as prepaid expenses until the services are rendered.

Leases

The Company has entered into lease agreements for its laboratory and office facilities. These leases qualify as and are accounted for as operating leases. Rent expense is recognized on a straight-line basis over the term of the lease and, accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Incentives granted under the Company’s facilities leases, including allowances to fund leasehold improvements and rent holidays, are capitalized and are recognized as reductions to rental expense on a straight-line basis over the term of the lease.

Income Taxes

The Company uses the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized. Due to the Company’s lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance. The Company’s policy is to recognize interest charges and penalties as interest expense and other, net.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits. The tax benefit recognized in the financial statements for a particular tax position is the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

Net Loss and Per Share

Basic net loss per common share is computed by dividing the net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per common share is computed by dividing the net loss by the weighted-average number of common shares and dilutive common share equivalents outstanding during the period. Because the Company has reported a net loss for the years ended December 31, 2014, 2013 and 2012, diluted net loss per common share is the same as basic net loss per common share for those periods.

Effective as of the completion of the IPO, all of the Company’s preferred stock was converted to common stock. For purposes of calculating net loss per common share for the year ended December 31, 2014, the preferred stock converted to common stock was included in the net loss per common share calculation on a post-conversion basis based on the conversion date.

The following table sets forth the computation of the basic and diluted net loss per share during the years ended December 31, 2014, 2013 and 2012 (in thousands, except share and per share data):

	Year Ended December 31,		
	2014	2013	2012
Net loss	$(20,176)	$(13,112)	$(18,365)
Weighted-average common shares outstanding used to calculate basic and diluted net loss per common share	14,210,098	387,547	347,993
Basic and diluted net loss per common share	$(1.42)	$(33.83)	$(52.77)

The following potentially dilutive securities outstanding have been excluded from the computations of diluted weighted-average shares outstanding because such securities have an anti-dilutive impact due to losses reported (in common stock equivalent shares):

	December 31,		
	2014	2013	2012
Convertible preferred stock	—	10,386,894	7,711,160
Warrants to purchase convertible preferred stock	—	40,454	40,454
Options to purchase common stock	1,885,372	1,405,550	1,340,433
Restricted stock units	168,200	—	—
Warrants to purchase common stock	40,454	909	909

Reverse Stock Split

In February 2014, the Company’s board of directors and stockholders approved an amended and restated certificate of incorporation to effect a reverse split of shares of our common stock and convertible preferred stock at a 1-for-11 ratio. The reverse split became effective on March 10, 2014. The par value and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, convertible preferred stock, warrants for common stock, warrants for preferred stock, and per share amounts contained in the financial statements have been retroactively adjusted to reflect this reverse split for all periods presented.

Recent Accounting Pronouncements

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 the revenue recognition requirements in ASC 605, Revenue Recognition. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The ASU also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. The ASU's effective date is for interim and annual periods beginning after December 15, 2016. Adoption of the ASU is either retrospective to each prior period presented or retrospective with a cumulative adjustment to retained earnings or accumulated deficit as of the adoption date. Early adoption is not permitted. The Company is assessing the potential effects of this ASU on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Topic 205-40), Going Concern. This ASU introduces an explicit requirement for management to assess if there is substantial doubt about an entity's ability to continue as a going concern, and to provide related footnote disclosures in certain circumstances. In connection with each annual and interim period, management must assess if there is substantial doubt about an entity's ability to continue as a going concern within one year after the issuance date. Disclosures are required if conditions give rise to substantial doubt. ASU 2014-15 is effective for all entities in the first annual period ending after December 15, 2016. The Company is currently assessing the potential effects of this ASU on its consolidated financial statements.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash, cash equivalents, contracts receivable, accounts payable, accrued liabilities, and certain related-party convertible notes approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair

value on a recurring basis in the consolidated balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value

is defined as the exchange price that would be received for an asset or an exit price that would be paid to transfer a liability in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at estimated fair value using Level 3 inputs. There were no transfers within the hierarchy during the years ended December 31, 2014 and 2013.

Financial instruments

Financial assets and liabilities measured and recognized at fair value on a recurring basis were as follows (in thousands):

As of December 31, 2014:

	December 31, 2014			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Assets				
Cash	620	—	—	620
Level 1:				
Restricted cash	127	—	—	127
Money market funds	18,261	—	—	18,261
Subtotal	18,388	—	—	18,388
Level 2:				
Corporate debt securities	44,830	—	(32)	44,798
Total	$63,838	$—	$(32)	$63,806
Reported as:				
Cash and cash equivalents				$18,881
Short-term investments				$44,798
Restricted cash				$127

As of December 31, 2013:

	December 31, 2013			
	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Assets				
Cash	$8,411	$—	$—	$8,411
Level 1:				
Restricted cash	127	—	—	127
Money market funds	2,327	—	—	2,327
Subtotal	2,454	—	—	2,454
Total	$10,865	$—	$—	$10,865
Reported as:				
Cash and cash equivalents				$10,738
Restricted cash				$127
Liabilities				
Level 3:				
Convertible preferred stock warrant liabilities				$244

All available-for-sale securities held as of December 31, 2014 had contractual maturities of less than one year. There were no sales of available-for-sale securities in any of the periods presented. The fair value of corporate debt obligations that were in unrealized loss positions totaled $40.7 million as of December 31, 2014. The Company has determined that (i) it does not have the intent to sell any of these investments, and (ii) it is not more likely than not that it will be required to sell any of these investments before recovery of the entire amortized cost basis. The Company anticipates that it will recover the entire amortized cost basis of such corporate debt obligations and has determined that no other-than-temporary impairments associated with credit losses were required to be recognized during the year ended December 31, 2014.

The following table provides a summary of changes in the estimated fair value of the Company’s liabilities measured at estimated fair value using significant Level 3 inputs for the years ended 2014, 2013 and 2012 (in thousands):

	Estimated Fair Value of Convertible Preferred Stock Warrant Liabilities	Estimated Fair Value of Derivative Liability
Balance at January 1, 2012	$126	$—
Initial estimated fair value of convertible preferred stock warrant liabilities for newly issued warrants	163	—
Change in estimated fair value of convertible preferred stock warrant liabilities included in other income and expense, net	(52)	—
Initial estimated fair value of derivative liability	—	1,398
Balance at December 31, 2012	237	1,398
Change in estimated fair value of convertible preferred stock warrant liabilities included in other income and expense, net	7	—
Extinguishment of derivative liability	—	(1,398)
Balance at December 31, 2013	244	—
Change in estimated fair value of convertible preferred stock warrant liabilities included in other income and expense, net	42	—
Reclassification of warrant liability to additional paid-in capital upon conversion of warrant to purchase convertible preferred stock to warrant to purchase common stock	(286)	—
Balance at December 31, 2014	$—	$—

The convertible preferred stock warrant liabilities and derivative liabilities associated with certain convertible loans were considered Level 3 liabilities. The estimated fair values of the outstanding preferred stock warrant liabilities were measured using the Black-Scholes option-pricing model. The estimated fair value of the derivative liability associated with the convertible loan due to

beneficial conversion features ("BCF"), on certain of the Company’s convertible loans was measured by multiplying (1) the intrinsic value of the 20% conversion discount on the effective date and (2) the number of shares converted. In connection with the conversion of the related-party loan payable to The Wellcome Trust to shares of Series D convertible preferred stock in March 2013, the estimated fair value of the derivative liability of $1,398,000 was reclassified to convertible preferred stock.

