TETRAPHASE PHARMACEUTICALS INC
Form 10-K
March 13, 2017

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended: December 31, 2016

Or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 001-35837

TETRAPHASE PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	04-3581650
(State or Other Jurisdiction of	(I.R.S. Employer
Incorporation or Organization)	Identification No.)

480 Arsenal Way

Watertown, Massachusetts 02472

(Address of Principal Executive Offices) (zip code)

Registrant’s telephone number, including area code: (617) 715-3600

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

Title of each class	Name of each exchange on which registered
Common Stock, $.001 par value	NASDAQ Global Select Market

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

None

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) 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.

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

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

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

The aggregate market value of the registrant's common stock, $0.001 par value per share ("Common Stock"), held by non-affiliates of the registrant, based on the last reported sale price of the Common Stock on the NASDAQ Global Select Market at the close of business on June 30, 2016, was $149,685,670. For purposes hereof, shares of Common Stock held by each executive officer and director of the registrant and entities affiliated with such executive officers and directors have been excluded from the foregoing calculation because such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's Common Stock as of March 10, 2017: 37,057,089

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2017 annual meeting of stockholders are incorporated by reference into Part III of this annual report on Form 10-K.

TETRAPHASE PHARMACEUTICALS, INC.

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References to Tetraphase

Throughout this annual report on Form 10-K, the "Company," "Tetraphase," "we," "us," and "our," except where the context requires otherwise, refer to Tetraphase Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of Tetraphase Pharmaceuticals, Inc.

The trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

Forward-Looking Information

This annual report on Form 10-K contains forward-looking statements regarding, among other things, our future discovery and development efforts, our future operating results and financial position, our business strategy, and other objectives for our operations. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "proj "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. You also can identify them by the fact that they do not relate strictly to historical or current facts. There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery and clinical development activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, our ability to obtain any necessary financing to conduct our planned activities, and other risk factors. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this annual report on Form 10-K, particularly in the section entitled "Risk Factors" in Part I that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make. Unless required by law, we do not undertake any obligation to publicly update any forward-looking statements.

PART I

ITEM 1. Business

Overview

We are a clinical-stage biopharmaceutical company using our proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. We are developing our lead product candidate, eravacycline, a fully synthetic fluorocycline, as an intravenous, or IV, and oral antibiotic for use as a first-line empiric monotherapy for the treatment of resistant and multidrug-resistant infections, including multidrug-resistant Gram-negative infections.

We are conducting a global phase 3 clinical program for eravacycline called IGNITE (Investigating Gram-Negative Infections Treated with Eravacycline), which is evaluating eravacycline in complicated intra-abdominal infections (or cIAI) and complicated urinary tract infections (or cUTI). We are also pursuing the discovery and development of additional antibiotics that target unmet medical needs, including multidrug-resistant, or MDR, Gram-negative bacteria.

We are conducting IGNITE4, a phase 3 randomized, double-blind, double-dummy, multicenter, prospective study that is designed to assess the efficacy, safety and pharmacokinetics of twice-daily IV eravacycline (1.0 mg/kg every 12 hours) compared with meropenem (1g every 8 hours), the control therapy in this trial, for the treatment of cIAI. The study is expected to enroll approximately 450 adult patients at 75 centers worldwide. The primary endpoint of IGNITE4 is clinical response at the test-of-cure (TOC) visit, which occurs 25 to 31 days after the initial dose of the study drug. The primary efficacy analysis will be conducted using a 12.5% non-inferiority margin in the microbiological intent-to-treat (“micro-ITT”) population. We previously conducted IGNITE1, our completed phase 3 clinical trial where eravacycline met the primary endpoint of statistical non-inferiority compared to ertepenem, the control therapy for the trial, for the treatment of cIAI. Consistent with draft guidance issued by the United States Food and Drug Administration, or FDA, with respect to the development of antibiotics for cIAI and our discussions with the FDA, positive results from our phase 3 clinical trials (IGNITE1 and IGNITE4) would be sufficient to support submission of a new drug application, or NDA, for eravacycline for the treatment of cIAI. We expect to report top-line data from IGNITE4 in the fourth quarter of 2017.

During the second half of 2017, we plan to submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for IV eravacycline for the treatment of cIAI. We expect the MAA submission will be supported by data from IGNITE1, our completed phase 3 clinical trial, which evaluated the efficacy and safety of twice-daily IV eravacycline for the treatment of cIAI. In this study, eravacycline was well tolerated, and met the primary endpoint of statistical non-inferiority compared to ertapenem, the control therapy for the trial.

In January 2017, we initiated IGNITE3, a randomized, multi-center, double-blind, phase 3 clinical trial evaluating the efficacy and safety of once-daily IV eravacycline (1.5mg/kg every 24 hours) compared to ertapenem (1g every 24 hours), the control therapy in this trial, for the treatment of cUTI. IGNITE3 is expected to enroll approximately 1,000 adult patients, who will be randomized 1:1 to receive eravacycline or ertapenem for a minimum of five days, and will then be eligible to switch to an approved oral antibiotic. The co-primary endpoints of responder rate (a combination of clinical cure rate and microbiological response) in the micro-ITT population at the end-of-IV treatment visit and at the test-of-cure, or TOC, visit (Day 5-10 post therapy) will be evaluated using a 10% non-inferiority margin.

In parallel with the clinical trials using IV eravacycline, we are continuing our development program for an oral formulation of eravacycline. We recently completed phase 1 clinical testing in which the administration of oral eravacycline to patients in the fasted state resulted in increased drug exposure. Further clinical tests designed to evaluate other important variables are currently ongoing, with the goal of optimizing the oral eravacycline dosing regimen. We expect to provide an update with top-line findings from this testing and potential next steps during the third quarter of 2017.

In January 2016, we initiated a phase 1 clinical trial of the IV formulation of TP-271, a fully synthetic fluorocycline being developed for respiratory disease caused by bacterial biothreat pathogens, in healthy volunteers. In addition to eravacycline and TP-271, we are pursuing development of TP-6076, a fully synthetic fluorocycline derivative, as a lead candidate under our second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria, and in July 2016 we initiated a phase 1 clinical trial of the IV formulation of TP-6076 in healthy volunteers.

Eravacycline has been designated by the FDA as a Qualified Infectious Disease Product, or QIDP, for both the cIAI and cUTI indications. The QIDP designation makes eravacycline eligible for priority review and an additional five years of U.S. market exclusivity, if approved. In addition, the FDA granted Fast Track designations for eravacycline for both the cIAI and cUTI indications

and in both the IV and oral formulations. Fast Track designation is intended to expedite the study and regulatory review of drugs intended to treat serious or life-threatening conditions that demonstrate the potential to address unmet medical needs.

Eravacycline is designed to treat a broad range of infections, including infections due to multidrug-resistant bacteria. In in vitro experiments, eravacycline has demonstrated the ability to cover a wide variety of multidrug-resistant Gram-negative, Gram-positive, anaerobic and atypical bacteria, including multidrug-resistant Klebsiella pneumoniae and multi-drug resistant Acinetobacter. Multidrug-resistant Klebsiella pneumoniae is one of the carbapenem-resistant Enterobacteriaceae (or CREs) listed as an urgent threat and multi-drug resistant Acinetobacter is listed as a serious threat by the Centers for Disease Control and Prevention, or CDC, in a September 2013 report and they are listed as Priority 1; Critical pathogens in the World Health Organization's priority pathogens list for R&D, published in February 2017. CREs were a confirmed area of great concern by the World Health Organization in an April 2014 global surveillance report. Gram-negative bacteria that are resistant to multiple available antibiotics are increasingly common and a growing threat to public health. We believe that the ability of eravacycline to cover multidrug-resistant Gram-negative bacteria, as well as multidrug-resistant Gram-positive, anaerobic and atypical bacteria, and its potential for IV-to-oral transition therapy, will enable eravacycline to become the drug of choice for first-line empiric treatment of a wide variety of serious and life-threatening infections.

We believe that our proprietary chemistry technology, licensed from Harvard University on an exclusive worldwide basis and enhanced by us, represents a significant innovation in the creation of tetracycline drugs that has the potential to reinvigorate the clinical and market potential of the class. Our proprietary chemistry technology makes it possible to create novel tetracycline antibiotics using a practical, fully synthetic process for what we believe is the first time. This fully synthetic process avoids the limitations of bacterially-derived tetracyclines and allows us to chemically modify many positions in the tetracycline scaffold, including most of the positions that we believe could not practically be modified by any previous conventional method. Using our proprietary chemistry technology, we can create a wider variety of tetracycline-based compounds than was previously possible, enabling us to pursue novel tetracycline derivatives for the treatment of multidrug-resistant bacteria that are resistant to existing tetracyclines and other classes of antibiotic products. We have used our proprietary chemistry technology to create more than 3,000 new tetracycline derivatives that we believe could not be practically created with conventional methods. We own exclusive worldwide rights to these compounds and our technology.

In 2011 and 2012, the U.S. government awarded contracts for potential funding of over $100 million for the development of our antibiotic compounds. These awards include a contract for up to $67.3 million from the Biomedical Advanced Research and Development Authority, or BARDA, an agency of the U.S. Department of Health and Human Services, for the development of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. We refer to this contract as the BARDA Contract. The funding under the BARDA Contract is also being used for certain activities in the development of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria. These awards also include a contract for up to $35.8 million from the National Institute of Allergy and Infectious Diseases, or NIAID, a division of the National Institutes of Health, for the development of TP-271. We refer to this contract as the NIAID Contract. In addition during 2011, NIAID awarded a separate grant for $2.9 million. We refer to this award as the NIAID Grant. These awards were made to CUBRC, Inc., or CUBRC, an independent, not-for-profit, research corporation that specializes in U.S. government-based contracts, with which we are collaborating. CUBRC serves as the prime contractor under these awards, primarily carrying out a program management and administrative role with additional responsibility for the management of preclinical studies. We serve as lead technical expert on all aspects of these awards and also serve as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. Under our subcontracts with CUBRC, we may receive funding of up to approximately $41.6 million reflecting the portion of the BARDA Contract funding that may be paid to us for our activities, up to approximately $15.1 million reflecting the portion of the NIAID Contract funding that may be paid to us for our activities, and up to approximately $0.9 million reflecting the

portion of the NIAID Grant that may be paid to us for our activities. Of these amounts, we have received a total of $43.7 million as of December 31, 2016. The BARDA Contract includes funding for some of the activities that we would otherwise be required to fund on our own in connection with an NDA submission for eravacycline.

Strategy

Our goal is to become a fully integrated biopharmaceutical company that discovers, develops and commercializes novel antibiotics for use in areas of unmet medical need. Key elements of our strategy include:

- Complete clinical development of eravacycline in its lead indications and seek regulatory approval. We are conducting our IGNITE4 clinical trial of IV eravacycline in patients with cIAI. Consistent with draft guidance issued by FDA with respect to the development of antibiotics for cIAI and our discussions with the FDA, positive results from our phase 3 clinical trials (IGNITE1 and IGNITE4) would be sufficient to support submission of a new drug application for eravacycline for the treatment of cIAI. As background, we previously conducted IGNITE1, our completed phase 3 clinical trial where eravacycline met the primary endpoint of statistical non-inferiority compared to ertapenem, the control therapy

for the trial, for the treatment of cIAI. We are also conducting our IGNITE3 clinical trial of the IV formulation of eravacycline in patients with cUTI. If IGNITE3 is successful, we plan to use the results from IGNITE3 to support submission of a supplemental new drug application, or sNDA, for IV eravacycline for the treatment of cUTI, assuming approval first of IV eravacycline for the treatment of cIAI. During the second half of 2017, we plan to submit an MAA to the EMA for IV eravacycline for the treatment of cIAI. We expect the MAA submission will be supported by data from IGNITE1.

- Maximize the commercial potential of eravacycline. If eravacycline is approved, we intend to directly commercialize eravacycline in the United States with a targeted hospital sales force and to commercialize eravacycline outside the United States through collaboration arrangements. We believe that eravacycline's potent coverage of multidrug-resistant Gram-negative bacteria and other multidrug-resistant bacteria, will allow it to be used to treat patients successfully in hospitals, emergency rooms and out-patient clinic settings.
- Pursue development of eravacycline in additional indications. We are initially developing eravacycline for the treatment of cIAI and cUTI, and, subject to obtaining additional financing, intend to pursue development of eravacycline for the treatment of additional indications, including other serious and life-threatening infections. We may pursue these development activities either by ourselves or with collaborators.
- Opportunistically advance development of other product candidates created using our proprietary chemistry technology. In addition to eravacycline, we are currently conducting phase 1 clinical trials of TP-271 and TP-6076. We have used our proprietary chemistry technology to create more than 3,000 new tetracycline derivatives that we believe could not be practically created with conventional methods. We intend to advance our antibiotic product pipeline with differentiated product candidates created using our proprietary chemistry technology and targeting hospital and acute care markets. We may pursue these activities either by ourselves or with collaborators.

Drug-Resistant Antibiotic Market

Physicians commonly prescribe antibiotics to treat patients with acute and chronic infectious diseases that are either known, or presumed, to be caused by bacteria. Inappropriate use of antibiotics and lack of new therapies has resulted in a rapid increase in bacterial infections that are resistant to multiple antibacterial agents. Global microbial resistance, including bacteria, viruses and fungi, now results in the death of at least 700,000 people each year, according to an analysis commissioned by the U.K. government in 2016. The report predicts that failing to develop effective treatments for drug-resistant bacteria by 2050 would lead to 10 million extra deaths a year. In a September 2013 report, the CDC estimated that every year in the United States, more than two million people acquire serious infections that are resistant to one or more of the antibiotics designed to treat those infections, with at least 23,000 dying as a result, and many more dying from other conditions that are complicated by the occurrence of an antibiotic-resistant infection. These antibiotic-resistant infections add considerable and avoidable costs to the U.S. healthcare system. In the same September 2013 report, the CDC noted that the total economic cost of antibiotic infections to the U.S. economy has been estimated to be as high as $20 billion in excess of direct healthcare costs. Over the last decade there has been an increase in antibiotics that target resistant Gram-positive bacteria, but there still remain limited therapeutic options for resistant Gram-negative infections. According to the CDC, among all of the bacterial resistance problems, Gram-negative pathogens are particularly worrisome because they are becoming resistant to nearly all drugs that would be considered for treatment, with the most serious Gram-negative infections being healthcare associated and the most common pathogens being Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter.

Antibiotics that treat bacterial infections can be classified as broad-spectrum or narrow-spectrum. Antibiotics that are active against a mixture of Gram-positive, Gram-negative and anaerobic bacteria are referred to as broad-spectrum. Antibiotics that are active only against a select subset of bacteria are referred to as narrow-spectrum. Because it usually takes from 24 to 72 hours from the time a specimen is received in the laboratory to definitively diagnose a particular bacterial infection, physicians may be required to prescribe antibiotics for serious infections without having identified the bacteria. As such, effective first-line treatment of serious infections requires the use of broad-spectrum

antibiotics with activity against a broad range of bacteria at least until the bacterial infection can be diagnosed.

Broad-spectrum antibiotics are used to treat major hospital infections such as cIAI, cUTI, hospital-acquired pneumonia, or HAP, and ventilator-associated pneumonia, or VAP. Based on an analysis from a variety of industry sources, we estimate that the number of patients treated with antibiotics in the United States and European Union annually includes approximately 4.6 million cIAI patients with each patient being treated for an average of 8.6 days for a combined estimated 40 million annual average days of treatment; approximately 8.6 million cUTI patients with each patient being treated for an average of 6.9 days for a combined estimated 60 million annual average days of treatment; and 2.8 million HAP/VAP patients with each patient being treated for an average of 9.6 days for a combined estimated 27 million annual average days of treatment. Of these patients, we believe that approximately 40% of cIAI patients require a change in therapy and more than 20% of cUTI patients fail therapy. 50% of patients with cIAI are receiving combination therapy and 30% of patients with cUTI are receiving combination therapy. Gram-negative bacteria account for 55-85% of

HAP/VAP infections, and greater than 60% of patients are receiving combination therapy. In hospitalized patients, rates of HAP/VAP infections due to multi-drug resistant, or MDR, pathogens are increasing. Late-onset HAP/VAP infections are more likely to be caused by MDR pathogens, and are associated with increased patient mortality and morbidity.

As such, at present, there is an acute need for new drugs to treat multidrug-resistant Gram-negative bacteria. Currently approved products, such as meropenem are becoming increasingly ineffective against Gram-negative bacteria due to increasing resistance, limiting patients' treatment options, particularly for patients with multidrug-resistant infections. Few new therapeutic agents have been approved or are in clinical development.

A survey of infectious disease specialists published in the June 2012 edition of Clinical Infectious Disease rated multidrug-resistant Gram-negative infections as the most important unmet clinical need in current practice. In the survey, 63% of physicians reported treating a patient in the past year whose bacterial infection was resistant to all available antibacterial agents. A nationwide electronic database looked at the prevalence of gram negative resistance from 2008-2015 in US Hospitals and it showed MDR rates continue to increase. Out of the 3,158,349 isolates tested 5.3% were considered MDR pathogens. Five bacteria accounted for 92.7% of all MDR isolates: E coli (39.4%), P aeruginosa (29.4%), K pneumoniae (13.2%), A baumannii (5.4%) and Enterobacter spp (5.2%). The highest rate of MDR was associated with the hospital onset setting (11.4%), followed by the admission period (6.6%), and the ambulatory setting (3.5%). The database showed that 42.9% of A baumannii were MDR related isolates. The rate of MDR A baumannii was highest in the inpatient setting (58.6% of isolates from all body sources), followed by admission setting (43.2%), and ambulatory setting (24.8%).