The fair value of the convertible preferred stock warrant liabilities was estimated to be $244,000 as of December 31, 2013 using the following assumptions:

	Year Ended December 31, 2013
Preferred stock fair value per share	$10.89–$12.43
Volatility	65%–68%
Risk-free interest rate	0.2%–2.6%
Remaining contractual term (in years)	1.2–7.8
Dividend yield	0%

In connection with the completion of the Company's IPO in March 2014, all of the outstanding warrants to purchase convertible preferred stock converted into warrants to purchase 40,454 shares of common stock at a weighted-average exercise price of $12.36 per share. The Company remeasured the estimated fair value of these remaining warrants at the date of the conversion and recorded a $42,000 loss related to the change in estimated fair value as part of other income and expense, net, and reclassified the estimated fair value of $286,000 to additional paid-in capital.

4. Balance Sheet Components

Property and Equipment

Property and equipment consist of the following (in thousands):

	December 31,	
	2014	2013
Office equipment	$1,033	$1,017
Laboratory equipment	2,932	2,739
Leasehold improvements	1,000	869
	4,965	4,625
Less: accumulated depreciation and amortization	(4,240)	(3,882)
Property and equipment, net	$725	$743

Depreciation and amortization expense for the years ended December 31, 2014, 2013 and 2012 was $358,000, $506,000 and $565,000, respectively.

Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2014	2013
Accrued clinical and development expenses	$1,618	$1,429
Payroll and related bonus expenses	1,171	760
Other	477	815
	$3,266	$3,004

5. License and Collaboration Agreements

Isis Pharmaceuticals

In January 2006, the Company entered into a license agreement with Isis Pharmaceuticals, Inc., or Isis. Isis granted the Company an exclusive, worldwide license with the right to grant and authorize sublicenses related to the research and development of aminoglycoside products. As an up-front fee, the Company issued 97,402 shares of preferred Series A convertible stock at a fair value of $15.40 per share. This license fee of $1,500,000 was recorded as research and development expense in 2006. In further consideration of this license, and in accordance with the terms of the agreement, the Company is required to make milestone payments with respect to development, regulatory and commercialization milestones, and to pay a percentage of revenue received from sublicensees (if any). All such milestone and sublicense revenue payments may total, in the aggregate, up to but no more than $19,500,000 for the first product and $9,750,000 following the second product commercialized under the agreement with Isis. The Company is also required to pay additional milestone payments of up to $20,000,000 in the aggregate upon the first achievement of specified threshold levels of annual net sales of all aminoglycoside products in a calendar year. The license agreement also provides that the Company shall pay royalties equal to a low single-digit percentage of annual worldwide net sales of all licensed products, including plazomicin.

Through December 31, 2013, the Company had compensated Isis $3,000,000 in connection with the first two milestones under the license for the first aminoglycoside product candidate. In 2014, the Company met its third milestone under the license with Isis when it dosed the first patients in the Phase 3 CARE trial for plazomicin, and made the milestone payment of $4,000,000, which was recorded as research and development expense. As of December 31, 2014 and December 31, 2013, the Company had no outstanding payments due under the agreement.

University of Washington

In December 2006, the Company entered into a license agreement with the University of Washington, referred to herein as the UW Agreement. Under the UW Agreement, the University granted the Company rights to the licensed patents resulting from the University’s research program on certain novel LpxC inhibitor antibacterial compounds and related technology. The Company paid an up-front fee, which was recorded as research and development expense in the Company’s consolidated statements of operations. The Company is obligated to reimburse the University for all reasonable out-of-pocket costs related to maintaining the licensed patents. Since December 2009, and until the grant of regulatory approval for products covered by the UW Agreement, the Company has been and will continue to be obligated to pay a nominal annual license maintenance fee to the University. If the Company commercializes products covered by the licensed patents, the Company will be obligated to pay royalties equal to a low single-digit percentage of annual worldwide net sales of such products, subject to a specified minimum annual royalty following the regulatory approval to market a licensed product. In further consideration of this license, the Company may be obligated to make product development and regulatory milestone payments of up to $2,150,000 for the first product commercialized under the UW Agreement to achieve the specified milestone, and up to $1,075,000 for each of the second and third products to achieve the specified milestones.

In April 2012, the Company met its first milestone under the UW Agreement when it filed an IND for a product candidate from the Company’s LpxC inhibitor program. During 2012, the Company paid $150,000 in cash and recorded the amount as research and development expense. At December 31, 2014 and 2013, the Company had no outstanding payments due under the UW Agreement.

6. Government Contracts

Certain of the Company’s drug discovery and development activities are performed under contracts with U.S. government agencies. Management has determined that the Company is the principal participant in the following contract arrangements, and, accordingly, the Company records amounts earned under the arrangements as revenue. Costs incurred under revenue contracts are recorded as operating expenses in the Company' consolidated statements of operations.

Biomedical Advanced Research and Development Authority

In August 2010, the Company was awarded a contract with the Biomedical Advanced Research and Development Authority, or BARDA, for the development, manufacturing, nonclinical and clinical evaluation of, and regulatory filings for, plazomicin as a countermeasure for disease caused by antibiotic-resistant pathogens and biothreats. The original contract included committed funding of $27,600,000 for the first two years of the contract and subsequent

options exercisable by BARDA to provide additional funding. In September 2012, BARDA modified the contract to increase the total contract committed funding to $43,398,000 through March 2014. In April 2013, the Company was awarded an additional $60,410,000 under the contract to support its Phase 3 CARE clinical trial of plazomicin which increased the total committed funding under this contract to $103,808,000. During the years ended December 31, 2014, 2013 and 2012, the Company recognized revenue of $19,970,000, $18,073,000 and $11,609,000, respectively, under this agreement, of which $5,234,000 and $7,188,000 were included in contracts receivable at December 31, 2014, and 2013, respectively.

Defense Threat Reduction Agency

In November 2012, the Defense Threat Reduction Agency ("DTRA") terminated for convenience a contract with the Company that provided funding for the Company's LpxC inhibitor program. In connection with the termination, the Company is seeking payment from DTRA for additional expenses the Company has incurred. The Company cannot be certain that it will be able to prevail upon DTRA to make such payments or that the Company would be successful in any subsequent legal proceeding to challenge DTRA’s decision.

In connection with the Company’s claim for payment from DTRA, the Defense Contract Audit Agency (“DCAA”) has audited the expenses for which the Company is seeking payment, as well as the $33,480,000 previously paid to the Company under the DTRA contract. The audit findings provided to the Company by DCAA have indicated no net repayment due from the Company. DTRA has indicated that they will consider DCAA’s audit findings, along with other internal information, in developing a recommendation for a settlement. The terms of a final settlement with DTRA may result in a payment to the Company or may require the Company to refund some of the amounts the Company previously received from DTRA.

During the year ended December 31, 2012, the Company recognized revenue of $1,542,000 under this agreement.

National Institute for Allergy and Infectious Disease

In September 2008, the Company was awarded a contract by the National Institute for Allergy and Infectious Disease, or NIAID, to conduct research and development of extended-spectrum aminoglycoside antibiotics for the treatment of serious gram-negative infections. As amended in September 2011, this contract provided the Company with up to $22,188,000 over a five-year term through August 2013. In July 2014, the Company was awarded a one-year, $407,000 grant by NIAID to conduct discovery research on novel antibiotics targeting gram-negative bacteria. During the years ended December 31, 2014, 2013 and 2012, the Company recognized revenue of zero, $168,000 and $2,561,000, respectively, under these agreements, of which zero and $42,000 were included in contracts receivable at December 31, 2014 and 2013, respectively.

U.S. Army Medical Research Acquisition Authority

In May 2012, the Company was awarded a one-year, $2,499,000 contract by the U.S. Army Medical Research Acquisition Authority to support its Phase 1 clinical study of ACHN-975, a product candidate from its LpxC inhibitor program. The Company recognized revenue of zero, $271,000 and $2,228,000 for the year ended December 31, 2014, 2013 and 2012, respectively. There were no outstanding receivables under this contract at December 31, 2014 and 2013.

7. Commitments

Facility Lease Agreement

In December 2010, the Company entered into an amended and restated lease agreement for its facility in South San Francisco, consisting of approximately 35,000 square feet. As part of the amended and restated lease agreement, the landlord agreed to complete certain leasehold improvement work on the additional premises in the amount of $362,000. Such tenant allowance was recorded as a leasehold improvement and is being amortized over the term of the lease. In April 2013, the Company subleased 19,000 square feet to a subtenant through March 2014. In June 2013, the Company further amended its lease to extend the lease term for the remaining space of approximately 16,000 square feet through April 2017 and to terminate the lease on the subleased space effective March 2014.

The Company has provided a letter of credit in the amount of $127,000 as a security deposit on the lease, which letter of credit is collateralized by a money market account. The Company records the collateralized deposit as restricted cash.

The Company recognizes rent expense on a straight-line basis over the lease period and has accrued for rent expense incurred but not paid. Aggregate rent expense, net of sublease income, was $405,000, $673,000 and $957,000 for the years ended December 31, 2014, 2013 and 2012, respectively. The Company received $97,000 and $291,000 of sublease income for the year ended December 31, 2014 and 2013, respectively.

Future minimum payments under all noncancelable operating leases, excluding expected future sublease income, as of December 31, 2014, are as follows (in thousands):

2015	$578
2016	595
2017	179

Total minimum lease payments	$1,352

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Guarantees and Indemnifications

As permitted under Delaware law and in accordance with the Company's bylaws, the Company is required to indemnify its officers and directors for certain events or occurrences while the officer or director is or was serving in such capacity. The Company is also party to indemnification agreements with its directors. The Company believes the fair value of the indemnification rights and agreements is minimal. Accordingly, the Company has not recorded any liabilities for these indemnification rights and agreements as of December 31, 2014 and 2013.

8. Borrowings

Oxford Finance and SVB Loan Agreement

In November 2011, the Company entered into a loan and security agreement, referred to herein as the Loan Agreement, with Oxford Finance LLC and Silicon Valley Bank, or SVB, under which the Company borrowed $4,000,000 in November 2011, and $8,000,000 in April 2012.

The interest rate, which was fixed at the closing of each tranche, equaled the three-month LIBOR plus 7.75%. The interest rates for the tranches under the Loan Agreement were 8.18% and 8.22% per annum. Payments were monthly in arrears and interest only until September 1, 2012, followed by equal monthly payments of principal and interest through June 2014, when the loan was repaid in full. In addition, a final payment equal to 8.25% of the aggregate amount drawn was due upon termination of the Loan Agreement, which was accreted as interest expense over the term of the loan using the effective-interest method, with the remaining balance charged to interest expense upon loan repayment. The loan principal balance, accrued interest and the final payment under the Loan Agreement totaling $4,454,000 were repaid in full in June 2014.

During 2012 and 2011, in connection with the loan agreement, the Company issued warrants to Oxford Finance LLC and SVB to purchase 20,016 and 10,008 shares, respectively, of its Series C convertible preferred stock at an exercise price of $11.99 per share. The fair value of these warrants at the date of issuance was approximately $163,000 and $86,000, respectively, and was recorded as a debt discount and was amortized as interest expense over the term of the loan using the effective-interest method, with the remaining balance charged to interest expense upon loan repayment. Immediately prior to the closing of the IPO, these warrants automatically converted into warrants exercisable for shares of common stock, resulting in the reclassification of the related preferred stock warrant liabilities to additional paid-in capital. As of December 31, 2014, these warrants remained outstanding and exercisable.

The Company recorded interest expense related to the loan of $397,000, $1,037,000 and $1,160,000 for the years ended December 31, 2014, 2013 and 2012, respectively.

Funding Agreement with The Wellcome Trust

In March 2010, the Company entered into a Funding Agreement, referred to herein as the 2010 Wellcome Funding Agreement, with The Wellcome Trust Limited, a company registered in England and Wales, as trustee for The Wellcome Trust, which is referred to herein as the Trust. Under the 2010 Wellcome Funding Agreement, the Trust provided an unsecured convertible loan of $5,594,000 to the Company to progress its aminoglycoside program. The funds were advanced to the Company in two tranches of (a) $3,148,000 upon the signing of the 2010 Wellcome Funding Agreement and (b) the remaining amount upon the satisfaction of a milestone defined under the 2010 Wellcome Funding Agreement.

The Trust, at its discretion, had the right to convert any outstanding balance on the loan into the Company's stock at a conversion price representing a 20% discount to the applicable share price after the first round of equity financing following the execution of the 2010 Wellcome Funding Agreement, using the share price from such round. The discount feature of the loan, and the control of conversion by the lender under this funding agreement created a beneficial conversion feature ("BCF"), which was accounted for as derivative liability and recorded in long-term liabilities, resulting in a discount on the convertible instrument. The fair value of the BCF is measured by multiplying (1) the intrinsic value of the 20% conversion discount on the effective date with (2) the number of shares converted. In March 2013, the outstanding balance under the 2010 Wellcome Funding Agreement of $5,594,000 was converted into 583,162 shares of Series D convertible preferred stock at a conversion price that represented a 20% discount to the issue price. The 20% discount feature was recorded as a debt discount on the funding dates and accreted over the life of the debt up to the date of redemption. The Company recorded interest expense related to the 2010 Wellcome Funding Agreement of $153,000 and $1,115,000 for the years ended December 31, 2013 and 2012, respectively.