The important need for new treatment options for serious bacterial infections was further highlighted by the passage in the United States in July 2012 of the Generating Antibiotic Incentives Now, or GAIN, Act, which provides regulatory incentives for the development of new antibacterial or antifungal drugs intended to treat serious or life-threatening infections that are resistant to existing treatment. In September 2014, the United States' President's Council of Advisors on Science and Technology issued a report providing recommendations to combat the rise in antibiotic resistant bacteria and advising that without rapid action, the United States risks losing the tremendous progress made in antibiotic development over the last century. Their recommendations focused on three areas: improving surveillance, increasing longevity of current antibiotics and increasing the rate at which new antibiotics are discovered and developed.

New legislative initiatives have recently been approved as part of the 21st Century Cures Act, including the Antibiotic Development to Advance Patient Treatment Act which would provide a pathway for approval of antibiotics in limited populations of patients with few or no suitable treatment options. Other legislation still pending include the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms, or DISARM, Act which would designate certain novel antibiotics used to treat serious bacterial infections to receive higher Medicare reimbursement, and an amendment to the GAIN Act, which would allow successful QIDP sponsors to transfer up to one year of exclusivity to another product, including products marketed by other companies.

Limitations of Available Treatment Options

When confronted with a new patient suffering from a serious infection caused by an unknown pathogen, a physician may be required to quickly initiate first-line empiric antibiotic treatment to stabilize the patient prior to definitively diagnosing the particular bacterial infection. However, current antibiotics for first-line empiric treatment of serious bacterial infections suffer from significant limitations, including one or more of the following:

Insufficient Coverage of Multidrug-resistant Bacteria. A physician cannot risk prescribing an inappropriate antibiotic when initially treating a patient for a serious infection where the pathogen has not yet been definitively identified.

Frequently used products, such as linezoid and daptomycin, are limited to Gram-positive bacteria and thus are rarely used as a first-line empiric monotherapy if broad bacterial coverage is required. Recently approved products are limited to specific Gram-negative bacteria and thus are rarely used as a first-line empiric monotherapy if broad bacterial coverage is required. In addition, other popular antibiotics that have been used as first-line empiric monotherapies, such as levofloxacin, piperacillin/tazobactam, carbapenems, and imipenem/cilastatin, have seen their utility as first-line empiric monotherapies diminished as the number of bacterial strains resistant to these therapies has increased.

Complicated and Expensive Multi-Drug Cocktails and Multi-Dose Regimens. Due to gaps in the spectrum of coverage of antibiotics, physicians are often confronted with the need to design complicated multi-drug cocktails for the first-line empiric treatment of patients with serious infections. The clinical situation is further complicated when each drug in the multi-drug cocktail has a different dosing regimen, such as three or four times a day, resulting in an added burden on the pharmacy and nursing staff, higher costs due to multiple drug administrations and an increased potential for medical errors or drug-drug interactions. We believe that, with the exception of eravacycline, most of the antibiotics that are in development or have recently been approved by the FDA that are intended to cover a broad range of bacteria, including Gram-negative bacteria, or solely to address Gram-negative bacteria, are

being developed or are approved for use in combination with one or more other antibiotics, and require the addition of a third drug such as metronidazole to address the presence of anaerobic bacteria.

Safety and Tolerability Concerns. Concerns about antibiotic safety and tolerability are among the leading reasons why patients stop treatment and fail therapy. Antibiotics on the market have been associated with adverse effects such as myelosuppression, seizures, nephrotoxicity and gastrointestinal disorders.

Given these limitations, there is an unmet medical need for a first-line empiric antibiotic treatment that has the following characteristics:

- Potency and effectiveness against a broad range of bacteria, including multidrug-resistant Gram-negative, Gram-positive, atypical and anaerobic bacteria;
- Capability of being used as a monotherapy in the majority of patients in the hospital with cIAI, cUTI and other multidrug-resistant infections;
- A convenient dosing regimen, such as once or twice-daily; and
- A favorable safety and tolerability profile.
- Availability in both IV dosage and potentially an oral dosage form.

Based on our belief that eravacycline has, or potentially has, each of these characteristics, our goal is to develop eravacycline to be the drug of choice for first-line empiric treatment of a wide variety of serious and life-threatening infections.

Eravacycline

Overview

We are developing our lead product candidate, eravacycline, as an IV and oral antibiotic for use as a first-line empiric monotherapy for the treatment of resistant and multidrug-resistant infections, including multidrug-resistant Gram-negative bacteria. We developed eravacycline using our proprietary chemistry technology. We own exclusive worldwide rights for the development and commercialization of eravacycline.

To date, we have completed two phase 3 clinical trials with eravacycline: IGNITE1, a phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cIAI, and IGNITE2, a phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV-to-oral transition therapy for the treatment of cUTI. In December 2014, we announced that in IGNITE1, eravacycline met the primary endpoint of statistical non-inferiority compared to the control therapy for the trial. In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority in IGNITE2 compared to the control therapy for this trial.

Following advice from with the FDA, we are conducting an additional phase 3 clinical trial of IV eravacycline in patients with cIAI, IGNITE4. If IGNITE4 is successful, we plan to use the results from IGNITE1 and IGNITE4 to support submission of an NDA for IV eravacycline for the treatment of cIAI. As background, we previously conducted IGNITE1, our completed phase 3 clinical trial where eravacycline met the primary endpoint of statistical non-inferiority compared to ertapenem, the control therapy for the trial, for the treatment of cIAI. We are also conducting a phase 3 clinical trial of IV eravacycline in patients with cUTI, IGNITE3. If IGNITE3 is successful, we plan to use the results from IGNITE3 to support submission of an sNDA for IV eravacycline for the treatment of cUTI, assuming approval first of IV eravacycline for the treatment of cIAI. Consistent with guidance from the EMA which requires only one successful phase 3 clinical trial, Tetraphase plans to submit an MAA to the EMA in the second half of 2017 supported by data from the successfully completed IGNITE1 clinical trial.

Tetracycline antibiotics have been in clinical use for over 50 years and have a demonstrated record of safety and effectiveness. However, as with most classes of antibiotics, a high incidence of resistance among many bacteria has limited their effectiveness and resulted in tetracyclines being relegated to second- or third-line therapy several decades after their introduction. Chemists have generally been unable to synthesize new tetracyclines that could overcome bacterial resistance mechanisms. We have used our proprietary chemistry technology to create more than 3,000 new tetracycline derivatives that we believe could not be practically created with conventional methods. Many of these new derivatives, including eravacycline, have been able to overcome bacterial resistance in in vitro studies.

Eravacycline is a novel, fully synthetic fluorocycline antibiotic. We selected eravacycline for development from tetracycline derivatives that we generated using our proprietary chemistry technology on the basis of the following characteristics of the compound that we observed in in vitro studies of the compound:

- potent antibacterial activity against a broad range of susceptible and multidrug-resistant bacteria, including Gram-negative, Gram-positive, atypical and anaerobic bacteria;
- potential to treat the majority of patients as a first-line empiric monotherapy with convenient dosing; and
- potential for IV-to-oral transition therapy.

In designing eravacycline, we inserted a fluorine atom into the tetracycline scaffold, which we call a fluorocycline, and modified the scaffold at another position. We believe that these modifications enable eravacycline to not be subject to tetracycline-specific mechanisms of drug resistance. As a result, we believe that eravacycline is active against multidrug-resistant bacteria in ways that tetracyclines currently on the market or in development are not.

In in vitro studies, including a surveillance study published in December 2014 using over 4,000 patient bacterial isolates collected in New York City, eravacycline has been highly active against emerging multidrug-resistant pathogens like Acinetobacter baumannii as well as clinically important species of Enterobacteriaceae, including those isolates that produce ESBLs or are resistant to the carbapenem class of antibiotics, and anaerobes, in comparison to commonly used antibiotics.

Data published in August 2016 demonstrated that eravacycline retained potency against E. coli clinical isolates containing a plasmid expressing mcr-1 (ERV MIC_{90}=0.5 µg/mL; colistin MIC_{90}=16 µg/mL). The in vitro potency of eravacycline was unaffected by inducible overexpression of the mcr-1 gene in an engineered laboratory E. coli strain.

Eravacycline has also demonstrated strong activity in vitro against Gram-positive pathogens, including both nosocomial and community-acquired methicillin susceptible or resistant Staphylococcus aureus strains, vancomycin susceptible or resistant Enterococcus faecium and Enterococcus faecalis, and penicillin-susceptible or resistant strains of Streptococcus pneumoniae. In in vitro studies of pathogens most prevalent in cIAI infections, eravacycline consistently exhibited strong activity against enterococci and streptococci. One of the most frequently isolated anaerobic pathogens in cIAI, either as the sole pathogen or often in conjunction with another Gram-negative bacterium, is Bacteroides fragilis. In these studies eravacycline demonstrated activity against Bacteroides fragilis and a wide range of Gram-positive and Gram-negative anaerobes.

Key Differentiating Attributes of Eravacycline

We believe that the following key attributes of eravacycline, observed in clinical trials and preclinical studies, differentiate eravacycline from other antibiotics targeting multidrug-resistant infections, including multidrug-resistant Gram-negative infections. We believe these attributes will make eravacycline a safe and effective treatment for cIAI, cUTI and other serious and life-threatening infections for which we may develop eravacycline.

- Offers a broad range of activity against a wide variety of multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria. In our phase 2 and phase 3 clinical trials of the IV formulation of eravacycline, eravacycline

demonstrated a high cure rate against a wide variety of multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria. In addition, in in vitro studies, eravacycline demonstrated potent antibacterial activity against Gram-negative bacteria, including ESBL-producing E. coli and the mcr-1 gene; ESBL-producing Klebsiella pneumoniae; Acinetobacter baumannii; Gram-positive bacteria, including MRSA and vancomycin-resistant enterococcus, or VRE; and anaerobic pathogens. As a result, we believe that eravacycline has the potential to be used as a first-line empiric monotherapy for the treatment of cIAI, cUTI and other serious and life-threatening infections.

- Lower probability of drug resistance. To date, in the clinical trials and preclinical studies of eravacycline that we have conducted we have seen little decrease in susceptibility that would suggest increased resistance to eravacycline. We believe that, as a fluorocycline, eravacycline will not be subject to tetracycline-specific mechanisms of drug resistance.

- Favorable safety and tolerability profile. Eravacycline has been evaluated in 1,348 subjects in the phase 1, phase 2 and phase 3 clinical trials that we have conducted through September 2016. In these trials, eravacycline has demonstrated a favorable safety and tolerability profile. In our phase 2 and phase 3 clinical trials of eravacycline in patients with cIAI, no patients suffered any drug-related serious adverse events, and safety and tolerability were comparable to ertapenem, the control therapy for the trials. In the phase 3 clinical trial of eravacycline in patients with cUTI, no patients suffered any drug-related serious adverse events, and safety and tolerability were comparable to levofloxacin, the control therapy for this trial. In addition, in these phase 2 and phase 3 clinical trials, the rate at which gastrointestinal adverse events such as nausea and emesis that occurred in the eravacycline arms was low.
- Convenient dosing regimen. In our clinical trials to date, we have dosed eravacycline once or twice a day as a monotherapy. We believe that eravacycline will be able to be administered as a first-line empiric monotherapy with once- or twice-daily dosing, avoiding the need for complicated dosing regimens typical of multi-drug cocktails and the increased risk of negative drug-drug interactions inherent to multi-drug cocktails.
- Potential for convenient IV-to-oral transition therapy. Notwithstanding the results of IGNITE2, we are continuing to seek to develop an oral formulation of eravacycline. We believe an oral formulation would enable patients who begin IV treatment with eravacycline in the hospital setting to transition to oral dosing of eravacycline either in hospital or upon patient discharge for convenient home-based care. We believe that the availability of both IV and oral transition therapy may reduce the length of a patient's hospital stay and the overall cost of care.

Clinical Experience

We have studied IV and oral formulations of eravacycline in 1,348 subjects in 19 clinical trials completed from October 2009 to September 2016.

Phase 3 Clinical Program

We designed our IGNITE phase 3 program for eravacycline to enable us to position eravacycline as a first-line empiric monotherapy for the treatment of cIAI and cUTI due to eravacycline's broad-range of coverage against resistant and multidrug-resistant infections, including multidrug-resistant Gram-negative infections.

cIAI

Our initial phase 3 clinical trial of eravacycline for the treatment of patients with cIAI was our IGNITE1 trial. Consistent with guidance issued by the FDA with respect to the development of antibiotics for cIAI and our discussions with the FDA, we had planned to utilize results from our IGNITE1 trial with the results of our IGNITE2 trial in patients with cUTI to support the submission of an NDA for both indications. In December 2014, we announced that eravacycline met the primary endpoint of statistical non-inferiority compared to ertapenem in IGNITE1 for the treatment of cIAI. In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin in IGNITE2 for the treatment of cUTI.

Following the results of IGNITE2, we held discussions with the FDA regarding the registration pathway for eravacycline. As part of these discussions, the FDA advised us that data from one additional positive phase 3 clinical trial would be required to support an NDA submission for IV eravacycline for cIAI. Based on this guidance, we initiated our IGNITE4 trial in patients with cIAI. If IGNITE4 is successful, we plan to use the results from IGNITE1 and IGNITE4 to support submission of an NDA for IV eravacycline for the treatment of cIAI. Consistent with guidance from the EMA which requires only one successful phase 3 clinical trial, we plan to submit an MAA to the EMA in the second half of 2017 for eravacycline for the treatment of cIAI, supported by data from our IGNITE1 clinical trial.

IGNITE4

Eravacycline Phase 3 IGNITE4 Study Design

In October 2016 we initiated IGNITE4 as a phase 3 randomized, double-blind, double-dummy, multicenter, prospective study designed to assess the efficacy, safety and pharmacokinetics of twice-daily eravacycline (1.0 mg/kg every 12 hours) compared with meropenem (1g every 8 hours) for the treatment of cIAI. The study is expected to enroll approximately 450 adult patients at 75 centers worldwide. The primary endpoint of IGNITE4 is clinical response at the test-of-cure, or TOC, visit, which occurs 25 to 31 days after the initial dose of the study drug. The primary efficacy analysis will be conducted using a 12.5% non-inferiority margin in the microbiological intent-to-treat, or micro-ITT, population. We expect top-line results in the fourth quarter of 2017.

IGNITE1

Eravacycline Phase 3 IGNITE1 Study Design

In the third quarter of 2013, we initiated a global, multi-center, randomized, double-blind, double-dummy phase 3 clinical trial, our IGNITE1 trial, to assess the efficacy, safety and pharmacokinetics of eravacycline compared to ertapenem in patients with cIAI. We enrolled 541 patients in the trial at 66 clinical sites worldwide. These patients were randomized into two arms on a 1:1 basis. Patients in the eravacycline arm received 1.0 mg/kg IV eravacycline administered twice per day. Patients in the ertapenem arm received 1.0 g IV ertapenem administered once per day.

Investigators obtained baseline intra-abdominal cultures at the time of operation and treated patients for a minimum of four days and a maximum of 14 days following the time of operation and until symptoms of cIAI were resolved. A test-of-cure, or TOC, visit took place 25 to 31 days after the initial dose of treatment and a final or follow-up visit occurred 38 to 50 days after the initial dose of treatment.

We designed the trial as a non-inferiority study, and to be responsive to both FDA and EMA guidance. Under FDA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the microbiological intent-to-treat, or micro-ITT, population which consisted of all randomized patients in the trial who had baseline bacterial pathogens that cause cIAI and against which eravacycline has antibacterial activity. Under EMA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the modified intent-to-treat, or MITT, population which consisted of all patients who received at least one dose of study drug, and in the clinically evaluable, or CE, patient population, which consisted of all randomized patients in the trial who meet key inclusion/exclusion criteria and follow other important components of the trial. Secondary endpoints included clinical response at the end-of-treatment, TOC and follow-up visits in the intent-to-treat population, the CE population, the micro-ITT population and the microbiologically evaluable, or ME, population. The ME population consists of all micro-ITT patients who meet key inclusion/exclusion criteria and follow other important components of the trial. In the trial, we also studied microbiologic response at the end-of-treatment and TOC visits in the micro-ITT and ME populations, the safety and tolerability of eravacycline in the safety population and pharmacokinetic parameters after eravacycline administration. We designed the trial to be consistent with the FDA's cIAI guidance, in which the FDA suggested that the primary efficacy endpoint for a trial of cIAI should be complete resolution of baseline signs and symptoms attributable to cIAI in the micro-ITT patient population 28 days after randomization and the absence of clinical failure including death and unplanned surgical procedures through the period ending 28 days following randomization.

In December 2014, we announced top-line data from IGNITE1. In the trial, eravacycline met the primary endpoint of statistical non-inferiority of clinical response at the TOC visit, under the guidance set by the FDA and the EMA. The primary analysis under the FDA guidance was conducted using a 10% non-inferiority margin in the micro-ITT population. In the micro-ITT population, the lower and upper bounds of the 95% confidence interval were -7.1% and 5.5%, respectively. Under the EMA guidance, the primary analysis was conducted using a 12.5% non-inferiority margin in the CE and MITT patient populations. In the CE population, the lower and upper bounds of the 95% confidence interval were -6.3% and 2.8%, respectively, and the lower and upper bounds of the 99% confidence interval were -7.9% and 4.4%, respectively. In the MITT population, the lower and upper bounds of the 95% confidence interval were -7.4% and 3.8%, respectively, and the lower and upper bounds of the 99% confidence interval were -9.2% and 5.6%, respectively. The secondary analyses were consistent with and supportive of the primary outcome. There were no drug-related serious adverse events in the trial. The most commonly reported drug-related adverse events for eravacycline were gastrointestinal, including nausea (3.3%) and emesis (2.2%). This adverse event profile for eravacycline was consistent with that seen in the phase 2 clinical trial of eravacycline in cIAI. The spectrum of pathogens in this trial was similar to that seen in other pivotal trials of antibiotics in this patient population. The most common Gram-negative pathogens in the trial included Escherichia coli, Klebsiella pneumonia, Pseudomonas and Bacteroides.

cUTI

Our initial phase 3 clinical trial of eravacycline for the treatment of patients with cUTI was our IGNITE2 trial. Our IGNITE2 trial was designed to evaluate the safety and efficacy of eravacycline with IV-to-oral transition therapy. Following the failure of eravacycline to meet the primary endpoint of IGNITE2, and based on discussions with the FDA, we determined to conduct our IGNITE3 phase 3 clinical trial evaluating the IV formulation of eravacycline in patients with cUTI and to continue our development program for an oral formulation of eravacycline. If IGNITE3 is successful, we plan to use the results from IGNITE3 to support submission of an sNDA, for IV eravacycline for the treatment of cUTI, assuming approval first of IV eravacycline for the treatment of cIAI.

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IGNITE3

Eravacycline Phase 3 IGNITE3 Study Design

In January 2017, we initiated dosing in IGNITE3, a phase 3 randomized, double-blind, double-dummy, multi-center, prospective study that is designed to assess the efficacy, safety and pharmacokinetics of once-daily IV eravacycline (1.5mg/kg every 24 hours) compared to ertapenem (1g every 24 hours), the control therapy in this trial, for the treatment of cUTI. The study is expected to enroll approximately 1,000 adult patients. Patients will be randomized 1:1 to receive eravacycline or ertapenem for a minimum of 5 days, and will then be eligible for transition to an approved oral agent. The co-primary endpoints of responder rate (a combination of clinical cure and microbiological success) in the micro-ITT population at the end-of-IV treatment visit and at the TOC visit (Day 5-10 post therapy) will be evaluated using a 10% non-inferiority margin.

IGNITE2

Eravacycline Phase 3 IGNITE2 Study Design

In the first quarter of 2014, we initiated a two-part, multi-center, randomized, double-blind phase 3 clinical trial, our IGNITE2 trial, to assess the efficacy and safety of eravacycline compared with levofloxacin in the treatment of cUTI. We enrolled 143 patients in the lead-in portion of the trial. These patients were randomized into three arms on a 1:1:1 basis: an arm in which patients received 1.5 mg/kg IV eravacycline every 24 hours followed by 200 mg of eravacycline orally every 12 hours; an arm in which patients received 1.5 mg/kg IV eravacycline every 24 hours followed by 250 mg of eravacycline orally every 12 hours; and an arm in which patients received 750 mg IV levofloxacin every 24 hours followed by 750 mg of levofloxacin orally every 24 hours.

After treatment was completed in the lead-in portion of the trial, we evaluated efficacy, safety and tolerability endpoints to determine the dose regimen for eravacycline to be studied in the pivotal portion of the trial. In the lead-in portion of IGNITE2 both IV-to-oral dosing regimens of eravacycline compared favorably to levofloxacin. The responder outcome, the primary endpoint for the FDA, is determined as the number of micro-ITT patients at the PT visit with both clinical cure and microbiological success. Clinical cure is measured by a complete or significant improvement in signs or symptoms and microbiological success is demonstrated if the baseline pathogen is cleared or reduced below a specified level in a urine sample. The responder rates in the micro-ITT population for the IV-to-oral 200 mg, IV-to-oral 250 mg and levofloxacin groups were 70.8% (n=24), 64.3% (n=28) and 52.2% (n=23), respectively. The microbiological response rates in the micro-ITT population were 75.0% (n=24), 64.3% (n=28) and 56.5% (n=23), respectively. The pharmacokinetics of both oral doses of eravacycline were comparable to the IV formulation in the trial. Overall, treatment was generally well tolerated in all three groups with the most common adverse events reported being nausea and emesis. Only two patients discontinued treatment as a result of drug related adverse events. In October 2014, we selected the 1.5 mg/kg IV followed by 200 mg oral dose as the IV-to-oral transition therapy to be evaluated in the pivotal portion of the trial and initiated patient enrollment.

We enrolled 908 patients in the pivotal portion of the trial. These patients were randomized on a 1:1 basis to receive 1.5 mg/kg IV eravacycline every 24 hours followed by 200 mg of eravacycline orally every 12 hours or 750 mg IV levofloxacin every 24 hours followed by 750 mg of levofloxacin orally every 24 hours. In both treatment arms, subjects received a minimum of three days of IV therapy and then, if clinically indicated, were eligible to transition to oral therapy for the remaining doses for a total treatment period of 7 days. We designed the pivotal portion of the trial as a non-inferiority study in compliance with both FDA and EMA guidance. Under FDA guidance, the primary endpoint of the pivotal portion of the trial was clinical and microbiological response in the micro-ITT population at the PT visit. Under EMA guidance, the primary endpoint of the pivotal portion of the trial was microbiological response in the micro-MITT and ME populations. The micro-MITT population consisted of any patient who received study drug who had baseline bacterial pathogens that cause cUTI and against which eravacycline has antibacterial activity. The ME population consisted of all micro-ITT patients who met key inclusion/exclusion criteria and followed other important components of the trial. In order to achieve the primary endpoint under both FDA and EMA guidance, eravacycline would have needed to demonstrate non-inferiority as compared to levofloxacin within a margin of no more than 10%. A key secondary endpoint in IGNITE2 was to test for

superiority of eravacycline over levofloxacin in the treatment of cUTI for those subjects with infections caused by quinolone-resistant pathogens by evaluation of clinical and microbiological response in the micro-ITT population at the PT visit.

In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin in IGNITE2 for the treatment of cUTI under the guidance set by the FDA. The primary analysis under the FDA guidance was conducted using a 10% non-inferiority margin in the micro-ITT population. In the micro-ITT population, the lower and upper bounds of the 95% confidence interval were -14.1% and 1.2%, respectively.

Eravacycline did show superiority to levofloxacin in patients with quinolone-resistant pathogens, a secondary endpoint of the trial. In patients with quinolone-resistant pathogens, the responder rate was 17.3% higher in the eravacycline arm than in the levofloxacin arm. The lower and upper bounds of the 95% confidence intervals were 2.1% and 31.8% respectively. In addition, results of a post hoc multivariate analysis of the study data showed that longer IV treatment with eravacycline resulted in improved responder rates relative to levofloxacin. For subjects who received only IV study drug, the responder rate was 12.2% higher in the eravacycline arm than in the levofloxacin arm. The lower and upper bounds of the 95% confidence interval were -5.7% and 29.3%. In this analysis the lower bound is above -10. There were no drug-related serious adverse events in the trial.

Previous clinical trial of eravacycline

Phase 2 clinical trial of IV formulation in cIAI

In June 2012, we completed a global, multi-center, randomized, double-blind phase 2 clinical trial to evaluate the efficacy, safety and pharmacokinetics of the IV formulation of eravacycline compared to ertapenem in patients with cIAI. We selected cIAI as the indication for the trial because we wanted to ensure that there would be a significant population of patients in the study with multidrug-resistant Gram-negative bacteria and because Gram-negative bacteria are prevalent in cIAI. We selected ertapenem as the comparison therapy because ertapenem is one of the antibiotics recommended by IDSA guidelines for the treatment of cIAI. We also established clinical sites in countries such as India, where multidrug-resistant Gram-negative pathogens have higher prevalence.

Trial Design. We enrolled 143 hospitalized patients with cIAI in the trial. These patients were randomized into three arms on a 2:2:1 basis: an arm in which patients received 1.5 mg/kg IV eravacycline administered once per day; an arm in which patients received 1.0 mg/kg IV eravacycline administered twice per day; and a control arm in which patients received 1.0 g IV ertapenem administered once per day, which is the standard dosing regimen for ertapenem.

Investigators obtained baseline intra-abdominal cultures at the time of operation and treated patients for a minimum of four days and a maximum of 14 days. The length of treatment for each patient was determined by the physician based on pre-set parameters. A TOC visit took place ten to 14 days after the last dose of drug was administered and a final or follow-up visit occurred within four to six weeks after the last dose of drug was administered.

Patient Disposition. Of the 143 patients in the trial, four did not receive drug. Two were excluded because of incorrect randomization, one withdrew consent for inclusion in the trial after randomization, and one was excluded for having received non-study antibiotics prior to the first dose. At least one pathogen or bacterium responsible for the cIAI was identified following enrollment in 119 of the 139 patients who received drug in the trial. We refer to this subset of patients as the microbiologically-modified intent-to-treat, or micro-MITT, patients. Of the 119 micro-MITT patients, 109 were deemed clinically evaluable based on key inclusion and exclusion criteria being validated and key visits and

assessments having been performed. We refer to this subset of the micro-MITT patients as the microbiologically evaluable, or ME, patients. The 10 micro-MITT patients that were not considered clinically evaluable were not classified as ME patients as a result of their withdrawing consent, failing to complete the trial, failing to attend a TOC visit or having indeterminate results at the TOC visit. The primary endpoint of the trial was clinical response at the TOC visit in the ME patients. Clinical response was defined as complete resolution or significant improvement of signs or symptoms of infection with no further systemic antibiotic treatment required. Clinical response was also included as one of the secondary endpoints in the trial at the follow-up visit in the micro-MITT population.

Patient Demographics. Patient demographics were similar across all three trial arms except for APACHE scores as, at baseline, the patients in the 1.5 mg/kg dose group exhibited slightly higher APACHE scores than the other treatment groups. APACHE scores are a commonly used severity of disease scoring system, where a higher number means that the patient had more severe disease and higher risk of death. In the majority of the MITT patient population, complicated appendicitis was the diagnosed disease underlying the infections, which were being treated with the antibiotics in the trial. Other diseases including perforation of intestine, complicated diverticulitis, gastric/duodenal perforation and complicated cholecystitis, comprised the other diagnoses.

Efficacy. In the trial, ME patients in the eravacycline arms experienced similar infection cure rates to the ME patients in the ertapenem arm, as summarized in the table below. The table also shows the 95% confidence interval, a statistical determination that

demonstrates the range of possible differences in the point estimates of success that will arise 95% of the time the endpoint is measured.

Eravacycline Phase 2 Trial Primary Endpoint Analysis

Population	Eravacycline (1.5 mg/kg every 24 hours)	Eravacycline (1.0 mg/kg every 12 hours)	Ertapenem (1.0 g Every 24 hours)
Microbiologically Evaluable (ME)	N=42	N=41	N=26
% Cure in ME (95% Confidence Interval)	92.9 (80.5-98.5)	100 (91.4-100)	92.3 (74.9-99.1)

Investigators in the trial had the discretion to determine the period that patients remained on the applicable treatment. The mean duration of treatment in the trial was 6.1 days for the patients receiving 1.5 mg/kg IV eravacycline administered once per day; 5.6 days for the patients receiving 1.0 mg/kg IV eravacycline administered twice per day; and 6.0 days for the patients receiving 1.0 g IV ertapenem administered once per day.

The figure below shows the overall pathogen mix identified in the phase 2 cIAI clinical trial. Of the pathogens isolated from the micro-MITT patients enrolled in the phase 2 clinical trial, approximately 60% were members of the Enterobacteriaceae family. Micro-MITT patients in the trial were infected with an average of 1.8 pathogens. The Gram-negative aerobic pathogens occurring most frequently were Escherichia coli, Klebsiella pneumonia, Klebsiella oxytoca, Pseudomonas aeruginosa, Acinetobacter baumannii complex and Morganella morganii. The Gram-positive aerobic pathogens occurring most frequently were Streptococcus spp., Enterococcus faecalis and Staphylococcus aureus. The anaerobic pathogens occurring most frequently were Bacteroides fragilis and Clostridium spp.

Of particular importance in the trial results was the performance of eravacycline against confirmed drug-resistant Gram-negative pathogens as well as other challenging Gram-negative pathogens. Due to the global, multi-center nature of the trial and our emphasis on sites in known geographic “hot spots” for multidrug-resistant Gram-negative bacteria, 25% of the Gram-negative pathogens identified in micro-MITT patients were confirmed to be multidrug-resistant as a result of being ESBL-positive and/or carbapenem-resistant. The figure below shows that the patients cured with eravacycline in the phase 2 cIAI clinical trial had 23 confirmed multidrug-resistant Gram-negative pathogens.

Safety and Tolerability. In the phase 2 clinical trial, eravacycline demonstrated a comparable safety and tolerability profile to ertapenem. No patients in the trial suffered any serious adverse events that were found to be related to eravacycline, and the percentage of patients in the trial arms that experienced treatment emergent adverse events, or TEAEs, were similar. In addition, gastrointestinal adverse events known to be associated with tetracyclines such as nausea and emesis, occurred at low rates in the eravacycline arms that were similar to the rates for the ertapenem arm. Adverse events associated with infusion sites were limited and similar in all treatment groups.

Pharmacokinetics. Patients in the phase 2 clinical trial were subjected to pharmacokinetic sampling during the period of treatment to enable us to assess plasma exposure levels of eravacycline in the trial. The mean area under the curve, or AUC, was 4,349.9 ng*h/mL (50% CV) for the 1.5 mg/kg dose of eravacycline administered every 24 hours (n=48) and 3,240.7 ng*h/mL (53.5% CV) for the 1.0 mg/kg dose of eravacycline administered every 12 hours (n=51). The C_{max}, which refers to the maximum observed peak plasma concentration, was 1,445.6 ng/mL (80.8% CV) for the 1.5 mg/kg dose of eravacycline administered every 24 hours and 952.6 ng/mL (79.8% CV) for the 1.0 mg/kg dose of eravacycline administered every 12 hours.

Efficacy for tetracycline-class molecules is driven by the ratio of AUC to MIC. MIC refers to minimum inhibitory concentration, which is the minimum concentration of an antibiotic needed to inhibit the growth of an organism. In the phase 2 clinical trial, we measured AUC for the 12 hours following dosing. As a result, in order to understand the AUC of the dose groups we studied in the trial over the 24 hours following dosing, we relied on modeling to predict the AUC of eravacycline in differing dose sizes and schedules over the 24 hours following dosing. We believe that these estimated AUCs for eravacycline are supportive of eravacycline’s potential to treat multidrug-resistant Gram-negative and other bacteria.

Phase 1 clinical trials of IV formulation

We studied the IV formulation of eravacycline in several phase 1 clinical trials in a total of 140 healthy volunteers and at doses ranging from 0.1 mg/kg to 3.0 mg/kg. No serious adverse events were reported during the phase 1 clinical trials and no clinically significant dose-related safety signals were reported. As expected in this class of antibiotics, transient gastrointestinal adverse events such as nausea and emesis were observed at the higher dose levels in the phase 1 clinical trials. Additionally, pharmacokinetic data demonstrates that eravacycline achieves high concentration levels in the blood and urine.

Phase 1 clinical trials of oral formulation

In order to assess the potential for eravacycline to be developed as an orally administered drug, we conducted a phase 1 single ascending dose clinical trial in 2010, a phase 1 multiple ascending dose clinical trial in 2011 and a second phase 1 multiple ascending dose clinical trial in 2013. In each of these trials, we evaluated the compound for safety, tolerability and pharmacokinetics. In these trials the oral formulation of eravacycline achieved drug levels equivalent to those in the patients that received IV infusions of 1.5 mg/kg of eravacycline once per day in our phase 2 cIAI clinical trial. As part of the phase 1 clinical trials, we evaluated the impact of food and fasting on the absorption of orally administered eravacycline and observed a significant food effect. As a result, we focused our development efforts on patients in a fasted state.

Across the phase 1 studies of the oral formulation, the most common adverse events reported were nausea and emesis. Doses up to 300 mg once daily were well tolerated with all adverse events mild to moderate in intensity. A single daily dose of 400 mg was not tolerated due to gastrointestinal-related adverse events.

In the second phase 1 multiple ascending dose clinical trial, oral doses of 200 mg and 250 mg provided twice-daily were well tolerated. The Day 7 mean AUC was 4520 ng*h/mL (43% CV) for the 200 mg twice-daily dose of eravacycline and 6200 ng*h/mL

(17% CV) for the 250 mg twice-daily dose of eravacycline. The C_{max} was 261 ng/mL (47% CV) for the 200 mg twice-daily dose of eravacycline and 398 ng/mL (14% CV) for the 250 mg twice-daily dose of eravacycline.

We continue to develop an oral dose formulation of eravacycline. A phase 1 clinical program is ongoing which is designed to evaluate and optimize the oral dosing regimen for eravacycline. During the second quarter of 2016, we completed preliminary clinical testing which indicates that the overall efficacy results in IGNITE2 were driven by lower systemic exposures after oral dosing due to a food effect. Preliminary clinical testing also suggests that administration of oral eravacycline in a fasted state results in increased drug exposure. Further clinical testing is now underway to evaluate several additional variables associated with optimizing the oral eravacycline dosing regimen. We expect to provide an update with top-line findings from this testing and potential next steps in the development of oral eravacycline during the third quarter of 2017.

Preclinical Studies

In preclinical studies, we have evaluated the in vitro activity of eravacycline against a broad range of bacterial pathogens including Gram-negative, Gram-positive, atypical and anaerobic pathogens. In these studies, we also compared the potency of eravacycline to the potency of other antibiotic compounds against the same pathogens. In many cases, the isolates measured were resistant to one or more of the antibiotic compounds against which eravacycline was compared. In each case, we measured potency by determining the concentration of drug required to inhibit the growth of 90% of a panel of bacterial strains isolated from patients. We refer to this measurement as a MIC_{90} measurement. A lower MIC_{90} indicates greater potency against a particular bacterium in vitro. Historically, with tetracyclines, MIC_{90} values of up to 2 μg/mL have indicated that Gram-positive bacteria were susceptible to tetracyclines and for most Gram-negative bacteria up to 4 μg/mL. Traditionally, bacteria considered resistant to an antibiotic have MIC_{90} values for Gram-positive bacteria of 8 μg/mL and for Gram-negative bacteria of 16 μg/mL and higher.

In Vitro Activity Against Gram-negative Bacteria

The figure below summarizes the in vitro activity of eravacycline and various antibiotics commonly used in hospitals today for the treatment of Gram-negative bacteria in panels that included 3,840 Gram-negative clinical isolates collected in 2014 and 2015. In each panel, isolates of a single species of bacteria were separately treated with each of the antibiotics in the study. The number specified in the figure below for each species of bacteria indicates the number of isolates of that species that were included in the studies. The bacteria selected for evaluation were chosen because they are commonly found in serious hospital infections.