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Convertible Notes Purchase Agreement

In November 2012, the Company entered into a Note Purchase Agreement, referred to herein as the 2012 Bridge Loan Agreement, with a group of existing investors. Under the 2012 Bridge Loan Agreement, the investors severally agreed to purchase convertible promissory notes for a principal amount of up to $3,000,000 in aggregate. For value received, the Company agreed to pay to the investors the principal loan amount plus accrued interest calculated at a rate equal to 6% per annum. The Company recorded interest expense related to the 2012 Bridge Loan Agreement of $26,000 and $19,000 for the years ended December 31, 2013 and 2012, respectively.

On March 6, 2013, the investors under the 2012 Bridge Loan Agreement converted the entire outstanding notes amount plus accrued interest totaling $2,732,000 into 227,784 shares of the Company's Series D convertible preferred stock at a conversion price of $11.99 per share, which was the issuance price of Series D convertible preferred stock.

9. Convertible Preferred Stock

Immediately prior to the completion of the Company's IPO, all of the outstanding shares of convertible preferred stock automatically converted into 10,386,894 shares of common stock. Each share of Series A, B, C, and D convertible preferred stock converted into common shares at a conversion rate of approximately 1.15, 1.33, 1.00 and 1.00 shares of common stock, respectively.

The authorized, issued and outstanding shares of convertible preferred stock, liquidation amount and carrying value per Series as of December 31, 2013 were as follows (in thousands, except for share amounts):

	Shares		Liquidation Amount	Carrying Value
Series	Authorized	Issued and Outstanding		
Series A	12,386,071	1,116,876	$17,200	$17,062
Series B	14,266,839	1,295,448	27,075	26,991
Series C	52,550,000	4,708,284	56,452	56,301
Series D	53,000,000	2,675,734	32,082	31,924
	132,202,910	9,796,342	$132,809	$132,278

The Company recorded Series A, B, C, and D convertible preferred stock at fair values on the dates of issuance, net of issuance costs. A redemption event will only occur upon the liquidation or winding up of the Company, a greater than 50% change of control, or a sale of substantially all of its assets. As the redemption event was outside of the Company's control, all shares of convertible preferred stock were presented outside of permanent equity in accordance with ASC 480-10-S99-3A, "Classification and Measurement of Redeemable Securities."

In May 2013, the Company completed the first of two tranches of its Series D round of financing. The majority of the first tranche was received in March 2013 and the Company issued 1,110,252 shares of Series D convertible preferred stock at $11.99 per share to existing investors in exchange for cash proceeds of $10,581,000 and conversion of outstanding loans and accrued interest in the aggregate of $2,732,000 under the 2012 Bridge Loan Agreement. The remaining amount of the first tranche was received in May 2013 from a new investor for additional cash proceeds of $1,778,000 for the issuance of 148,289 shares at a price of $11.99 per share. The second tranche was closed in November 2013. The Company issued 834,031 additional shares of Series D convertible preferred stock at $11.99 per share for gross cash proceeds of $10,000,000.

Warrants

In connection with a loan agreement in 2005, the Company issued warrants to two lenders, SVB and Gold Hill Venture Lending 03, L.P., referred to herein as Gold Hill, to purchase 9,090 shares of the Company's Series A convertible preferred stock at an exercise price of $15.40 per share. The warrants are exercisable immediately and expire ten years from the issuance date, or March 15, 2015. Upon completion of the Company's IPO in March 2014, these warrants converted into warrants to purchase 10,430 shares of common stock at an exercise price of $13.42 per share.

In connection with the Loan Agreement described in Note 8, the Company issued warrants to Oxford Finance LLC and SVB to purchase 20,016 and 10,008 shares of the Company's Series C convertible preferred stock at an exercise price of $11.99 per share during 2012 and 2011, respectively. Upon completion of the Company's IPO in March 2014, these warrants converted into warrants to purchase 30,024 shares of common stock at an exercise price of $11.99 per

share. The warrants are exercisable immediately and expire November 1, 2021.

As of December 31, 2014, the following warrants to purchase shares of common stock were outstanding and exercisable:

Warrant Holder	Issue Date	In Connection With	Warrant to Purchase	Shares	Purchase Price	Expiration Date
Oxford Finance LLC	4/30/2012	Loan agreement	Common stock	11,676	$11.99	11/1/2021
SVB	4/30/2012	Loan agreement	Common stock	8,340	$11.99	11/1/2021
Oxford Finance LLC	11/1/2011	Loan agreement	Common stock	5,838	$11.99	11/1/2021
SVB	11/1/2011	Loan agreement	Common stock	4,170	$11.99	11/1/2021
SVB	3/16/2005	Loan agreement	Common stock	3,723	$13.42	3/15/2015
Gold Hill	3/16/2005	Loan agreement	Common stock	6,707	$13.42	3/15/2015
Total				40,454		

In January 2014, a common stock warrant was exercised for 909 shares with an exercise price of $1.54 per share.

10. Equity Incentive Plans

2014 Plan

In February 2014, the Company’s stockholders approved the 2014 Equity Incentive Award Plan (the "2014 Plan"), which became effective as of March 11, 2014. Under the 2014 Plan, the Company may grant incentive stock options ("ISOs"), nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock units awards and other stock-based awards for the purchase of that number of shares of common stock equal to the sum of (i) 963,636 shares of common stock, (ii) 121,555 shares of common stock that were reserved for issuance under the 2003 Plan that remained available for issuance under the 2003 Plan immediately prior to effectiveness of the 2014 Plan and (iii) any shares of common stock subject to awards under the 2003 Plan which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company without having been fully exercised or resulting in any common stock being issued. In addition, the number of shares of common stock that may be issued under the 2014 Plan is subject to annual increases, to be added on January 1 of each year beginning in 2015 and ending in 2024, in each case subject to the approval of the board of directors or the compensation committee of the board of directors, equal to the lesser of (i) 4% of the shares of the Company’s common stock outstanding on the last day of the immediately preceding fiscal year or (ii) such smaller number of shares of stock as determined by the Company’s board of directors; provided, however, that no more than 14,545,454 shares of stock may be issued under the 2014 Plan upon the exercise of ISOs. As of December 31, 2014, 461,470 shares were available for future issuance under the 2014 Plan.

Under the 2014 Plan, the terms of stock award agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2014 Plan. Options granted by the Company typically vest over a four years period and the exercise price may not be less than fair market value on the date of grant. Certain of the options are subject to acceleration of vesting in the event of certain change of control transactions. Options granted under the 2014 Plan expire no later than 10 years from the date of grant.

2014 Employment Commencement Incentive Plan

In December 2014, the Company adopted a 2014 Employment Commencement Incentive Plan (the "Inducement Plan"). The Inducement Plan is designed to comply with the inducement exemption contained in Nasdaq’s Rule 5635(c)(4), which provides for the grant of non-qualified stock options, restricted stock units, restricted stock awards, performance awards, dividend equivalents, deferred stock awards, deferred stock units, stock payment and stock appreciation rights to a person not previously an employee or director of the Company, or following a bona fide period of non-employment, as an inducement material to the individual’s entering into employment with the Company. The number of shares of common stock initially reserved for issuance under the Inducement Plan was 650,000 shares. As of December 31, 2014, there were no awards issued under the Inducement Plan.