As shown in the figure, eravacycline demonstrated potent activity against Gram-negative bacteria. In the majority of instances, the MIC_{90} of eravacycline was equivalent to or lower than the MIC_{90} values of the other antibiotics studied for each bacterium. Key observations from these in vitro studies include:

- Eravacycline had MIC_{90} values of ≤1 µg/mL against clinical isolates of E. coli, K. pneumoniae, and K. oxytoca including ESBL-producing isolates; E. cloacae and C. freundii.
- Eravacycline was twice as potent as the next most active comparator, tigecycline, against A. baumannii with an MIC_{90} values of ≤2 µg/mL in a panel that was 65% resistant to carbapenems, 73% resistant to fluoroquinolones and 4% resistant to colistin.
- Eravacycline was eight times more potent than tigecycline against ESBL-producing K. pneumoniae isolates.
- 83%, 29%, and 43% of the isolates were fully resistant to fluoroquinolones, carbapenems and gentamicin, respectively.
- P. aeruginosa isolates were largely not susceptible to eravacycline (MIC_{90} of 16 µg/mL) or tigecycline (MIC_{90} in excess of 16 µg/mL) [data not shown].

The figure below further demonstrates the potent activity of eravacycline against Gram-negative bacteria, including multidrug-resistant Gram-negative pathogens, in comparison to commonly used antibiotic treatments. This surveillance study was conducted using over 4,000 patient bacterial isolates collected in New York City from November 2013 through January 2014, and was published in the Antimicrobial Agents and Chemotherapy Journal in December 2014.

In Vitro Activity Against Gram-positive Bacteria

The figure below summarizes the in vitro activity of eravacycline and various antibiotics commonly used in hospitals today for the treatment of Gram-positive bacteria in panels that included 3,180 Gram-positive clinical isolates collected in 2014 and 2015. The bacteria selected for evaluation were chosen because they are commonly found in serious hospital infections.

Eravacycline demonstrated excellent in vitro potency against methicillin-susceptible and resistant Staphylococcus aureus and Staphylococcus epidermidis, vancomycin-susceptible and resistant Enterococcus faecium and Enterococcus faecalis, penicillin-susceptible and -resistant Streptococcus pneumoniae, Streptococcus anginosus, Streptococcus intermedius, Streptococcus mitis, Streptococcus sanguis, Streptococcus pyogenes, and Streptococcus agalactiae. The MIC_{90} values for eravacycline against all of the streptococci and enterococci in the panels were less than 0.12 μg/mL. For staphylococci, including MRSA confirmed to contain Panton-Valentine leukocidin virulence factor, the MIC_{90} values were less than 0.5 μg/mL in 464 MRSA isolates tested.

In Vitro Activity Against Anaerobic Bacteria

The figure below summarizes the in vitro activity of eravacycline and various antibiotics commonly used in hospitals today for the treatment of anaerobic bacteria in panels that included 422 anaerobic clinical isolates collected in 2014 and 2015. The bacteria selected for evaluation were chosen because they are commonly found in serious hospital infections.

Key observations from these in vitro studies include that eravacycline:

- had a MIC_{90} against B. fragilis, the most prevalent anaerobe in human infections, of 1 μg/mL, which was four times lower than tigecycline;
- had excellent activity against a wide range of anaerobes important in cIAI
- provided broader coverage than the other antibiotics tested in the panel.

In addition, in the studies, many of the isolates from the Bacteroides, Prevotella and Clostridium perfringens species were vancomycin-resistant, and many of the isolates of the Peptostreptococcus spp. and C. perfringens species were metronidazole-resistant. Eravacycline showed strong activity against these isolates, including the mcr-1 gene.

Other Indications

We have received funding for our lead product candidate, eravacycline, under an award from BARDA. In January 2012, BARDA awarded to CUBRC a five-year contract that provided a total of up to $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline as a potential empiric countermeasure for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including Francisella tularensis, which causes tularemia, Yersinia pestis, which causes plague, and Bacillus anthracis, which causes anthrax disease, as well as bacterial pathogens associated with moderate-to-severe community-acquired bacterial pneumonia and other serious hospital infections. The funding under the BARDA Contract is also being used for certain activities in the development of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria. Under this program, we have conducted a number of in vitro, toxicology and animal studies to evaluate the efficacy of eravacycline against biothreat pathogens. Eravacycline has performed as well as, or better than, standard-of-care comparators in studies in murine respiratory infection models challenged with public health pathogens. In addition we have also completed a phase 1 clinical trial assessing the bronchial pulmonary disposition, safety and tolerability of eravacycline, the first clinical assessment of its potential use for treating pneumonia. In connection with the BARDA Contract, in February 2012, we entered

into with CUBRC a cost-plus-fixed-fee subcontract under which we can receive funding of up to $41.6 million to fund specific work performed by us related to eravacycline. The term of the subcontract runs through May 10, 2018.

Although the BARDA Contract, and our subcontract with CUBRC under the BARDA Contract, have terms running through May 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from Congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is $41.6 million from the initial contract date through May 10, 2018, of which $32.4 million had been received through December 31, 2016.

Technology Platform

We believe that our proprietary chemistry technology, licensed from Harvard on an exclusive worldwide basis and enhanced at our company, represents a significant innovation in the creation of tetracycline drugs and has the potential to reinvigorate the clinical and market potential of the class.

The tetracycline class of antibiotics has been used successfully for more than 50 years. Unlike our tetracycline compounds, all tetracyclines on the market and under development of which we are aware are produced semi-synthetically, first in bacteria and then modified in a limited number of ways by available chemistry. These conventional methods have only been able to produce tetracycline antibiotics with limited chemical diversity, making it difficult for conventional technology to create tetracycline antibiotics that address a wide variety of multidrug-resistant bacteria. In part, because of the challenges in creating novel tetracycline molecules, only one tetracycline antibiotic has been developed and approved by the FDA for sale in the United States in the past 30 years.

By contrast, our proprietary technology makes it possible to create novel tetracycline antibiotics using a practical, fully synthetic process for what we believe is the first time. This fully synthetic process avoids the limitations of bacterially derived tetracyclines and allows us to chemically modify many positions in the tetracycline scaffold, including most of the positions that we believe could not practically be modified by any previous method. Using our proprietary chemistry technology, we can create a wider variety of tetracycline-based compounds than was previously possible, enabling us to pursue novel tetracycline derivatives for the treatment of multidrug-resistant bacteria that are resistant to existing tetracyclines and other classes of antibiotic products.

The diagram below illustrates the tetracycline core scaffold. Scaffold positions marked with dots have been modified to date using conventional chemistry to create either tetracycline drugs that have been marketed or drug candidates of which we are aware that are currently in development. Our fully synthetic process also allows for modification of the positions marked with dots, but with greater opportunity for substitution than is possible using conventional chemistry. The scaffold positions marked with stars in the diagram below indicate useful positions that we have modified through our fully synthetic process that could not practically be modified by conventional chemistry.

While the four positions on the bottom of the scaffold in the diagram above that are not marked with dots or stars can also be modified using our proprietary chemistry technology, these positions are involved in the binding of tetracyclines to the bacterial ribosome and, consequently, changes to these positions greatly reduce antibacterial activity of compounds. As a result, we are not pursuing compounds based on modifications of these positions.

We believe that our approach to tetracycline drug development provides us with strong intellectual property protection. We hold or have licensed rights under patents and patent applications that protect both our synthetic processes for developing tetracyclines and the compositions of matter of the individual compounds themselves. These include patents and patent applications directed towards the composition of matter for key intermediates like the enone used in the synthesis of eravacycline and our other product candidates. Unless a new synthetic method is created, we believe that, for the life of our intellectual property, our proprietary chemistry technology will be the only practical way of modifying the positions on the tetracycline core scaffold that have not been previously modified using conventional chemistry.

Our proprietary chemistry technology has allowed us to develop compounds that have been highly active in in vitro studies against tetracycline-resistant bacterial strains, including multidrug-resistant Gram-negative bacteria, and that have novel pharmacokinetic properties. To date, we have used our proprietary chemistry technology to create more than 3,000 new tetracycline derivatives that we believe could not be practically created with conventional methods. Our discovery program is focused on identifying novel compounds that will be effective against the toughest multidrug-resistant Gram-negative bacteria.

A number of potential tetracycline uses in non-antibiotic therapeutic areas, including oncology and inflammatory diseases, have been reported in the scientific literature. Until now, these opportunities could not be fully exploited because of limited synthetic access and availability of analogs. With our tetracycline chemistry expertise and our extensive tetracycline library, we are uniquely positioned to explore serious conditions beyond bacterial infections.

Drug Development Programs

The following table sets forth our clinical and earlier-stage antibiotic compounds that we are developing for the treatment of serious and life-threatening infections and their status.

Candidate	Indication	Status
Eravacycline	cIAI (IV)	Phase 3 IGNITE1 study completed; met primary end point
		Phase 3 IGNITE4 study initiated October 2016
	cUTI (IV/oral)	Phase 3 IGNITE2 study completed; did not meet primary end point
		Phase 1 clinical trials ongoing for oral formulation
	cUTI (IV)	Phase 3 IGNITE3 study initiated January 2017
	Pneumonia (IV)	Phase 1 completed
TP-271	Bacterial biothreats	Phase 1 clinical trials ongoing
TP-6076	Multidrug-resistant Gram-negative infections	Phase 1 clinical trials ongoing

TP-271

TP-271 is a fully synthetic broad-spectrum preclinical compound that we are developing for respiratory diseases caused by bacterial biothreat pathogens under funding provided by NIAID. We are collaborating with CUBRC on the TP-271 program funded by NIAID.

We created TP-271 using our proprietary chemistry technology. In doing so, we made modifications to the tetracycline scaffold that were designed to improve potency and effectiveness against a broader spectrum of bacteria as compared to tetracycline and doxycycline, which are currently used for the treatment of pneumonia and other

respiratory ailments.

In our development program for TP-271, we have conducted a number of in vitro, toxicology and animal studies to evaluate the efficacy of TP-271 against biothreat pathogens. TP-271 has performed as well as, or better than, standard-of-care comparators in studies in murine respiratory infection models challenged with public health pathogens. In susceptibility studies, TP-271 also demonstrated broad-spectrum activity against NIAID Category A and B public health bacterial pathogens including Francisella tularensis, Yersinia pestis, Burkholderia mallei, Burkholderia pseudomallei, Bacillus anthracis, and NIAID Category C public health bacterial pathogens (in vitro and in vivo) that are associated with CABP, including Streptococcus pneumoniae, including multidrug-resistant pneumococci, Staphylococcus aureus (methicillin-susceptible and methicillin-resistant), Haemophilus influenzae, Moraxella catarrhalis and Legionella pneumophila, including strains that are tetracycline-resistant. In January 2016, we initiated a phase 1 clinical trial of the IV formulation of TP-271. This trial is a randomized, double-blind, placebo-controlled, single-ascending-dose study in up to 56 healthy volunteers.

Funding for TP-271 is covered by two awards from NIAID. The first award is a grant awarded to CUBRC in July 2011 that provides up to approximately $2.9 million in funding, which we refer to as the NIAID Grant. The second award is a contract awarded to CUBRC in September 2011 that provides up to approximately $35.8 million in funding. The NIAID Grant and the NIAID Contract

each support the development, manufacturing and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including Francisella tularensis, Yersinia pestis and Bacillus anthracis, as well as bacterial pathogens associated with community-acquired bacterial pneumonia.

In connection with the NIAID Contract, in October 2011, we entered into a cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $15.1 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities. In connection with the NIAID Grant, in November 2011, CUBRC awarded us a subaward of approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to us for our activities.

Although the NIAID Contract, the NIAID Grant and our subcontract with CUBRC under the NIAID Contract have terms which currently expire on December 31, 2018, and our subaward under the NIAID Grant has a term which currently expires on May 31, 2017, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond December 31, 2018. To the extent that NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. As of December 31, 2016, committed funding from CUBRC under the our subcontract with respect to the NIAID Contract is $15.1 million, of which $10.4 million had been received through December 31, 2016. Committed funding from CUBRC under our subaward with respect to the NIAID Grant is $0.9 million, of which $0.8 million had been received through December 31, 2016.

Second-generation Gram-negative Program

We are using our proprietary chemistry technology to pursue the discovery and development of tetracycline-derived compounds effective against the most urgent multidrug-resistant Gram-negative bacterial health threats identified by the CDC, in a September 2013 report. Pathogens targeted include carbapenem-resistant variants of Klebsiella pneumoniae, Acinetobacter baumanni, Escherichia coli and Pseudomonas aeruginosa. We have generated compounds that have demonstrated potent activity against a broad range of these multidrug-resistant Gram-negative pathogens. We identified TP-6076, a fully synthetic fluorocycline, as a lead candidate from these compounds to target unmet medical needs, including multidrug-resistant Gram-negative bacteria, and in July 2016, we initiated a phase 1 clinical trial of the IV formulation of TP-6076 in healthy volunteers.

Commercialization Strategy

Our commercialization strategy is to develop our product candidates into leading therapies that will be available worldwide for the treatment of serious multidrug-resistant infections. We have retained worldwide commercial rights to all of our product candidates. We intend to retain control over the commercial execution of each of our product candidates in the United States.

We are currently developing our lead product candidate, eravacycline, as an IV and oral antibiotic for use as a first-line empiric monotherapy for the treatment of serious and life-threatening infections, including a wide variety of multidrug-resistant infections. Assuming the successful completion of clinical trials and receipt of regulatory approvals, we intend to directly commercialize eravacycline in the United States. We currently have limited marketing capabilities and no sales or distribution capabilities. We intend to build a commercial organization in the United States and recruit experienced marketing, sales and medical education professionals and to develop a commercial strategy to target institutions with the greatest use of drugs for multidrug-resistant serious and life-threatening infections. We expect that our sales force will focus on educating hospital and institution-based physicians, nurses, pharmacy directors and payers about the benefits of eravacycline for the product’s approved indications.

Manufacturing and Supply

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. All of our product candidates are organic compounds of low molecular weight, commonly referred to as small molecules. They are manufactured in a fully synthetic process from readily available starting materials.

We currently rely on a limited number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our product candidates after they are approved. 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. We currently employ internal resources to manage our manufacturing.

Intellectual Property

We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our product candidates and compositions, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will significantly depend on our ability to obtain and maintain patent and other proprietary protection for commercially important technology and inventions and know-how related to our business, defend and enforce our patents, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and continuing technological innovation to develop and maintain our proprietary position.

As of February 21, 2017, we owned eight U.S. patents, 21 foreign patents, eight pending U.S. patent applications, two pending applications filed under the Patent Cooperation Treaty, or PCT, and 67 pending foreign patent applications in Europe and 20 other jurisdictions. The PCT is an international patent law treaty that provides a unified procedure for filing a single initial patent application for an invention simultaneously in each of the member states. Although a PCT application is not itself examined and cannot issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications. In addition we have exclusively licensed from Harvard University rights under ten U.S. patents, 26 foreign patents, two pending U.S. patent applications and 14 pending foreign patent applications in Europe and ten other jurisdictions. Certain of our patents and patent applications are directed to the composition of matter and/or use of eravacycline and applications are pending in the United States, Europe, Japan and other countries.

Tetraphase-Owned Intellectual Property Relating to Eravacycline and Other Compounds Under Development

We have patent applications directed to the composition of matter and/or use of eravacycline and other fluorocyclines, such as TP-271, pending in the United States, Europe, Japan and other countries. Patents specific to pharmaceutical compositions and/or use of eravacycline have been granted in the United States, Europe, Australia, China, Colombia, Japan, Mexico, New Zealand, Hong Kong, Taiwan, Israel and Singapore. The granted patents have an expiration date of August 7, 2029, and any patents that may issue from the pending applications will also have an expiration date of August 7, 2029, absent any term extensions or adjustments that may be available. The term of one of the U.S. patents has received 508 days of patent term adjustment under the America Invents Act.

We have also filed patent applications directed to the composition of matter and use of various derivatives of tetracycline and pentacycline (a tetracycline scaffold extended to five rings) in the United States, Europe and other foreign countries. Any patents that might issue from these pending applications will have an expiration date no earlier than 2030, with some expiration dates as late as 2033.

Exclusively Licensed Intellectual Property Relating to Our Proprietary Chemistry Technology

The patents and patent applications that we exclusively license from Harvard provide patent protection for the proprietary chemistry technology used in our fully synthetic process to make eravacycline and other tetracycline derivatives. The key intermediates that enable our fully synthetic process are commonly referred to as enone intermediates. The licensed patents and patent applications are directed towards the composition of matter of enone intermediates and compounds used to make the enone intermediates, referred to as key precursors, as well as synthetic routes to those enone intermediates, precursors and our tetracycline derivatives under development.

Composition of matter for the enone intermediates and precursors used in preparing the enone intermediates, and methods of making the precursors and enone intermediates are covered by the U.S. patents we license from Harvard, which will expire no earlier than 2027, taking into consideration patent term adjustment. Corresponding patent applications have been filed in foreign jurisdictions and any patents that have issued and might issue from these applications expire or will expire no earlier than 2025.

Exclusively Licensed Intellectual Property Relating to Pentacycline and Tetracycline Derivatives

Our license from Harvard also includes patent applications directed to the composition of matter and use of other novel tetracycline or pentacycline derivatives. These applications are pending in the United States, Europe and other countries. Any patents that might issue from these pending applications will have an expiration date no earlier than 2027.

Patent Term and Patent Term Extensions

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

Trademark Applications Relating to the Company Name and Logo

As of February 1, 2017 we had eight intent-to-use trademark applications at the United States Patent and Trademark Office relating to the Company Name, the Company Logo, combinations thereof, design marks relating to eravacycline and potential commercial names of eravacycline.