2014 Employee Stock Purchase Plan

In February 2014, the Company’s stockholders approved the 2014 Employee Stock Purchase Plan (the “ESPP”), which became effective as of March 11, 2014. The number of shares of common stock initially reserved for issuance under the ESPP was 145,454 shares. The ESPP provides for an annual increase on the first day of each year beginning in 2015 and ending in 2024, in each case subject to the approval of the board of directors or the compensation committee of the board of directors, equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the

prior fiscal year or (ii) such number of shares as determined by the board of directors; provided, however, that no more than 3,181,818 shares of common stock may be issued under the ESPP. The option

price per share of common stock to be paid by a participant upon exercise of the participant's option on the applicable exercise date for an offering period shall be equal to 85% of the lesser of the fair market value of a share of common stock on (a) the applicable grant date or (b) the applicable exercise date. As of December 31, 2014, 17,795 shares of common stock have been issued to employees participating in the ESPP, and 127,659 shares were available for issuance under the ESPP.

Amended and Restated 2003 Stock Plan

The Company's Amended and Restated 2003 Stock Plan, referred to herein as the 2003 Plan, provided for the granting of incentive and non-statutory stock options to employees, directors and consultants at the discretion of the board of directors. The Company granted options under its 2003 Plan until January 2014 when it was terminated as to future awards, although it continues to govern the terms of options that remain outstanding under the 2003 Plan.

Options granted under the 2003 Plan expire no later than 10 years from the date of grant. Options granted under the 2003 Plan vest over periods determined by the board of directors, generally over four years. The board of directors determined the fair value of common stock at the date of grant.

The 2003 Plan allows for early exercise of certain options prior to vesting. Upon termination of employment, the unvested shares are subject to repurchase at the original exercise price. Stock options granted or modified after March 21, 2002, that are subsequently exercised for cash prior to vesting, are not deemed to be issued until those shares vest. As of December 31, 2014 and 2013 there were no shares subject to repurchase relating to the early exercise of options.

In connection with the Board of Directors and stockholders approval of the 2014 Equity Incentive Award Plan (the "2014 Plan"), all remaining shares available for future awards under the 2003 Plan were transferred to the 2014 Plan, and the 2003 Plan was terminated as to future awards. As of December 31, 2014, a total of 1,242,203 shares of common stock are subject to options outstanding under the 2003 plan, which shares will become available under the 2014 Plan to the extent the options are forfeited or lapse unexercised.

Total stock-based compensation recognized in the Company's consolidated statements of operations for the years ended December 31, 2014, 2013 and 2012, was classified as follows (in thousands):

	Year Ended December 31,		
	2014	2013	2012
Research and development	$570	$351	$241
General and administrative	1,480	702	588
Total	$2,050	$1,053	$829

A summary of stock option activity is as follows:

		Outstanding Options			
	Shares Available for grant	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Balance, January 1, 2012	271,014	939,843	$ 5.36		
Additional shares reserved	227,272	—			
Options granted	(789,942)	789,942	$ 6.25		
Options exercised	—	(49,934)	$ 3.87		$135
Options forfeited	232,785	(232,785)	$ 6.93		
Option expired	106,633	(106,633)	$ 4.85		
Balance, December 31, 2012	47,762	1,340,433	$ 5.72		
Additional shares reserved	163,636	—			
Options granted	(168,231)	168,231	$ 5.28		
Options exercised	—	(19,004)	$ 3.65		$65
Options forfeited	75,673	(75,673)	$ 6.21		
Option expired	8,437	(8,437)	$ 5.55		
Balance, December 31, 2013	127,277	1,405,550	$ 5.68		
Additional shares reserved	1,190,908	—			
Shares reserved for the 2014 Employment Commencement Incentive Plan	650,000	—			
Options granted	(876,163)	876,163	$ 10.15		
RSUs granted	(168,200)	—			
Options exercised	—	(208,693)	$ 3.38		$1,704
Options forfeited	187,648	(187,648)	$ 6.29		
Balance, December 31, 2014	1,111,470	1,885,372	$ 7.95	7.62	$9,816
At December 31, 2014:					
Vested and exercisable		768,284	$ 6.61	5.93	$4,970
Vested and expected to vest		1,655,136	$ 7.81	7.41	$8,848

The following table summarizes information about stock options outstanding as of December 31, 2014:

	Options Outstanding		Vested and Exercisable	
Exercise Price	Number of Options	Weighted-Average Remaining Contractual Life (in Years)	Number of Options	Weighted-Average Exercise Price
$1.65 - $4.62	106,332	2.51	106,332	$ 3.82
$4.73	267,212	7.87	160,050	$ 4.73
$6.60	38,736	8.74	12,404	$ 6.60
$6.93	304,788	5.10	226,378	$ 6.93
$7.26	324,073	6.65	167,750	$ 7.26
$8.04	230,000	9.73	—	$ —
$9.21	125,900	9.89	7,857	$ 9.21
$9.24	201,062	8.88	37,513	$ 9.24
$12.00 - $12.22	212,909	9.28	45,000	$ 12.00
$14.89 - $18.03	74,360	9.42	5,000	$ 18.03
	1,885,372	7.62	768,284	$ 6.61

Stock Options Granted to Employees and Non-Employee Directors

During the years ended December 31, 2014, 2013 and 2012, the Company granted stock options to employees and directors to purchase 876,163, 168,231 and 783,125 shares, respectively, of common stock under the stock plans with a weighted-average estimated grant-date fair value of $6.41, $3.74 and $2.53 per share, respectively. As of December 31, 2014, there were unrecognized

compensation costs of $5,070,000 related to outstanding employee and non-employee director stock options, which are expected to be recognized over a weighted-average period of 3.1 years.

The Company estimated the fair value of stock options using the Black-Scholes option valuation model for options with time-based vesting terms. The Black-Scholes model requires the input of highly complex and subjective assumptions, including (a) the expected term of the award, (b) the expected stock price volatility, (c) the risk-free interest rate and (d) expected dividends. The estimated fair value of these employee stock options is being amortized on a straight-line basis over the requisite service period of the awards. The fair value of the employee stock options was estimated using the following weighted-average assumptions:

	Year Ended		
	2014	2013	2012
Expected term	5.3–6.1 years	5.4–6.1 years	6.0–6.1 years
Expected volatility	67%–77%	68%–69%	56%–69%
Risk-free interest rate	1.7%–2.0%	1.2%–1.7%	0.8%–1.2%
Expected dividend yield	0%	0%	0%
Expected forfeiture rate	8%	8%	9%

The Company has opted to use the “simplified method” for estimating the expected term of options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the option. Due to the Company’s limited operating history and company specific stock price volatility data, the Company has based its estimate of expected volatility on the historical price volatility of a group of similar companies that are publicly traded. Beginning in 2014 the Company began to include the historical price volatility of its own stock, along with data for the group of similar companies, to estimate expected volatility. When selecting these public companies to use in estimating its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, stages of clinical development, risk profiles, position within the industry and with historical share price information sufficient to meet the expected life of the stock-based awards. The risk-free rate assumption is based on the U.S. Treasury instruments with maturities similar to the expected term of the Company’s stock options. The expected dividend assumption is based on the Company’s history of not paying dividends and its expectation that it will not declare dividends for the foreseeable future.

During the years ended December 31, 2014, 2013 and 2012, the Company issued 168,977, 23,770 and 242,104 shares of options to purchase common stock, respectively, that vests upon the achievement of market-based common stock price targets. The fair value was estimated at the grant date using a Monte-Carlo simulation model. The Monte-Carlo simulation model requires the use of a range of assumptions. The range of risk-free interest rates was 0.4% to 2.8%, expected volatility rates ranged from 60.0% to 70.0% and the dividend rate was 0%. The expected life assumption is not used in the Monte-Carlo simulation model, but the output of the model indicated an expected life of 2.9 to 6.3 years. The associated stock-based compensation expense is being recognized on a graded basis over the implicit service period derived from that simulation model.

Forfeitures of unvested grants are estimated at the time of the grant. The estimated rate of forfeitures is re-evaluated periodically and adjusted as necessary. Ultimately, the actual expense recognized will be only for those options that vest.

Restricted Stock Units Granted to Employees and Non-Employee Directors

During the year ended December 31, 2014, the Company granted restricted stock units ("RSUs") to employees to purchase 168,200 shares of common stock under the stock plans with a weighted-average estimated grant-date fair value of $9.33 per share. RSUs generally vest annually over a 4-year service period and vesting is contingent on continued service. As of December 31, 2014, there were unrecognized compensation costs of $1,520,000 related to outstanding RSUs, which are expected to be recognized over a weighted-average period of 3.75 years.

A summary of RSU activity is as follows:

	RSUs Outstanding		
	Number of Shares	Weighted-Average Grant Date Fair Value per Share	Aggregate Intrinsic Value (in thousands)
Balance, December 31, 2013	—	$ —	
RSUs granted	168,200	$ 9.33	
Balance, December 31, 2014	168,200	$ 9.33	$626

Stock Options Granted to Non-Employees

During the year ended December 31, 2012, the Company granted to non-employees options to purchase 6,817 shares of common stock. The Company did not grant stock options to non-employees during the years ended December 31, 2014 and 2013. Stock-based compensation expense of approximately zero, $35,000 and $10,000 was recorded for the years ended December 31, 2014, 2013 and 2012, respectively. The Company measures the estimated fair value of the award each period until the award is fully vested. The fair value of stock compensation expense recognized upon vesting of options granted to non-employees during the years ended December 31, 2013 and 2012 was estimated using the Black-Scholes method with the following weighted-average assumptions.

	Year Ended December 31,	
	2013	2012
Remaining contractual term	6.1–9.9 years	6.3–9.9 years
Expected volatility	68%–69%	56%–70%
Risk-free interest rate	1.1%–2.5%	0.9%–1.8%
Expected dividend yield	0%	0%

11. Income Taxes

A reconciliation of the statutory tax rates and the effective tax rates for the years ended December 31, 2014, 2013 and 2012 is as follows:

	Year ended December 31,		
	2014	2013	2012
Statutory tax rate	34.00 %	34.00 %	34.00 %
State taxes, net of federal benefits	5.04 %	7.10 %	3.98 %
Stock-based compensation	(0.76)%	(0.81)%	(1.18)%
Credits	3.21 %	7.65 %	0.00 %
True-ups	(0.39)%	0.44 %	(2.79)%
Other	(1.35)%	(0.45)%	(0.63)%
Valuation allowance	(39.75)%	(47.93)%	(33.38)%
Effective tax rate	— %	— %	— %

The tax effects of temporary differences and carryforwards that give rise to significant portions of the deferred tax assets are as follows (in thousands):

	December 31,	
	2014	2013
Deferred tax assets:		
Net operating loss carry forwards	$51,039	$45,455
Research and development credit	7,680	6,856
Intangible assets	2,293	1,113
Depreciation	120	98
Other	1,567	1,227
Gross Deferred tax assets	62,699	54,749
Less: valuation allowance	(62,699)	(54,749)
Net deferred tax assets	$—	$—

Realization of the deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The net valuation allowance increased by $7,950,000, $6,295,000 and $6,067,000 during the years ended December 31, 2014, 2013 and 2012, respectively.

The Company had federal and state net operating loss carryforwards of approximately $129,713,000 and $127,390,000, respectively, at December 31, 2014, and approximately $114,024,000 and $114,689,000, respectively, at December 31, 2013. The federal and state net operating loss carryforwards are available to reduce future taxable income, if any. If not utilized, the federal and state operating loss carryforwards will begin to expire in various amounts beginning 2023 and 2015, respectively. The Company also had federal and state research and development credit carryforwards of approximately $5,345,000 and $3,539,000, respectively, at December 31, 2014, and approximately $4,797,000 and $3,120,000, respectively, at December 31, 2013. The federal research and development credits will begin to expire in 2025. The state research and development credits can be carried forward indefinitely. Utilization of the net operating loss and research and development credits carryforwards may be subject to an annual limitation due to the ownership change limitations provided by the Internal Revenue Code of 1986 and similar state provisions. The annual limitation may result in the expiration of the net operating loss and research and development credits before utilization.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. The Company is subject to U.S. federal and state income tax examinations by tax authorities for tax years from 2003 due to net operating losses and tax credits that are being carried forward for tax purposes.

The Company does not have any unrecognized tax benefits, or interest and penalties accrued on unrecognized tax benefits, at December 31, 2014 or 2013.

12. Employee Benefit Plan

In 2003, the Company adopted a 401(k) plan for its employees whereby eligible employees may contribute up to 100% of their compensation, on a pretax basis, subject to the maximum amount permitted by the Internal Revenue Code. In December 2010, the Company approved a plan to provide matching contributions equal to 50% of employees' contributions, up to 6% of annual earnings, starting in January 2011. Company contributions were $184,000, $152,000 and $196,000 for the years ended December 31, 2014, 2013 and 2012, respectively.

13. Related-Party Transactions

In 2010, the Company entered into the 2010 Wellcome Funding Agreement with the Trust, one of the Company's preferred stockholders. As of December 31, 2012, the Company had received $5,594,000 under the 2010 Wellcome Funding Agreement, and recorded the amount as a related-party convertible loan payable. The loan was convertible, at the holder's option, into the Company's next round of preferred stock. In March 2013, the outstanding balance of the 2010 Wellcome Funding Agreement, $5,594,000, was converted into Series D convertible preferred stock at a conversion price that represented a 20% discount to the issue price. Refer to Note 8, "Borrowings."

In November 2012, the Company entered into the 2012 Bridge Loan Agreement with certain existing investors. The Company received $2,687,000 under the 2012 Bridge Loan Agreement. Refer to Note 8, "Borrowings."

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14. Restructuring Charges

In July 2012, the Company initiated a reduction in workforce resulting in an aggregate restructuring charge of approximately $592,000, consisting of severance and benefit payments for terminated employees, of which $367,000 and $225,000 were included as part of research and development and general and administrative expenses, respectively, in the consolidated statement of operations for the year ended December 31, 2012. Cash payments related to employee severance were all made by March 31, 2013.