Trade Secrets

We rely, in some circumstances, on trade secrets to protect our unpatented technology. However, trade secrets can be difficult to protect. We seek to protect our trade secrets and proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached. We may not have adequate remedies for any breach and could lose our trade secrets through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions.

License Agreement

On August 3, 2006, we entered into a license agreement with The President and Fellows of Harvard College, under which Harvard granted us an exclusive worldwide license under specified Harvard patent rights to develop and commercialize tetracycline-based products such as eravacycline. Under the license agreement, we also have the right to expand the patent rights subject to the license to include improvement patents that may be owned by Harvard in the future and that meet specified criteria by paying to Harvard an additional license issuance fee in an amount to be agreed between Harvard and us. We also have a right of negotiation to expand the license to include additional patents relating to tetracycline chemistry within a specified category that may be owned by Harvard in the future, including patents covering inventions made by Andrew Myers, Ph.D., our scientific founder, under his consulting agreement with us. Since entering into the license agreement, we have entered into amendments to the license agreement pursuant to which we expanded the patent rights subject to the license in accordance with these rights. Under the license agreement, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts

to develop and commercialize licensed compounds and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. Our license grant from Harvard is subject to academic rights retained by Harvard and United States government rights and obligations that are customary in patent license agreements with universities in the United States.

In consideration for the rights granted to us by Harvard under the license agreement, as of December 31, 2016, we have paid Harvard an aggregate of $4.4 million in upfront license fees and development milestone payments, and issued 31,379 shares of our common stock to Harvard. In addition, we have agreed to make payments to Harvard upon the achievement of specified future development and regulatory milestones totaling up to $15.1 million for each licensed product candidate ($3.1 million of which has already been paid with respect to eravacycline), and to pay tiered royalties in the single digits based on annual worldwide net sales, if any, of licensed products by us, our affiliates and sublicensees. We are also obligated to pay Harvard a specified share of non-royalty sublicensing revenues that we receive from sublicensees for the grant of sublicenses under the license and to reimburse Harvard for specified patent prosecution and maintenance costs.

The license agreement expires on a licensed product-by-licensed product and country-by-country basis upon the expiration of the last-to-expire patent covering the applicable product in the applicable country that is included in the license. Harvard may terminate the license agreement based on our uncured material breach or insolvency or bankruptcy. We have the right to terminate the license agreement for any or no reason at any time on sixty (60) days prior written notice to Harvard.

Government Contracts

Eravacycline

We received funding for eravacycline under an award from BARDA. In January 2012, BARDA awarded a five-year contract that provided a total of up to $67.3 million in funding that BARDA awarded to CUBRC in January 2012. The contract contemplates that CUBRC will collaborate with us on the development, manufacturing and clinical evaluation of a novel tetracycline antibiotic with potential as an empiric countermeasure for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including Francisella tularensis, which causes tularemia, Yersinia pestis, which causes plague, and Bacillus anthracis, which causes anthrax disease, as well as bacterial pathogens associated with moderate-to-severe CABP and other serious hospital infections. The funding under the BARDA Contract is also being used for certain activities in the development of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria. In connection with the BARDA Contract, in February 2012, we entered into a cost-plus-fixed-fee subcontract with CUBRC under which we can receive up to $41.6 million to fund specific work performed by us related to eravacycline. The terms of the subcontract expire on May 10, 2018.

We collaborated with CUBRC in seeking government funding of this development program because we did not have any expertise in bidding for, or the administration and management of, government-funded contracts. Because CUBRC had the expertise to manage and administer awards issued by government funding agencies, we agreed with CUBRC that CUBRC would serve as the prime contractor under the BARDA Contract, primarily carrying out a program management and administrative role with additional responsibility for the management of certain preclinical studies. We serve as lead technical experts on all aspects of the BARDA Contract and serve as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. The flow of funds under this arrangement follows the respective activities being conducted by us and by CUBRC, with funds being paid to us under our subcontract with CUBRC reflecting payment for our activities.

We have agreed upon a research plan with CUBRC detailing the activities to be conducted by CUBRC and by us. In addition to our obligations to conduct the activities provided for by the research plan, we are also obligated under the CUBRC subcontract to satisfy various federal reporting requirements, extending to technical reporting with respect to our activities, reporting with respect to intellectual property and financial reporting.

Payments under our subcontract with CUBRC are made in installments as activities are conducted in accordance with the research plan. Payments are based on direct and indirect costs incurred plus fixed fees, where applicable.

Under the subcontract, CUBRC’s use of our eravacycline data is expressly limited to purposes of performing CUBRC’s obligations under the BARDA Contract, and CUBRC and its other subcontractors must assign to us, subject to government rights, all intellectual property rights relating to our compounds and related data that arise from the project. 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 government receives unlimited rights to use and disclose new data first produced under the project with BARDA funding, and the government is entitled to at least 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.

BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from Congressionally approved annual appropriations, and CUBRC has a right to terminate its subcontract with us only to the extent that BARDA first cancels the corresponding portions of CUBRC's prime contract.

We retain a right to terminate CUBRC's rights to use eravacycline. Permissible grounds for such termination of CUBRC's rights include but are not limited to the sale of our assets relating to the project, an acquisition of us or our granting an exclusive or partially exclusive license to use eravacycline to a licensee that declines to continue CUBRC's license rights. In such an event, the subcontract may be terminated upon CUBRC's negotiation of a corresponding termination of CUBRC's obligations to BARDA.

TP-271

Our program to develop TP-271 is funded by NIAID through the NIAID Grant, a grant awarded in July 2011 that provided up to approximately $2.9 million in funding, and the NIAID Contract, a separate agreement that provides up to $35.8 million in funding that

NIAID awarded to CUBRC in October 2011. The NIAID Contract and the NIAID Grant contemplate that CUBRC will collaborate with us on the development, manufacturing and clinical evaluation of a novel broad-spectrum tetracycline antibiotic for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including Francisella tularensis, Yersinia pestis and Bacillus anthracis, as well as bacterial pathogens associated with CABP.

In connection with the NIAID Contract, in October 2011, we entered into a subcontract with CUBRC under which we may receive funding of up to approximately $15.1 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities. The term of the NIAID subcontract now runs through December 31, 2018. In connection with the NIAID Grant, in November 2011, CUBRC awarded us a subaward of approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to us for our activities. The term of the sub-award under the NIAID grant now runs through May 31, 2017.

We collaborated with CUBRC in seeking government funding of this development program because we did not have any expertise in bidding for, or the administration and management of, government-funded contracts. Because CUBRC had the expertise to manage and administer awards issued by government funding agencies, we agreed with CUBRC that CUBRC would serve as the prime contractor under the NIAID Contract, primarily carrying out a program management and administrative role with additional responsibility for the management of certain preclinical studies. We serve as lead technical experts on all aspects of the NIAID Contract and serve as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. The flow of funds under this arrangement follows the respective activities being conducted by us and by CUBRC, with funds being paid to us under our subcontract with, and subaward from, CUBRC reflecting payment for our activities.

We have agreed upon a research plan with CUBRC detailing the activities to be conducted by CUBRC and by us. In addition to our obligations to conduct the activities provided for by the research plan, we are also obligated under the CUBRC subcontract to satisfy various federal reporting requirements, extending to technical reporting with respect to our activities, reporting with respect to intellectual property and financial reporting.

Payments under our subcontract with CUBRC are made in installments as activities are conducted in accordance with the research plan. Payments are based on direct and indirect costs incurred plus fixed fees, where applicable.

Under the subcontract, CUBRC’s use and disclosure of our proprietary data pertaining to the project are expressly subject to a separate confidentiality agreement between CUBRC and us. CUBRC and its other subcontractors or subawardees must assign to us, subject to government rights, all intellectual property rights relating to our compounds and related data that arise from the project. Under standard government contracting terms and grant conditions, the government is entitled to at least 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.

NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond May 31, 2017 in the case of the NIAID Grant, and December 31, 2018 in the case of the NIAID Contract, and CUBRC has a right to terminate its subcontract with, or subaward to, us only to the extent that NIAID first cancels the corresponding portions of CUBRC’s prime contract or award.

We retain rights to terminate the subcontract if CUBRC breaches the subcontract, subject in certain cases to CUBRC’s failure to cure such breach, or by written notice to CUBRC, effective upon CUBRC’s negotiation of a corresponding termination of CUBRC’s obligations to NIAID.

Research and Development Expenses

For the years ended December 31, 2016, 2015 and 2014, we incurred $63.8 million, $73.8 million, and $61.9 million, respectively, in expenses on research and development activities.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical companies and generic drug companies. Many of our potential competitors have greater financial, technical and human resources than we do, as well as greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our potential competitors may be more successful than us in obtaining FDA approval for drugs and achieving widespread market acceptance. We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates non-competitive or obsolete.

We believe the key competitive factors that will affect the development and commercial success of our most advanced product candidate, eravacycline, if approved, will be efficacy, coverage of drug-resistant strains of bacteria, safety and tolerability profile, reliability, convenience of dosing, including the capability for IV-to-oral transition therapy, price, availability of reimbursement from governmental and other third-party payers and susceptibility to drug resistance.

We are developing eravacycline as an IV and oral antibiotic for use as a first-line empiric monotherapy for the treatment of resistant and multidrug-resistant infections. If approved, eravacycline would compete with a number of currently marketed antibiotics, including meropenem, which is marketed by AstraZeneca as Merrem, imipenem/cilastatin, which is marketed by Merck & Co., or Merck, as Primaxin, tigecycline, which is marketed by Pfizer as Tygacil, piperacillin/tazobactam, which is marketed by Pfizer as Zosyn, ceftolozane/tazobactam, which is marketed by Merck as Zerbaxa, and ceftazidime/avibactam, which is marketed by Allergan, Inc. and AstraZeneca as Avycaz, as well as several antibiotics currently in phase 3 development. We also expect that eravacycline, if approved, would compete with future and current generic versions of marketed antibiotics.

If approved, we believe that eravacycline would compete effectively against these compounds on the basis of:

- broad range of activity against a wide variety of resistant and multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria;
- lower probability of drug resistance;
- a favorable safety and tolerability profile;
- a convenient dosing regimen;
- allows for monotherapy;
- potentially, convenient IV-to-oral transition therapy

Recent Changes in the Regulatory Landscape

The FDA's Division of Anti-Infective Products, or DAIP, has undergone evolution in recent years, primarily driven by concerns that increasingly less effective antibiotics may have been approved in the last 10 to 15 years and a desire to bring what DAIP perceives to be greater statistical rigor to their analyses. The impact of this was a rethinking of how antibiotic efficacy is measured in clinical trials, and a review of the statistical tools used to analyze the data. In February 2015, the FDA published guidance documents for industry entitled "Complicated Urinary Tract Infections: Developing Drugs for Treatment" and guidance entitled "Complicated Intra-Abdominal Infections: Developing Drugs for Treatment." The purpose of these guidance documents was to address considerations surrounding the clinical development of drugs for cUTI and cIAI indications, including clinical trial design and efficacy considerations.

On December 13, 2016, President Obama signed into law the 21st Centuries Cures Act, which builds on the FDA's ongoing efforts to advance medical product innovation. One key component of this Act is the Limited Population pathway, which is designed to help streamline the development programs for certain antibacterials intended to treat targeted groups of patients suffering from serious or life-threatening infections where unmet need exists due to lack of available therapies. Approvals of these antimicrobials are expected to rely on data primarily targeting these limited populations. The statement "Limited Population" will appear prominently next to the drug's name in labeling, which will provide notice to healthcare providers that the drug is indicated for use in a limited and specific population of patients. There is additional legislation pending in the U.S. Congress, including the DISARM Act, which would designate certain novel antibiotics used to treat serious bacterial infections to receive higher Medicare reimbursement, and an amendment to the GAIN Act, which would successful QIDP sponsors to transfer up to one year exclusivity to another product, including products marketed by other companies.

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, clinical trials, testing, manufacture, including any manufacturing changes, authorization, pharmacovigilance, adverse event reporting, recalls, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products and product candidates 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 applicable 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, or FDCA, and 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 and/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, or GLP, 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, or 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 practices, or GCP, 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 pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, 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. Preclinical tests intended for submission to the FDA to support the safety of a product candidate must be conducted in compliance with the FDA's Good Laboratory Practice (GLP) regulations and the United States Department of Agriculture's Animal Welfare Act. A drug 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.

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 along with the requirement to ensure that the data and results reported from the clinical trials are credible and accurate. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the criteria for determining subject eligibility, the dosing plan, the parameters to be used in monitoring safety, the procedure for timely reporting of adverse events, 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, or 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. During phase 1 clinical trials, sufficient information about the investigational drug's or biological product's

pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid phase 2 clinical trials.

Phase 2: The drug is administered to a larger, but still limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dosage tolerance and optimal dosage. Phase 2 clinical trials are typically well-controlled and closely monitored.

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. Phase 3 clinical trials usually involve a larger number of participants than a phase 2 clinical trial.

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. Results from one trial may not be predictive of results from subsequent trials. 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 special protocol assessment, or 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. Generally, the trial must have already been discussed with the relevant FDA review division at an end-of-phase 2/pre-phase 3 meeting to be eligible for SPA review. 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, or 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. Furthermore, the FDA is not required to

complete its review within the established ten-month timeframe and may extend the review process by issuing requests for additional information or clarification.

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.

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation. Our product candidates are not designated as orphan drugs.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to mitigate any identified or suspected serious risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and 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 is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. 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 will typically inspect one or more clinical trial sites to assure compliance with GCP.

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 GCPs 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 if 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. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted. The FDA granted eravacycline fast track designation as a QIDP in April 2014; granted fast track designation and as a QIDP for the IV formulation of TP-271 in September 2015 and for the oral formulation of TP-271 in February 2017. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

The FDA may give a priority review designation to drugs that offer major advances in treatment for a serious condition, or provide a treatment where no adequate therapy exists. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. 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.

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 receive accelerated approval, meaning that it may be approved on (1) 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 (2) on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. 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 new Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 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.

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 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.

The FDA strictly regulates the marketing, labeling, advertising and promotion of drug products that are placed on the market. A product cannot be commercially promoted before it is approved, and approved drugs may generally be promoted only for their approved indications. Promotional claims must also be consistent with the product's FDA-approved label, including claims related to safety and effectiveness. The FDA and other federal agencies also closely regulate the promotion of drugs in specific contexts such as direct-to-consumer advertising, industry-sponsored scientific and education activities, and promotional activities involving the Internet and social media.

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 of regulatory non-compliance include, among other things:

- restrictions on, or suspensions of, the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- interruption of production processes, including the shutdown of manufacturing facilities or production lines or the imposition of new manufacturing requirements;
- fines, warning letters or other enforcement 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.

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.

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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 eravacycline and our other product candidates are new chemical entities. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or 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, such as tetracycline, the statute imposes certain limitations on the award of non-patent exclusivity. However, we do not believe these limitations would apply to eravacycline or any of our other investigational antibiotics.

Qualified Infectious Disease Product Exclusivity

Under the GAIN provisions of FDASIA, which was signed into law in July 2012, the FDA may designate a product as a “qualified infectious disease product,” or QIDP. 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 obtained a QIDP designation for the IV formulation of eravacycline for cUTI and cIAI in July 2013, the oral formulation in March 2014, the IV formulation of TP-271 in September 2015, the oral formulation of TP-271 in February 2017, and expect to request QIDP designations for our other 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 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 addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the European Union, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product authorization, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicines, and optional for other medicines which are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency where it will be evaluated by the Committee for Medicinal Products for Human Use and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all European Union member states within 67 days of receipt of the opinion. The initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

Pharmaceutical Coverage and Reimbursement

Sales of our products will depend, in part, on the availability and extent of coverage and reimbursement by third-party payors, such as government health programs, including Medicare and Medicaid, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the price and limiting the coverage and reimbursement amounts for medical products and services.

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement, and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

In the U.S., the federal government provides health insurance for people who are 65 or older, and certain people with disabilities or certain conditions irrespective of their age, through the Medicare program, which is administered by the Centers for Medicare & Medicaid Services, or CMS. Coverage and reimbursement for products and services under Medicare are determined in accordance with the Social Security Act and pursuant to regulations promulgated by CMS, as well as the agency's subregulatory coverage and reimbursement guidance and determinations.

Medicaid is a health insurance program for low-income children, families, pregnant women, and people with disabilities that is jointly funded by the federal and state governments, but administered by the states. In general, state Medicaid programs are required to cover drugs and biologicals of manufacturers that have entered into a Medicaid Drug Rebate Agreement, although such drugs and biologicals may be subject to prior authorization or other utilization controls.

The U.S. Congress and state legislatures from time to time propose and adopt initiatives aimed at cost containment, which could impact our ability to sell our products profitably. Recently, a number of legislative reform measures have been passed to contain healthcare reimbursement for pharmaceuticals, including drugs such as our product candidates.

For example, the federal Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, known collectively as ACA, among other things, establishes annual fees to be paid by manufacturers for certain branded prescription drugs, requires manufacturers to participate in a discount program for certain outpatient drugs under Medicare Part D, increases manufacturer rebate liabilities under the Medicaid Drug Rebate Program for outpatient drugs dispensed to Medicaid recipients, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are line extensions of current drugs, and expands oversight and support for the federal government's comparative effectiveness research of services and products. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. We cannot predict the full impact of ACA or future reform measures on our operations.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the EU, the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC, or the Price Transparency Directive. The aim of this Directive is to ensure that pricing and reimbursement mechanisms established in the EU Member States are transparent and objective, do not hinder the free movement of and trade in medicinal products in the EU, and do not hinder, prevent or

distort competition on the market. The Price Transparency Directive does not provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual EU Member States, nor does it have any direct consequence for pricing or reimbursement levels in individual EU Member States. The EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices and/or reimbursement levels of medicinal products for human use. An EU Member State may approve a specific price or level of reimbursement for the medicinal product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the medicinal product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including the United Kingdom, France, Germany, Ireland, Italy and Sweden. The HTA process in the EU Member States is governed by the national laws of these countries. HTA is the procedure according to which the assessment of the public health impact, therapeutic impact, and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally focuses on the clinical efficacy and effectiveness, safety, cost, and cost-effectiveness of individual medicinal products as well as their potential implications for the healthcare system. Those elements of medicinal products are compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product vary between EU Member States. A negative HTA of one of our products by a leading and recognized HTA body, such as the National Institute for Health and Care Excellence in the United Kingdom, could not only undermine our ability to obtain reimbursement for such product in the EU Member State in which such negative assessment was issued, but also in other EU Member States. For example, EU Member States that have not yet developed HTA mechanisms could rely to some extent on the HTA performed in countries with a developed HTA framework, such as the United Kingdom, when adopting decisions concerning the pricing and reimbursement of a specific medicinal product.

Other Healthcare Laws

Although we currently do not have any products on the market, if our drug candidates are approved and we begin commercialization, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security and physician sunshine laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

Legal Proceedings

In January 2016 and March 2016, two securities class action lawsuits were filed against us, our chief executive officer, our former chief operating officer and our former chief financial officer in the United States District Court for the District of Massachusetts. In May 2016, the court consolidated the two lawsuits and appointed lead plaintiffs and lead counsel. The lead plaintiffs filed a consolidated amended complaint in July 2016 and filed a second consolidated amended complaint in August 2016. The second amended complaint is brought on behalf of an alleged class of those who purchased our common stock between March 5, 2015 and September 8, 2015, and alleges claims arising under Sections 10 and 20 of the Securities Exchange Act of 1934, as amended. The complaint generally alleges that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions

concerning IGNITE2. The complaint seeks, among other relief, unspecified compensatory damages, attorneys' fees, and costs. In October 2016, defendants filed a motion to dismiss the second amended complaint in its entirety, which plaintiffs have opposed. That motion is pending. We believe we have valid defenses against these claims, and will engage in a vigorous defense of such litigation.

In addition, in May 2016, Donald Britton filed a shareholder derivative complaint against our chief executive officer; our former chief operating officer; our former chief financial officer; all the members of our current board of directors; a former board member; and against Tetraphase as nominal defendant, in Massachusetts Superior Court (Suffolk County). The complaint generally alleges that the individual defendants breached fiduciary duties owed to Tetraphase and its shareholders by disseminating materially false and misleading statements to the market concerning IGNITE2. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets, and seeks to recover on behalf of the Company for any liability the Company incurs as a result of the individual defendants' alleged misconduct. The complaint seeks declaratory, equitable and monetary relief, an unspecified amount of damages, with interest, and

attorney's fees and costs. In August 2016, this action was dismissed by the Massachusetts Superior Court without prejudice due to plaintiff's failure to perfect service of process in a timely manner.

In management's opinion, it is not possible to predict the final outcome of these proceedings, nor is any potential liability estimable at this time.

Employees

As of March 10, 2017, we had 66 full-time employees, 47 of whom were primarily engaged in research and development activities. A total of 21 employees have an M.D. or Ph.D. degree. None of our employees is represented by a labor union and we consider our employee relations to be good.

Available Information

We file reports and other information with the Securities and Exchange Commission as required by the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. You can find, copy and inspect information we file at the SEC's Public Reference Room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549, on official business days during the hours of 10:00 a.m. to 3:00 p.m. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's Public Reference Room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov.

We were incorporated under the laws of the State of Delaware on July 7, 2006 as Tetraphase Pharmaceuticals, Inc. Our principal executive offices are located at 480 Arsenal Way, Watertown, Massachusetts, 02472, and our telephone number is (617) 715-3600. Our Internet website is http://www.tphase.com. We make available free of charge through our website our Annual Report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. In addition, we regularly use our website to post information regarding our business, product development programs and governance, and we encourage investors to use our website, particularly the information in the section entitled "Investor Relations," as a source of information about us.

The foregoing references to our website are not intended to, nor shall they be deemed to, incorporate information on our website into this annual report on Form 10-K by reference.

Item 1A. Risk Factors

Our business faces many risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this annual report on Form 10-K and other filings with the SEC, press releases, communications with investors and oral statements. The risks described below may not be the only risks we face. Additional risks we do not yet know of or which we currently believe are immaterial may also impair our business operations. If any of the events or circumstances described in the following risks actually occurs, our business, financial condition or results of operations could suffer and the trading price of our common stock could decline.

Risks Relating to Our Financial Position and Need for Additional Capital

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

We have incurred annual net operating losses in every year since our inception. Our net loss was $77.5 million for the year ended December 31, 2016, $83.2 million for the year ended December 31, 2015 and $66.7 million for the year ended December 31, 2014. As of December 31, 2016, we had an accumulated deficit of $347.1 million. We have not generated any product revenues and have financed our operations primarily through the public offering and private placements of our equity securities, debt financings and revenue from U.S. government grants and contract awards. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development.

We expect to continue to incur significant expenses and operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect that our expenses will increase in 2017 compared to 2016 as we commence and conduct our IGNITE3 and IGNITE4 trials, conduct pre-commercialization and launch-related activities for eravacycline, seek marketing approval for eravacycline, conduct additional manufacturing process activities related to eravacycline, manufacture drug product for our clinical trials, advance our other product candidates and satisfy our obligations under our license agreement with Harvard University, or Harvard. If we obtain marketing approval of eravacycline or any other product candidate, we also expect to incur significant sales, marketing, and distribution and outsourced manufacturing expenses, as well as ongoing research and development expenses. Our expenses also will increase if and as we:

- maintain, expand and protect our intellectual property portfolio;
- in-license or acquire other products and technologies;
- hire additional development personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we obtain marketing approval for, and commercialize, eravacycline, which will require us to be successful in a range of challenging activities, including:

- commencing, conducting and successfully completing IGNITE3 and IGNITE4;
- applying for and obtaining marketing approval for eravacycline;
- protecting and maintaining our rights to our intellectual property portfolio related to eravacycline;
- contracting for the manufacture of commercial quantities of eravacycline; and
- establishing sales, marketing and distribution capabilities to effectively market and sell eravacycline.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Our expenses could increase if we are required by the U.S. Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, to perform clinical trials and non-clinical studies in addition to those that are currently being conducted or are currently expected, or if there are any delays in completing our clinical trials, the development of any of our product candidates or the manufacture of any of our product candidates.

We may be unable to develop and commercialize eravacycline or any other product candidate and, even if we do, may never achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, expand our business or continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investment in us.

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

Developing pharmaceutical products, including conducting preclinical studies, clinical trials and manufacturing activities, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase in 2017 compared to 2016 for a number of reasons, including, but not limited to, costs associated with our IGNITE3 and IGNITE4 clinical trials, and conducting pre-commercialization and launch-related activities for eravacycline. If we obtain marketing approval for eravacycline or any other product candidate that we develop, we also expect to incur significant sales, marketing, distribution and outsourced manufacturing expenses, as well as ongoing research and development expenses.

We believe that our available funds will be sufficient to support our operations into the second half of 2018, which we believe would allow us to obtain results from IGNITE4 and submit a new drug application, or NDA, for IV eravacycline for the treatment of cIAI. We do not believe these funds will be sufficient, however, to enable us to commercially launch eravacycline, complete IGNITE3 or submit a supplemental new drug application, or sNDA, for IV eravacycline for the treatment of cUTI. It is also possible that we will not achieve the progress that we expect with respect to eravacycline because the actual costs and timing of clinical development activities are difficult to predict and are subject to substantial risks and delays. As a result, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

These estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to spend more money than currently expected because of circumstances beyond our control.

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.

Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the timing, design and costs of IGNITE3 and IGNITE4;
- the timing and costs of our ongoing clinical trials for our other product candidates;
- the timing and costs of manufacturing activities related to regulatory filings and anticipated commercial launch;
- the amount of funding that we receive under our subcontracts awarded to us by our collaborator CUBRC, Inc., or CUBRC, under its government contracts with the Biomedical Advanced Research and Development Authority, or BARDA, and with the National Institutes of Health's, or NIH's, National Institute of Allergy and Infectious Diseases, or NIAID, and under our subaward from CUBRC under its grant from NIAID, and the activities funded under these contracts;
- the number and characteristics of product candidates that we pursue;
- the timing and costs of developing eravacycline for additional indications;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for eravacycline and other product candidates if we receive marketing approval, including the timing and costs of establishing product sales, marketing, distribution and manufacturing capabilities;
- revenue received from commercial sales of eravacycline, subject to receipt of marketing approval;
- the terms and timing of any future collaborations, partnerships, licensing, marketing, distribution or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay to Harvard pursuant to our license agreement;
- the costs of maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

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

Currently, our only external source of funds is funding under subcontracts and a subaward awarded to us by CUBRC pursuant to government contracts from BARDA and NIAID and a grant from NIAID. Although the BARDA contract and our subcontract with CUBRC under the BARDA contract have terms which currently expire on May 10, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is up to $41.6 million from the initial contract date through May 10, 2018, of which $32.4 million had been received through December 31, 2016.

Similarly, although the NIAID contract and our subcontract with CUBRC under the NIAID contract have terms which currently expire on December 31, 2018, NIAID is entitled to terminate the project for convenience at any time, and is

not obligated to provide continued funding beyond December 31, 2018. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subcontract with respect to the NIAID contract is up to $15.1 million, of which $10.4 million had been received through December 31, 2016. In addition, although the NIAID grant has a term which currently expires on May 31, 2017 and our subaward from CUBRC has a term which currently expires on May 31, 2017, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond May 31, 2017. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to

cease providing funding to us. Committed funding from CUBRC under our subaward with respect to the NIAID grant is $0.9 million from the initial grant date through May 31, 2017, of which $0.8 million had been received through December 31, 2016.

As a result, unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings or collaborations and licensing arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interest of our stockholders may be materially diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect their rights. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific corporate actions, such as incurring additional debt, merging with or acquiring another entity, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or to grant licenses on terms that may not be favorable to us.

We have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We began operations in the third quarter of 2006. Our operations to date have been limited to financing and staffing our company, developing our technology and developing eravacycline and other product candidates. We have not yet demonstrated an ability to obtain marketing approval, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

Risks Related to Product Development and Commercialization

We are dependent on the success of our lead product candidate, eravacycline, and our ability to develop, obtain marketing approval for and successfully commercialize eravacycline. If we are unable to develop, obtain marketing approval for and successfully commercialize eravacycline or experience significant delays in doing so, our business could be materially harmed.

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of eravacycline for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections. In December 2014, we announced that eravacycline met the primary endpoint of statistical non-inferiority in IGNITE1, a phase 3 clinical trial evaluating the safety and efficacy of eravacycline with intravenous, or IV, administration for the treatment of complicated intra-abdominal infections, or cIAI, compared to ertapenem, an intravenously, or IV, administered antibiotic, the control therapy for this trial. In September 2015, we announced that eravacycline did not meet the primary endpoint of statistical non-inferiority in IGNITE2, a phase 3

clinical trial evaluating the safety and efficacy of eravacycline for the treatment of complicated urinary tract infection, or cUTI, with IV-to-oral transition therapy, compared to levofloxacin, an IV and orally administered antibiotic that was the control therapy for the trial. Consistent with guidance issued by the FDA with respect to the development of antibiotics for cIAI and our previous discussions with the FDA, we had planned to utilize results from these two phase 3 clinical trials to support submission of an NDA for eravacycline for the treatment of cIAI and cUTI.

Following the result of IGNITE2 and further discussion with the FDA, the FDA advised us that data from one additional positive phase 3 clinical trial would be required to support an NDA submission for IV eravacycline. We are conducting our IGNITE4 phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cIAI. If IGNITE4 is successful, we plan to use the results from IGNITE1 and IGNITE4 to support submission of an NDA for IV eravacycline for the treatment of cIAI. We are also conducting our IGNITE3 phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cUTI. If IGNITE3 is successful, we plan to use the results from IGNITE3 to support submission of an sNDA for IV eravacycline for the treatment of cUTI, assuming approval first of IV eravacycline for the treatment of cIAI.

In addition, we plan to submit a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI in the second half of 2017 on the basis of the results of IGNITE1.

Our prospects are substantially dependent on our ability to develop, obtain marketing approval for and successfully commercialize eravacycline. The success of eravacycline will depend on several factors, including the following:

- successful outcome of discussions with regulatory agencies regarding our planned marketing applications;
- successful completion and favorable results of IGNITE3 and IGNITE4, and any additional clinical trials involving eravacycline that we may conduct;
- successful manufacturing and validation of registration batches for regulatory filings for eravacycline;
- timely filing for and receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;
- obtainment and maintenance of patent and trade secret protection and regulatory exclusivity;
- protection of our rights in our intellectual property portfolio;
- successful manufacturing of commercial scale batches of eravacycline;
- commercial launch of eravacycline, if and when approved, whether alone or in collaboration with others;
- acceptance of eravacycline, if and when approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of eravacycline following approval.

Successful development of eravacycline for additional indications will be subject to these same risks.

If we are unable to develop, receive marketing approval for, or successfully commercialize eravacycline, or experience delays as a result of any of these matters or otherwise, our business could be materially harmed.

If clinical trials of eravacycline or of any other product candidate that we advance to clinical trials fail to demonstrate safety and efficacy to the satisfaction of the FDA or comparable foreign regulatory authorities or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of eravacycline or any other product candidate.

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. We must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted an NDA to the FDA, an MAA to the EMA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates.

The clinical development of eravacycline and other product candidates is susceptible to the risk of failure inherent at any stage of drug development, including failure to achieve efficacy in a trial or across a broad population of patients, the occurrence of severe adverse events, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a drug product is not approvable. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, although eravacycline achieved favorable results in the lead-in part of IGNITE2, the pivotal portion of IGNITE2 did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin. In October 2016, we initiated dosing in IGNITE4. In January 2017, we initiated IGNITE3. We may fail to achieve success in either or both of these phase 3 trials or any other future clinical trial of eravacycline or any other product candidate.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of our

clinical trials warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial

participants. For instance, the results of IGNITE1 may not be predictive of the results of IGNITE4 as we are using a different control therapy in IGNITE4 than we used in IGNITE1, and the results of the lead-in portion of IGNITE2 may not be predictive of the results of IGNITE3. In addition, in the case of our clinical trials, results may differ on the basis of the type of bacteria with which patients are infected. We cannot be certain that IGNITE4, IGNITE3, any phase 2, phase 3 or other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent us from obtaining regulatory approval for eravacycline or any of our other product candidates, including:

- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

If we are required to conduct additional clinical trials or other testing of eravacycline, either in an intravenous or oral dosage form, or any other product candidate that we develop beyond the trials and testing that we contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with eravacycline or our other product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- remove the product from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals and we may be required to obtain additional funds to complete clinical trials. We cannot be certain that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays

also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of eravacycline or any other product candidate.

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

We may not be able to initiate or continue clinical trials for eravacycline or any other product candidate that we develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials for eravacycline or such other product candidate as required by the FDA or comparable foreign regulatory authorities, such as the EMA. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial; and
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

The inclusion and exclusion criteria for IGNITE3 and IGNITE4 may adversely affect our enrollment rates for patients in these trials. In addition, many of our competitors also have ongoing clinical trials for product candidates that treat the same indications as eravacycline, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. 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 process and jeopardize our ability to commence product sales and generate revenues, which would cause the value of our company to decline and limit our ability to obtain additional financing if needed.

Serious adverse events or undesirable side effects or other unexpected properties of eravacycline or any other product candidate may be identified during development or after approval, if obtained, that could delay, prevent or cause the withdrawal of the product candidates' regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if obtained.

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board, 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 eravacycline 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. In our clinical trials of eravacycline, some treatment-related adverse events have been reported. The most common

treatment-related adverse events observed in clinical trials of eravacycline have been nausea and emesis. Additional adverse events, undesirable side effects or other unexpected properties of eravacycline 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, eravacycline or our other product candidates. If such an event occurs after eravacycline 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 postmarketing 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 revenues from the sale of our products and harm our business and results of operations.

Even if eravacycline or any other product candidate that we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success and the market opportunity for eravacycline or other product candidates may be smaller than we estimate.

We have never commercialized a product candidate for any indication. Even if eravacycline or any other product candidates that we develop are approved by the appropriate regulatory authorities for marketing and sale, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If physicians, rightly or wrongly, associate our product candidates with antibiotic resistance issues of other products of the same class, physicians might not prescribe our product candidates for treating a broad range of infections. If eravacycline or any other product candidate that we develop does not achieve an adequate level of market acceptance, we may not generate significant product revenues and, therefore, we may not become profitable. The degree of market acceptance of eravacycline, if approved, or any other product candidate that is approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved;
- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved risk evaluation and mitigation strategy;
- our ability to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments, including, in the case of eravacycline, the availability of the oral formulation that we are developing for use in intravenous-to-oral transition therapy;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- 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 strength of marketing and distribution support;
- the approval of other new products for the same indications;
- the timing of market introduction of our approved products as well as competitive products;
- the cost of treatment in relation to alternative treatments;
- availability and level of coverage and amount of reimbursement from government payors, managed care plans and other third-party payors;
- the effectiveness of our sales and marketing efforts;
    - adverse publicity about the product or favorable publicity about competitive products; and
- the development of resistance by bacterial strains to the product.

In addition, the potential market opportunity for eravacycline is difficult to estimate. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment

on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, then the actual market for eravacycline could be smaller than our estimates of the potential market opportunity. If the actual market for eravacycline is smaller than we expect, or if the product fails to achieve an adequate level of acceptance by physicians, health care payors and patients, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing eravacycline or such other product candidates that we develop if and when eravacycline or any other product candidates are approved.