For the year ended December 31, 2013, as a result of the Company ceasing to use certain areas of its leased property, additional restructuring charges of $319,000 were recorded relating to the impairment of certain leasehold improvements of $194,000, net of cash from asset disposal of $2,000, and the recognition of the remaining lease obligation on the subleased ceased-used property of $125,000 in general and administrative expenses. The Company paid accrued facility charges of $274,000, net of cash received from the Company's subtenant, through March 2014.

The following table summarizes the accrual balances and utilization by cost type for the restructuring plan (in thousands):

	Employee severance and related benefits	Facilities related and other costs
Beginning at January 1, 2012	$ —	$ —
Charges during the period	592	—
Cash payments during the period	(541)	—
Balance at December 31, 2012	51	—
Charges during the period	—	319
Cash payments during the period	(51)	—
Non-cash settlement	—	(250)
Balance at December 31, 2013	—	69
Cash payments during the period	—	(69)
Balance at December 31, 2014	$ —	$ —

15. Selected Unaudited Quarterly Financial Data

The following tables show a summary of the Company's unaudited quarterly financial data for each of the four quarters of 2014 and 2013 (in thousands, except per share amounts):

	Three Months Ended			
	December 31, 2014	September 30, 2014	June 30, 2014	March 31, 2014
Contract revenue	$4,259	$4,520	$5,203	$5,988
Operating expenses	$9,140	$12,853	$8,541	$9,222
Other income (expense), net	$27	$21	$(217)	$(221)
Net loss	$(4,854)	$(8,312)	$(3,555)	$(3,455)
Basic and diluted net loss per common share [(1)]	$(0.27)	$(0.47)	$(0.20)	$(1.00)
Cash, cash equivalents and short-term investments	$63,679	$72,030	$74,496	$84,937

	Three Months Ended			
	December 31, 2013	September 30, 2013	June 30, 2013	March 31, 2013
Contract revenue	$6,192	$4,289	$4,498	$3,533
Operating expenses	$8,373	$6,584	$8,704	$6,815
Other income and expense, net	$(305)	$(268)	$(104)	$(471)
Net loss	$(2,486)	$(2,563)	$(4,310)	$(3,753)
Basic and diluted net loss per common share[(1)]	$(6.33)	$(6.52)	$(11.08)	$(10.00)
Cash, cash equivalents and short-term investments	$10,738	$8,212	$9,826	$13,136

(1) Basic and diluted net loss per common share are computed independently for each of the quarters presented. Therefore, the sum of quarterly basic and diluted per share information may not equal annual basic and diluted net loss per common share.

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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

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and the rules and regulations thereunder, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) under the Exchange Act, our management, under the supervision and with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2014. Based on such evaluation, our principal executive officer and principal financial officer have concluded that, as of December 31, 2014, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal controls over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the year ended December 31, 2014 that have materially affected, or are 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.

The information required by this item will be contained in our definitive Proxy Statement for our 2015 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission on Schedule 14A in connection with our 2015 Annual Meeting of Stockholders (the “Proxy Statement”), which will be filed not later than 120 days after the end of our fiscal year ended December 31, 2014, under the headings “Executive Officers,” “Election of Directors,” “Corporate Governance,” and “ Section 16(a) Beneficial Ownership Reporting Compliance,” and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our website at www.achaogen.com. The Code of Business Conduct and Ethics is intended to qualify as a “code of ethics” within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (1) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (2) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation.

The information required by this item will be contained in our definitive Proxy Statement for our 2015 Annual Meeting of Stockholders under the headings "Executive Compensation and "Director Compensation," and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this item will be contained in our definitive Proxy Statement for our 2015 Annual Meeting of Stockholders under the headings “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information,” and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions and Director Independence.

The information required by this item will be contained in our definitive Proxy Statement for our 2015 Annual Meeting of Stockholders under the headings “Certain Relationships and Related Party Transactions” and “Corporate Governance,” and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this item will be contained in our definitive Proxy Statement for our 2015 Annual Meeting of Stockholders under the heading “Principal Accountant Fees and Services,” and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) The following documents are filed as part of this report:

1. Financial Statements

See Index to Financial Statements at Item 8 herein.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

See the Exhibit Index immediately following the signature page of this Annual Report on Form 10-K.

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.

Date: March 16, 2015

ACHAOGEN, INC.

By: /s/ Kenneth J. Hillan
Kenneth J. Hillan, M.B., Ch.B.
President and Chief Executive Officer
(principal executive officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of Kenneth J. Hillan, M.B., Ch.B. and Derek A. Bertocci his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this annual report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite his/her name.

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

Signature	Title	Date
/s/ Kenneth J. Hillan Kenneth J. Hillan, M.B., Ch.B.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 16, 2015
/s/ Derek A. Bertocci Derek A. Bertocci	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 16, 2015
/s/ Bryan E. Roberts Bryan E. Roberts	Chairman of the Board of Directors	March 16, 2015
/s/ Chris Boerner Chris Boerner, Ph.D.	Director	March 16, 2015
/s/ Scott M. Rocklage Scott M. Rocklage, Ph.D.	Director	March 16, 2015
/s/ Camille D. Samuels Camille D. Samuels	Director	March 16, 2015
/s/ Alan B. Colowick Alan B. Colowick, M.P.H., M.D.	Director	March 16, 2015
/s/ John C. Doyle John C. Doyle	Director	March 16, 2015
/s/ Kent E. Lieginger Kent E. Lieginger, Pharm.D.	Director	March 16, 2015
/s/ John W. Smither John W. Smither	Director	March 16, 2015
/s/ Christopher T. Walsh Christopher T. Walsh, Ph.D.	Director	March 16, 2015

EXHIBIT INDEX

Exhibit Number	Description of Document	Incorporated by Reference from				Filed Herewith
		Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number	
3.1	Amended and Restated Certificate of Incorporation of Achaogen, Inc.	8-K	001-36323	3/17/2014	3.1	
3.2	Amended and Restated Bylaws of Achaogen, Inc.	8-K	001-36323	3/17/2014	3.2	
4.1	Form of Common Stock Certificate	S-1/A	333-193559	2/25/2014	4.1	
4.2	Warrant issued to Oxford Finance LLC on November 1, 2011.	S-1	333-193559	1/24/2014	4.4	
4.3	Warrant issued to Silicon Valley Bank on November 1, 2011.	S-1	333-193559	1/24/2014	4.5	
4.4	Warrant issued to Oxford Finance LLC on April 30, 2012 (Term A Loan (2)).	S-1	333-193559	1/24/2014	4.6	
4.5	Warrant issued to Oxford Finance LLC on April 30, 2012 (Term B Loan).	S-1	333-193559	1/24/2014	4.7	
10.1(A)†	Exclusive Patent License Agreement, dated as of December 1, 2006, by and between the registrant and the University of Washington.	S-1/A	333-193559	2/27/2014	10.4(A)	
10.1(B)†	Amendment No. 1, effective March 1, 2009, to that certain Exclusive Patent License Agreement, dated December 1, 2006, by and between the registrant and the University of Washington.	S-1	333-193559	1/24/2014	10.4(B)	
10.1(C)†	Amendment No. 2, effective January 5, 2011, to that certain Exclusive Patent License Agreement, dated December 1, 2006, by and between the registrant and the University of Washington.	S-1	333-193559	1/24/2014	10.4(C)	
10.2(A)†	License Agreement, dated January 25, 2006, by and between the registrant and Isis Pharmaceuticals, Inc.	S-1/A	333-193559	2/27/2014	10.5(A)	
10.2(B)†	Letter Agreement, dated January 25, 2006, by and between the registrant and Isis Pharmaceuticals, Inc.	S-1	333-193559	1/24/2014	10.5(B)	
10.3†	Development Services Agreement, dated August 19, 2013, by and between the registrant and ARK Diagnostics, Inc.	S-1/A	333-193559	2/27/2014	10.6	
10.4(A)†	Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1/A	333-193559	2/27/2014	10.7(A)	
10.4(B)	Modification 0001, dated February 24, 2011, to Contract Award issued by the Biomedical Advanced Research and Development	S-1	333-193559	1/24/2014	10.7(B)	