We do not have a sales, marketing or distribution infrastructure and as a company have little experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We intend to develop and build a commercial organization in the United States and recruit experienced sales, marketing and distribution professionals, which will require substantial resources, will be time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we intend to target. If we are unable to establish a sales force and marketing and distribution capabilities, our operating results may be adversely affected.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the ability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

We plan to commercialize eravacycline outside the United States with the assistance of collaborators. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us may be lower than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to eravacycline and our other product candidates that we may seek to develop or commercialize in the future. There

are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of multidrug-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 or less costly than any product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete or noncompetitive.

There are a variety of available therapies marketed for the treatment of resistant or even multidrug-resistant infections that we would expect would compete with eravacycline, including ceftazidime/avibactam, which is marketed by Allergan, Inc. as Avycaz; meropenem, which is marketed by AstraZeneca as Merrem; ceftolozane/tazobactam, imipenem/cilastatin, and ertapenem which are marketed by Merck & Co., Inc. as Zerbaxa, Primaxin and Invanz, respectively; tigecycline, which is marketed by Pfizer, Inc. as Tygacil; and piperacillin/tazobactam, which is marketed by Pfizer, Inc. as Zosyn. 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 eravacycline is approved, it may be priced at a significant premium over other competitive products. This may make it difficult for eravacycline to compete with these products.

There are also a number of products currently in phase 3 development by third parties to treat multidrug-resistant infections, including meropenem/vaborbactam, which is being developed by The Medicines Company as Carbavance, plazomicin, which is being developed by Achaogen, Inc., imipenem/relebactam, which is being developed by Merck & Co., Inc., and cefiderocol, which is being developed by Shionogi. Some of these companies may obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market.

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

In July 2012, the Food and Drug Administration Safety and Innovation Act was passed, which included the GAIN Act. The GAIN Act is intended to provide incentives for the development of new, qualified infectious disease products. These incentives may result in more competition in the market for new antibiotics, and may cause pharmaceutical and biotechnology companies with more resources than we have to shift their efforts towards the development of products that could be competitive with eravacycline and our other product candidates.

Even if we are able to commercialize eravacycline or any other product candidate that we develop, the product may become subject to unfavorable pricing regulations, third-party payor coverage and reimbursement policies or healthcare reform initiatives that could harm our business.

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

Our ability to commercialize eravacycline or any other product candidate will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government authorities, private health insurers, health maintenance organizations and other third-party payors. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. As a result, government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell our product candidates profitably.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical

outcomes of new technologies and are challenging the prices charged. Moreover, obtaining coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based in part on existing reimbursement amounts for lower cost drugs or may be bundled into the payments for other services.

We cannot be sure that coverage will be available for eravacycline or any other product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we commercially sell eravacycline or any other product candidate that we develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

Although we maintain general liability insurance of $6 million in the aggregate and clinical trial liability insurance of $6 million in the aggregate for all product candidates, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we begin selling eravacycline or any other product candidate that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could adversely affect our business, financial condition, results of operations and prospects.

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

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

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

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

Our research and development efforts may not result in additional drug candidates being discovered on anticipated timelines, which could limit our ability to generate revenues.

Some of our research and development programs are at preclinical stages. Additional drug candidates that we may develop or acquire will require significant commitment of resources. We cannot predict whether our research will lead to the discovery and development of any additional drug candidates that could generate revenues for us.

Risks Related to Our Dependence on Third Parties

We expect to depend on collaborations with third parties for the development and commercialization of some of our product candidates. Our prospects with respect to those product candidates will depend in part on the success of those collaborations.

Although we expect to commercialize eravacycline ourselves in the United States, we intend to seek to commercialize eravacycline outside the United States through collaboration arrangements. In addition, we may seek third-party collaborators for development and commercialization of other product candidates. Our likely collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangements.

We may derive revenue from research and development fees, license fees, milestone payments and royalties under any collaborative arrangement into which we enter. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, our collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms. As a result, we can expect to relinquish some or all of the control over the future success of a product candidate that we license to a third party.

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or in compliance with applicable regulatory requirements;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product

candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

We may have to alter our development and commercialization plans if we are not able to establish collaborations.

We will require additional funds to complete the development and potential commercialization of eravacycline and our other product candidates. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we intend to utilize a variety of types of collaboration arrangements for commercialization of eravacycline outside the United States. Our ability to enter into any such collaboration may be significantly delayed, or the terms on which we enter into collaborations may be adversely affected, due to the unfavorable results of IGNITE2 or if the results from one or both IGNITE3 or IGNITE4 are unfavorable.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

- the design or results of clinical trials;
- the likelihood of approval by the FDA or comparable foreign regulatory authorities;
- the potential market for the subject product candidate;
- the costs and complexities of manufacturing and delivering such product candidate to patients;
- the potential for competing products;
- our patent position protecting the product candidate, including any uncertainty with respect to our ownership of our technology or our licensor's ownership of technology we license from them, which can exist if there is a challenge to such ownership without regard to the merits of the challenge;
- the need to seek licenses or sub-licenses to third-party intellectual property; and
- industry and market conditions generally.

The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to 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 fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and our business may be materially and adversely affected.

We rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business may be materially harmed.

We do not independently conduct clinical trials of eravacycline. We rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as

current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

We contract with third parties for the manufacture of eravacycline for clinical trials and expect to continue to do so in connection with the commercialization of eravacycline and for clinical trials and commercialization of any other product candidates that we develop. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not currently have nor do we plan to build the internal infrastructure or capability to manufacture eravacycline or our other product candidates for use in the conduct of our clinical trials or for commercial supply. We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture clinical supplies of eravacycline and our other product candidates, and we expect to rely on third-party contract manufacturers to manufacture registration batches and commercial quantities of any product candidate that we commercialize following approval for marketing by applicable regulatory authorities. Reliance on third-party manufacturers entails risks, including:

- delays in the manufacture of our clinical drug supply, registration and validation batches and commercial supply if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- equipment malfunctions, power outages or other general disruptions experienced by our third-party manufacturers to their respective operations and other general problems with a multi-step manufacturing process;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;

- the possible breach of the manufacturing agreement by the third-party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We currently rely on a small number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationships for the manufacture of commercial supplies of any of our other product candidates. If any of our existing manufacturers should become unavailable to us for any reason, we may incur some delay in identifying or qualifying replacements.

If any of our product candidates are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may

face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be inspected by the FDA after we submit an NDA and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate as alternative qualified manufacturing facilities may not be available on a timely basis or at all. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us or the contract manufacturer, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse impact on our business, financial condition and results of operations.

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

If we fail to comply with our obligations in the agreements under which we in-license or acquire development or commercialization rights to products or technology from third parties, we could lose commercial rights that are important to our business.

We are a party to a license agreement with Harvard that imposes, and we may enter into additional agreements, including license agreements, with other parties in the future that impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. For instance, under our license agreement with Harvard, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize licensed compounds and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. If we fail to comply with these obligations, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by these agreements, which could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

Our reliance on government funding for certain of our programs adds uncertainty to our research and commercialization efforts with respect to those programs.

Our development of eravacycline for the treatment of disease caused by bacterial biothreat pathogens and certain life-threatening multidrug-resistant bacteria is currently being partially funded through a subcontract with funding from BARDA. In addition, our development of TP-271 is being funded through a subcontract and grant subaward

from the NIH's NIAID division. Contracts and grants funded by the U.S. government and its agencies, including our agreements funded by BARDA and NIAID, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including, but not limited to 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;
- suspend the contractor or grantee 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;

- control and potentially prohibit the export of products;
- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

We may not have the right to prohibit the U.S. government from using 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 takes the position that it has the right to royalty-free use of technologies that are developed under U.S. government contracts.

In addition, government contracts and grants, and subcontracts and subawards awarded in the performance of those contracts and grants, 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.

As an organization, we are relatively new to government contracting and new to the regulatory compliance obligations that such contracting entails. If we fail to maintain compliance with those obligations, we may be subject to potential liability and to termination of our contracts.

Risks Related to Our Intellectual Property

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

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 proprietary chemistry technology and product candidates. 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. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. The patent application and approval process is expensive and time consuming. 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.

Under our license agreement with Harvard, Harvard retains the right to prosecute and maintain specified Harvard patents and patent applications in the field of tetracycline chemistry, which are exclusively licensed to us under the agreement. Moreover, if we license technology or product candidates from third parties in the future, those licensors may retain the right to prosecute, maintain and enforce the patent rights that they license to us with or without our involvement. Because control of prosecution and maintenance rests with Harvard, and prosecution, maintenance and enforcement could rest with future licensors, we cannot be certain that these in-licensed patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If Harvard fails to prosecute or maintain, or future licensors fail to prosecute, maintain or enforce, those patents necessary for any of our product candidates, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making and selling competing products.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the

United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings which may be brought by us related to our patent rights.

Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

As a result of the America Invents Act of 2011, the United States transitioned to a first-inventor-to-file system in March 2013, under which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. However, as a result of the lag in the publication of patent applications following filing in the United States, we are not able to be certain upon filing that we are the first to file for patent protection for any invention. Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, inter partes review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting Abbreviated New Drug Applications to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

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

Competitors may infringe our patents, trademarks, copyrights or other intellectual property, or those of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent’s claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we

have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. 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 litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

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.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our proprietary chemistry technology without infringing the intellectual property and other proprietary rights of third parties. Numerous third-party U.S. and non-U.S. issued patents and pending applications exist in the area of antibacterial treatment, including

compounds, formulations, treatment methods and synthetic processes that may be applied towards the synthesis of antibiotics. If any of their patents or patent applications cover our product candidates or technologies, we may not be free to manufacture or market our product candidates as planned. We are aware of a third-party U.S. patent claiming pharmaceutical compositions of tetracyclines. The third-party U.S. patent could be asserted against us with respect to eravacycline. We believe we have defenses in the event that the third party seeks to assert such patent against us, including the invalidity of the relevant claims of such patent. However, we may not be successful in asserting these defenses, including proving invalidity, and could be found to infringe the third party's patent, which would have a material adverse effect on us.

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 patent infringement litigation with respect to the third-party U.S. patent referred to above, and eravacycline. Other possible adversarial proceedings include interference proceedings before the U.S. Patent and Trademark Office. 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 invalidity 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, such as the third-party U.S. patent referred to above, we could be ordered by a court, to cease developing, manufacturing, using, selling or offering for sale the infringing product. Alternatively, we may conclude that we need to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product or 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. 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 subject to claims that we or our employees have misappropriated the intellectual property of a third-party, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the intellectual property and other proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed such intellectual property or other proprietary information. Litigation may be necessary to defend against these claims.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Moreover, because we have licensed intellectual property from Harvard, we must rely on Harvard's practices with regard to the assignment of intellectual property to it. To the extent we or Harvard have failed to obtain such assignments or such assignments are breached, we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and scientific personnel.

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 seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, in seeking to develop and maintain a competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our consultants, independent contractors, advisors, corporate collaborators, outside scientific collaborators, contract manufacturers, suppliers and other third parties. We, as well as our licensors, also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we or Harvard have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third-party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

We have not yet completed registration of our trademarks. Failure to secure those registrations could adversely affect our business.

Four trademark applications for TETRAPHASE PHARMACEUTICALS, our logo, and combinations of those have been allowed in the United States, meaning that we can perfect our registrations when we have commenced use in commerce. TETRAPHASE PHARMACEUTICALS is registered in nine other jurisdictions and pending in four others. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. We have also completed registration of trademarks for eravacycline in two jurisdictions. While we have filed trademark applications for the proposed tradename of eravacycline in the U.S. and other jurisdictions, those applications are pending and may not be allowed for registration, and registered trademarks may not be obtained, maintained or enforced. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the United States Patent and Trademark Office and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. We have also obtained registration for our design work in two jurisdictions, and applications remain pending for those design marks in the United States and one other jurisdiction.

In addition, any proprietary name we propose to use with eravacycline or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize eravacycline or any other product candidate that we develop, and our ability to generate revenue will

be materially impaired.

Our product candidates, including eravacycline, and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, marketing, export, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable 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. We currently do not have any products approved for sale in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

We are not permitted to market our product candidates in the United States until we receive approval of an NDA from the FDA. We have not submitted an NDA for any of our product candidates. An NDA must include extensive preclinical and clinical data and supporting information to establish 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 approval of an NDA is a lengthy, expensive and uncertain process. The FDA review process typically takes years to complete. The FDA has substantial discretion in the approval process and may refuse to accept for filing any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies or additional information regarding chemistry, manufacturing and controls for the product candidate. For example, our progress in the development and commercialization of eravacycline has been significantly delayed as a result of the failure of eravacycline to achieve the primary endpoint in IGNITE2 and may be further delayed as a result of additional clinical outcomes, manufacturing process challenges or other unforeseeable causes. Foreign regulatory authorities have differing requirements for approval of drug candidates with which we must comply prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively impact our ability to obtain marketing approval in other jurisdictions. Delays in approvals or rejections of marketing applications in the United States or foreign countries may be based upon many factors, including regulatory requests for additional analyses, reports, data and studies, regulatory questions regarding, or different interpretations of, data and results, changes in regulatory policy during the period of product development and the emergence of new information regarding product candidates or related products. The FDA or equivalent foreign regulatory authorities may determine that eravacycline 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. The FDA may also find during its pre-approval inspection that the facilities identified in our NDA fail to comply with cGMP requirements, thereby delaying or preventing approval. 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. If we experience delays in obtaining approval or if we fail to obtain approval of eravacycline or any other product candidate that we develop, the commercial prospects for eravacycline or such other product candidate may be harmed and our ability to generate revenues will be materially impaired.

A fast track designation by the FDA does not guarantee approval and may not actually lead to a faster development, regulatory review or approval process.

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for that condition, the treatment sponsor may apply for FDA fast track designation. The FDA granted eravacycline fast track designation as a QIDP in April 2014 and granted fast track designation and as a QIDP for the IV formulation of TP-271 in September 2015, and the oral formulation of TP-271 in February 2017. Fast track designation does not ensure approval or a faster development, regulatory review or approval process compared to conventional FDA procedures. Additionally, 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 we are unable to obtain marketing approval in international jurisdictions, we will not be able to market our product candidates abroad.

In order to market and sell eravacycline and any other product candidate that we develop in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted

by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

If we receive regulatory approval for any product candidates, including eravacycline, we will be subject to ongoing obligations and continuing regulatory review, which may result in significant additional expense. Our product candidates, including eravacycline, if approved, could be subject to restrictions or withdrawal from the market, and we may be subject to penalties, if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if approved.

Any product candidate, including eravacycline, for which we obtain marketing approval, will also be subject to ongoing regulatory requirements for labeling, manufacturing, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. 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.

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. 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 a regulatory agency 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, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us. In addition, if any product fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning or untitled letters;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners and patients;
- impose restrictions on the product or its manufacturers or manufacturing processes;
- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require 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;
- suspend, vary, modify or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions, levy fines or impose other civil and/or criminal penalties.

Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Our future arrangements with third-party payors, healthcare professionals and customers who purchase, recommend or prescribe our product candidates will be subject to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. These laws and regulations include, for example, the false claims and anti-kickback statutes and regulations. At such time as we market, sell and distribute any products for which we obtain marketing approval, it is possible that our business activities could be subject to challenge under one or more of these laws and regulations. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federally funded healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, which can be enforced by private citizens through civil whistleblower and qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and creates federal criminal laws that prohibit knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, requires manufacturers of covered drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to implement compliance programs, comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or track and report gifts, compensation and other remuneration provided to physicians and other health care providers; and state and foreign laws that govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, which complicates compliance efforts.

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Even then, governmental authorities may conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Recent healthcare reform legislation has strengthened these federal and state healthcare laws. For example, the ACA amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or a specific intent to violate them. In addition, the ACA provides that the government may assert that a claim that includes 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. If governmental authorities find that our operations violate any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare

and Medicaid, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud and abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

If we successfully commercialize one of our drug candidates, failure to comply with our reporting and payment obligations under U.S. governmental pricing programs could have a material adverse effect on our business, financial condition and results of operations.

If we participate in the Medicaid Drug Rebate Program once we successfully commercialize a drug, we will be required to report certain pricing information for our products to the Centers for Medicare & Medicaid Services, the federal agency that

administers the Medicaid and Medicare programs. We may also be required to report pricing information to the Department of Veterans Affairs. If we become subject to these reporting requirements, we will be liable for errors associated with our submission of pricing data, for failure to report pricing data in a timely manner, and for overcharging government payers, which can result in civil monetary penalties under the Medicaid statute, the federal civil False Claims Act, and other laws and regulations.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access to healthcare. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals.

In March 2010, the ACA became law in the United States with the goals of broadening access to health insurance, reducing or constraining the growth of healthcare spending, enhancing remedies against fraud and abuse, adding new transparency requirements for health care and health insurance industries and imposing additional health policy reforms. Further, the new law includes annual fees to be paid by manufacturers for certain branded prescription drugs, requires manufacturers to participate in a discount program for certain outpatient drugs under Medicare Part D, increases manufacturer rebate responsibilities under the Medicaid Drug Rebate Program for outpatient drugs dispensed to Medicaid recipients, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for line extensions and for drugs that are inhaled, infused, instilled, implanted or injected and expands oversight and support for the federal government’s comparative effectiveness research of services and products.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 which 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 product candidates or additional pricing pressures.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of our executive management team, as well as the other principal members of our management, scientific and clinical team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. For instance, in December 2015, both our former chief financial officer and our former chief operating officer terminated their employment with us.

We do not have formal employment agreements with any of our other employees. If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and

biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize drug candidates will be limited.

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

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy.

The business that we conduct outside the United States may be adversely affected by international risk and uncertainties.

Although our operations are based in the United States, we conduct business outside the United States and expect to continue to do so in the future. For instance, many of the sites at which our clinical trials are or may be conducted are outside the United States. In addition, we plan to seek approvals to sell our products in foreign countries. Any business that we conduct outside the United States will be subject to additional risks that may materially adversely affect our ability to conduct business in international markets, including:

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

We are increasingly dependent on information technology systems, infrastructure and data security. Any attack on our systems, infrastructure or data security could cause serious harm to our business.