	Authority of the United States Department of Health and Human Services, dated August 30, 2010.				
10.4(C)†	Modification 0003, dated August 18, 2011, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(C)
10.4(D)†	Modification 0004, dated July 16, 2012, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(D)
10.4(E)†	Modification 0006, dated September 20, 2012, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(E)

Exhibit Number	Description of Document	Incorporated by Reference from				Filed Herewith
		Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number	
10.4(F)†	Modification 0007, dated January 23, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(F)	
10.4(G)†	Modification 0008, dated February 28, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(G)	
10.4(H)†	Modification 0009, dated April 22, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(H)	
10.4(I)†	Modification 0010, dated August 14, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(I)	
10.4(J)†	Modification 0011, dated August 30, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(J)	
10.4(K)†	Modification 0012, dated November 5, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(K)	
10.4(L)†	Modification 0013, dated December 17, 2013, to Contract Award issued by the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services, dated August 30, 2010.	S-1	333-193559	1/24/2014	10.7(L)	
10.5	Loan and Security Agreement, dated November 1, 2011, by and among the	S-1	333-193559	1/24/2014	10.8	

	registrant, Oxford Finance LLC and Silicon Valley Bank.				
10.6	Third Amended and Restated Investors' Rights Agreement, dated March 6, 2013, by and among the registrant and certain stockholders.	S-1	333-193559	1/24/2014	10.15
10.7(A)	Amended and Restated Lease Agreement, dated December 29, 2010, by and between the registrant and ARE-San Francisco No. 17, LLC.	S-1	333-193559	1/24/2014	10.9(A)
10.7(B)	Letter Agreement, dated January 4, 2011, by and between the registrant and ARE-San Francisco No. 17, LLC.	S-1	333-193559	1/24/2014	10.9(B)
10.7(C)	Letter Agreement, dated June 15, 2011, by and between the registrant and ARE-San Francisco No. 17, LLC.	S-1	333-193559	1/24/2014	10.9(C)
10.7(D)	First Amendment, dated April 1, 2013, to that certain Amended and Restated Lease Agreement, dated December 29, 2010, by and between the registrant and ARE-San Francisco No. 17, LLC.	S-1	333-193559	1/24/2014	10.9(D)
10.7(E)	Second Amendment, dated June 28, 2013, to that certain Amended and Restated Lease Agreement, dated as of December 29, 2010, by and between the registrant and ARE-San Francisco No. 17, LLC.	S-1	333-193559	1/24/2014	10.9(E)
10.8(A)#	Achaogen, Inc. Amended and Restated 2003 Stock Plan, as amended.	S-8	333-195348	4/17/2014	99.1

Exhibit Number	Description of Document	Incorporated by Reference from				Filed Herewith
		Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number	
10.8(B)#	Amendment to Amended and Restated 2003 Stock Plan, as amended.					X
10.8(C)#	Form of Stock Option Agreement under Achaogen, Inc. Amended and Restated 2003 Stock Plan.	S-1	333-193559	1/24/2014	10.1(B)	
10.9(A)#	Achaogen, Inc. 2014 Equity Incentive Award Plan.	S-8	333-195348	4/17/2014	99.3	
10.9(B)#	Form of Stock Option Agreement under Achaogen, Inc. 2014 Equity Incentive Award Plan.	S-1/A	333-193559	2/12/2014	10.2(B)	
10.9(C)#	Form of Restricted Stock Agreement under Achaogen, Inc. 2014 Equity Incentive Award Plan.	S-1/A	333-193559	2/12/2014	10.2(C)	
10.9(D)#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under Achaogen, Inc. 2014 Equity Incentive Award Plan.					X
10.10#	Achaogen, Inc. 2014 Employee Stock Purchase Plan.	S-8	333-195348	4/17/2014	99.7	
10.11(A)#	Achaogen, Inc. 2014 Employment Commencement Incentive Plan.					X
10.11(B)#	Form of Stock Option Grant Notice and Stock Option Agreement under the Achaogen, Inc. 2014 Employment Commencement Incentive Plan.					X
10.11(C)#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the Achaogen, Inc. 2014 Employment Commencement Incentive Plan.					X
10.12#	Change in Control Plan	S-1	333-193559	1/24/2014	10.14	
10.13#	Form of Indemnification Agreement between the registrant and its directors and officers.	S-1/A	333-193559	2/12/2014	10.3	
10.14#	Offer Letter, dated January 24, 2011, by and between the registrant and Kenneth J. Hillan M.B., Ch.B.	S-1	333-193559	1/24/2014	10.10	
10.15#	Offer Letter, dated February 14, 2014, by and between the registrant and Derek A. Bertocci.	S-1/A	333-193559	2/25/2014	10.17	
10.16#	Offer Letter, dated June 24, 2014, by and between the registrant and Ian Friedland, M.D.	10-Q	001-36323	8/11/2014	10.1	
10.17#	Offer Letter, dated May 2, 2011, by and between the registrant and Becki Filice.	S-1	333-193559	1/24/2014	10.11	
10.18#	Offer Letter, dated July 27, 2011, by and between the registrant and Christine Murray.	S-1	333-193559	1/24/2014	10.12	

10.19#	Offer Letter, dated December 29, 2012, by and between the registrant and Dennis Hom.	S-1	333-193559	1/24/2014	10.13	
10.20#	Separation Agreement, dated March 31, 2014, by and between the registrant and Dennis Hom.	10-Q	001-36323	5/12/2014	10.1	
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.					X
31.1	Certification of Principal Executive Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of Principal Financial Officer Required Under Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1*	Certification of Principal Executive Officer and Principal Financial Officer Required Under Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and 18 U.S.C. §1350.					X
101.INS	XBRL Instance Document.					X
101.SCH	XBRL Taxonomy Extension Schema Document.					X

Exhibit Number	Description of Document	Incorporated by Reference from				Filed Herewith
		Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number	
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.					X

† Confidential treatment has been granted for certain information contained in this exhibit. Such information has been omitted and filed separately with the SEC.
# Indicates management contract or compensatory plan.
* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Achaogen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.