Data privacy, security breaches or service interruptions may pose a risk that sensitive data including intellectual property, trade secrets or personal information belonging to us or our business partners may be exposed to unauthorized persons or to the public. Cyber-attacks are growing in their frequency, sophistication and intensity. Our third-party vendors face similar risks and any security breach of their systems could adversely affect us. While we have not yet experienced cyber-attacks and intrusions into our information technology infrastructure, there can be no assurance that our efforts will prevent or detect future service interruptions or breaches in our systems. Any such future breach may adversely affect our business and operations.

Risks Related to Our Common Stock

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. For example, our stock traded within a range of a high price of $52.90 per share and a low price of $3.11 per share for the period beginning March 20, 2013, our first day of trading on the NASDAQ Global Select Market, through March 10, 2017. As a result of this volatility, investors may not be able to sell their common stock at or above the prices they paid for it. The market price for our common stock may be influenced by many factors, including:

- the timing of clinical trials of eravacycline and any other product candidate;
- results of clinical trials of eravacycline and any other product candidate;
- the filing and approval of marketing applications;
- regulatory actions by the FDA or equivalent authorities in foreign jurisdictions with respect to eravacycline and any other product candidate;
- failure or discontinuation of any of our development programs;
- the success of existing or new competitive products or technologies;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop, in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

We are currently subject to class action litigation and have been subject to shareholder derivative litigation due to stock price volatility, which could distract our management and could result in substantial costs or large judgments against us.

The stock market frequently experiences extreme price and volume fluctuations. In September 2015, we experienced a significant decline in our stock price based, in large part, on our announcement that the phase 3 clinical trial for eravacycline for the treatment of patients with cUTI did not meet the primary endpoint of statistical non-inferiority compared to levofloxacin. In addition, the market prices of securities of companies in the biotechnology and pharmaceutical industry have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. These fluctuations could adversely affect the market price of our common stock. In the past, securities class action litigation has often been brought against companies following periods of volatility in the market prices of their securities. In fact, in January 2016 and March 2016, two class action lawsuits were filed against us, our chief executive officer and certain former executives

in the United States District Court for the District of Massachusetts. In addition, in May 2016 a shareholder derivative action was filed against our chief executive officer, certain former executive officers, all the members of our current board of directors, a former board member, and

against Tetraphase as nominal defendant, in Massachusetts Superior Court (Suffolk County). This case was subsequently dismissed by the court without prejudice due to the plaintiff's failure to properly perfect service of process. Due to the volatility in our stock price, we may be the target of similar litigation in the future.

In connection with such litigation, we could incur substantial costs and such costs and any related settlements or judgments may not be covered by insurance. We could also suffer an adverse impact on our reputation and a diversion of management's attention and resources, which could cause serious harm to our business, operating results and financial condition.

An active trading market for our common stock may not be sustained.

Although we have listed our common stock on The NASDAQ Global Select Market, an active trading market for our common stock may not be sustained. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the price at which they acquired the common stock or at the times that they would like to sell. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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

The trading market for our common stock will depend on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. There can be no assurance that analysts will cover us, or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

We have broad discretion in the use of our cash reserves and may not use them effectively.

Our management has broad discretion to use our cash reserves and could spend these reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

We have incurred increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly especially since we are no longer an "emerging growth company", as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer able to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are "emerging growth companies" and that were applicable to us prior to January 1, 2016.

Failure to maintain effective internal controls in accordance with Section 404 of the Sarbanes-Oxley Act in the future could have a material adverse effect on our ability to produce accurate financial statements and on our stock price.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls. To maintain compliance with Section 404, we are required to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, continue to engage outside consultants and follow a detailed work plan to continue to assess and document the adequacy of internal control over financial reporting, continue to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that in the future neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future; accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation, development and growth of our business. The terms of our term loan facility with Silicon Valley Bank and Oxford Finance that we repaid precluded us from paying dividends, and any future debt agreements may also preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

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

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

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or by-laws.

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

ITEM 1B. Unresolved Staff Comments

None

ITEM 2. Properties

We lease our principal facilities, which consist of approximately 37,438 square feet of office, research and laboratory space located at 480 Arsenal Way, Watertown, Massachusetts. The leases covering this space expire on November 30, 2019. We believe that our existing facilities are sufficient for our current needs for the foreseeable future. In the third quarter of 2016, we entered into a sublease with respect to a portion of our principal facilities with an unrelated third party. The term of the sublease expires in November 2019.

ITEM 3. Legal Proceedings

In January 2016 and March 2016, two securities class action lawsuits were filed against us, our chief executive officer, our former chief operating officer and our former chief financial officer, in the United States District Court for the District of Massachusetts. In May 2016, the court consolidated the two lawsuits and appointed lead plaintiffs and lead counsel. The lead plaintiffs filed a consolidated amended complaint in July 2016 and filed a second consolidated amended complaint in August 2016. The second amended complaint is brought on behalf of an alleged class of those who purchased our common stock between March 5, 2015 and September 8, 2015, and alleges claims arising under Sections 10 and 20 of the Exchange Act of 1934, as amended. The complaint generally alleges that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning IGNITE2. The complaint seeks, among other relief, unspecified compensatory damages, attorneys' fees, and costs. In October 2016, we filed a motion to dismiss the second amended complaint in its entirety, which plaintiffs have opposed. That motion is pending. We believe we have valid defenses against these claims, and will engage in a vigorous defense of such litigation.

In addition, in May 2016, Donald Britton filed a shareholder derivative complaint against our chief executive officer, our former chief operating officer, our former chief financial officer, all the members of our current board of directors, a former board member, and against Tetraphase as nominal defendant, in Massachusetts Superior Court (Suffolk County). The complaint generally alleges that the individual defendants breached fiduciary duties owed to Tetraphase and its shareholders by disseminating materially false and misleading statements to the market concerning IGNITE2. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets, and seeks to recover on behalf of Tetraphase for any liability Tetraphase incurs as a result of the individual defendants' alleged misconduct. The complaint seeks declaratory, equitable and monetary relief, an unspecified amount of damages, with interest, and attorney's fees and costs. In August 2016, this action was dismissed by the Massachusetts Superior Court without prejudice due to plaintiff's failure to perfect service of process in a timely manner.

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 Securities

Market Price Information

Our common stock began trading on the NASDAQ Global Select Market on March 20, 2013 under the symbol "TTPH". Prior to that date, there was no established public trading market for our common stock. The following table sets forth, for the periods indicated, the high and low intraday sales prices of our common stock as reported by the NASDAQ Global Select Market:

	High	Low
2016		
First Quarter	$9.98	$3.48
Second Quarter	$6.28	$3.12
Third Quarter	$4.65	$3.62
Fourth Quarter	$5.12	$3.11

	High	Low
2015		
First Quarter	$44.55	$32.40
Second Quarter	$48.68	$34.68
Third Quarter	$52.90	$7.24
Fourth Quarter	$12.45	$7.20

Holders

At March 9, 2017, there were approximately 8 holders of record of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Dividends

We have never declared or paid any cash dividends on our common stock. We currently intend to retain earnings, if any, for use in our business and do not anticipate paying cash dividends on our common stock in the foreseeable future. Payment of future dividends, if any, on our common stock will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results, anticipated cash needs, and plans for expansion.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be set forth in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein.

Purchase of Equity Securities

We did not purchase any of our equity securities during the period covered by this Annual Report on Form 10-K.

Unregistered Sales of Equity Securities

We did not issue any unregistered securities during the period covered by this Annual Report on Form 10-K.

Comparative Stock Performance Graph

The information included under the heading “Comparative Stock Performance Graph” in this Item 5 of Part II of this annual report on Form 10-K shall not be deemed to be “soliciting material” or subject to Regulation 14A or 14C, shall not be deemed “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

Set forth below is a graph comparing the total cumulative returns of Tetraphase, the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes $100 was invested on March 20, 2013 in our common stock and each of the indices and that all dividends, if any, are reinvested.

	3/20/13	12/31/13	12/31/14	12/31/15	12/31/16
Tetraphase Pharmaceuticals	$100.00	$193.14	$567.29	$143.29	$143.29
NASDAQ Composite Index	$100.00	$128.34	$145.54	$153.88	$153.88
NASDAQ Biotechnology Index	$100.00	$145.52	$195.14	$217.42	$217.42

ITEM 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with our Consolidated Financial Statements and the Notes thereto and Management's Discussion and Analysis of Financial Condition and Results of Operations included elsewhere in this annual report on Form 10-K. The selected consolidated financial data in this section are not intended to replace our financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future.

The consolidated statement of operations data for each of the three years in the period ended December 31, 2016 and the consolidated balance sheet data at December 31, 2016 and 2015 have been derived from our audited consolidated financial statements

for such years, included elsewhere in this annual report on Form 10-K. The statement of operations data for the years ended December 31, 2013 and 2012 and the consolidated balance sheet data at December 31, 2014, 2013 and 2012 have been derived from the audited consolidated financial statements for such years not included in this annual report on Form 10-K.

Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
	(in thousands, except per share data)				
Statement of Operations data:					
Contract and grant revenue	$5,145	$11,686	$9,098	$10,486	$7,600
Operating expenses:					
Research and development	63,764	73,768	61,932	31,508	17,294
General and administrative	19,211	20,916	12,932	7,168	4,309
Total operating expenses	82,975	94,684	74,864	38,676	21,603
Loss from operations	(77,830)	(82,998)	(65,766)	(28,190)	(14,003)
Other income (expense):					
Interest income	350	42	17	10	-
Interest expense	-	(231)	(1,017)	(1,719)	(1,021)
Other income (expense)	-	(2)	24	263	(63)
Total other income (expense)	350	(191)	(976)	(1,446)	(1,084)
Net loss	$(77,480)	$(83,189)	$(66,742)	$(29,636)	$(15,087)
Net loss per share-basic and diluted	$(2.11)	$(2.36)	$(2.49)	$(1.78)	$(47.54)
Weighted-average number of common shares used in net loss per share-basic and diluted	36,704	35,261	26,807	16,665	317

	As of December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents	$142,086	$205,912	$121,042	$102,712	$9,079
Working capital	138,962	203,071	109,321	92,229	3,720
Total assets	151,710	214,917	127,204	105,886	14,072
Current liabilities	11,495	10,697	17,276	13,191	8,661
Long-term obligations	162	165	1,362	4,887	8,619
Convertible preferred stock	—	—	—	-	79,841
Accumulated deficit	(347,132)	(269,652)	(186,463)	(119,721)	(90,085)
Total stockholders' equity (deficit)	$140,053	$204,055	$108,566	$87,808	$(83,049)

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 our consolidated financial statements and related notes appearing in this annual report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this annual report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. 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 the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company using our proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. We are developing our lead product candidate, eravacycline, a fully synthetic fluorocycline, as an intravenous, or IV, and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant, or MDR, Gram-negative infections.

We are conducting a global phase 3 clinical program for eravacycline called IGNITE (Investigating Gram-Negative Infections Treated with Eravacycline). We are also pursuing the discovery and development of additional antibiotics that target unmet medical needs, including multidrug-resistant Gram-negative bacteria.

We are conducting IGNITE4, a phase 3 randomized, double-blind, double-dummy, multicenter, prospective study that is designed to assess the efficacy, safety and pharmacokinetics of twice-daily eravacycline (1.0 mg/kg every 12 hours) compared with meropenem (1g every 8 hours) for the treatment of complicated intra-abdominal infections, or cIAI. The study is expected to enroll approximately 450 adult patients at 75 centers worldwide. The primary endpoint of IGNITE4 is clinical response at the test-of-cure (TOC) visit, which occurs 25 to 31 days after the initial dose of the study drug. The primary efficacy analysis will be conducted using a 12.5% non-inferiority margin in the microbiological intent-to-treat (micro-ITT) population. We previously conducted IGNITE1, our completed phase 3 clinical trial where eravacycline met the primary endpoint of statistical non-inferiority compared to ertapenem, the control therapy for the trial, for the treatment of cIAI. Consistent with draft guidance issued by the United States Food and Drug Administration, or FDA, with respect to the development of antibiotics for cIAI and our discussions with the FDA, positive results from our phase 3 clinical trials (IGNITE1 and IGNITE4) would be sufficient to support submission of a new drug application, or NDA, for eravacycline for the treatment of cIAI. We expect to report top-line data from IGNITE4 in the fourth quarter of 2017.

During the second half of 2017, we plan to submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for IV eravacycline for the treatment of cIAI. We expect the MAA submission will be supported by data from IGNITE1, our completed phase 3 clinical trial, which evaluated the efficacy and safety of twice-daily IV eravacycline for the treatment of cIAI. In this study, eravacycline was well tolerated, and met the primary endpoint of statistical non-inferiority compared to ertapenem, the control therapy for the trial.

In January 2017, we initiated IGNITE3, a randomized, multi-center, double-blind, phase 3 clinical trial evaluating the efficacy and safety of once-daily IV eravacycline (1.5mg/kg every 24 hours) compared to ertapenem (1g every 24 hours), the control therapy in this trial, for the treatment of complicated urinary tract infections, or cUTI. IGNITE3 is expected to enroll approximately 1,000 adult patients, who will be randomized 1:1 to receive eravacycline or ertapenem for a minimum of five days, and will then be eligible to switch to an oral antibiotic. The co-primary endpoints of responder rate (a combination of clinical cure rate and microbiological response) in the micro-ITT population at the end-of-IV treatment visit and at the test-of-cure visit (Day 5-10 post therapy) will be evaluated using a 10% non-inferiority margin.

In parallel with the clinical trials using IV eravacycline, we are continuing our development program for an oral formulation of eravacycline. We recently completed phase 1 clinical testing in which the administration of oral eravacycline to patients in the fasted state resulted in increased drug exposure. Further clinical tests designed to evaluate other important variables are currently ongoing, with the goal of optimizing the oral eravacycline dosing regimen. We expect to provide an update with top-line findings from this testing and potential next steps during the third quarter of 2017.

In January 2016, we initiated a phase 1 clinical trial of the IV formulation of TP-271, a fully synthetic fluorocycline being developed for respiratory disease caused by bacterial biothreat pathogens, in healthy volunteers. In addition to eravacycline and TP-271, we are pursuing development of TP-6076, a fully synthetic fluorocycline, as a lead candidate under our second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria, and in July 2016 we initiated a phase 1 clinical trial of the IV formulation of TP-6076 in healthy volunteers.

We commenced business operations in July 2006. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our proprietary chemistry technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of our product candidates. To date, we have not generated any product revenue and have primarily financed our operations through public offerings and private placements of our equity securities, debt financings and funding from the United States government. As of December 31, 2016, we had received an aggregate of $460.5 million in net proceeds from the issuance of equity securities and borrowings under debt facilities and an aggregate of $43.7 million from government grants and contracts. As of December 31, 2016, our principal source of liquidity was cash and cash equivalents, which totaled $142.1 million.

As of December 31, 2016, we had an accumulated deficit of $347.1 million. Our net losses were $77.5 million, $83.2 million and $66.7 million for the years ended December 31, 2016, 2015 and 2014, respectively. We expect that our expenses will increase as we continue development of eravacycline, seek marketing approval for eravacycline, conduct pre-commercialization and launch-related activities for eravacycline, pursue development of eravacycline for additional indications, manufacture drug product for our clinical and pre-clinical trials, conduct our phase 1 clinical trial of TP-271in healthy volunteers, and our phase 1 clinical trial of TP-6076 in healthy volunteers and satisfy our obligations under our license agreement with Harvard University. If we obtain marketing approval of eravacycline, we also expect to incur significant sales, marketing, distribution and manufacturing expenses. Furthermore, we expect to incur ongoing research and development expenses relating to our product candidates other than eravacycline and that our general and costs will increase as we grow and continue to operate as a public company, and comply with increased disclosure requirements since we are no longer an emerging growth company.

We believe that our available funds will be sufficient to support our operations into the second half of 2018, which we believe will allow us to obtain results from IGNITE4 and file the NDA for IV eravacycline for the treatment of cIAI. We do not believe these funds will be sufficient, however, to enable us to commercially launch eravacycline, complete IGNITE3 or submit an sNDA for IV eravacycline for the treatment of cUTI. It is also possible that we will not achieve the progress that we expect with respect to eravacycline because the actual costs and timing of clinical development activities are difficult to predict and are subject to substantial risks and delays. We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations 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. Moreover, we will need to generate significant revenue to achieve profitability, and we may never do so.

Financial overview

Contract and Grant Revenue

We have derived all of our revenue to date from funding provided under three U.S. government awards for the development of our compounds as potential counter measures for the treatment of disease caused by bacterial biothreat pathogens through our collaborator CUBRC Inc., or CUBRC, an independent, not-for-profit, research corporation that specializes in U.S. government-based contracts:

- We have received funding for our lead product candidate, eravacycline, under an award from the Biomedical Advanced Research and Development Authority, or BARDA, an agency of the U.S. Department of Health and Human Services. In January 2012, BARDA awarded CUBRC a five-year contract that provides for up to a total of $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. The funding under the BARDA Contract is also being used for the development, manufacturing and clinical evaluation of eravacycline to treat certain infections caused by

life-threatening multidrug-resistant bacteria. We refer to this contract as the BARDA Contract.

- We have received funding for our preclinical compound TP-271 under two awards from the National Institute of Allergy and Infectious Diseases, or NIAID, a division of National Institutes of Health, for the development, manufacturing and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia:
  - a grant awarded to CUBRC in July 2011 that provides up to a total of approximately $2.9 million through May 31, 2017, which we refer to as the NIAID Grant; and
  - a contract awarded to CUBRC in September 2011 that provides up to a total of approximately $35.8 million in funding through December 31, 2018, which we refer to as the NIAID Contract.

We are collaborating with CUBRC, because when we initially decided to seek government funding, we recognized that we did not have any expertise in bidding for, administrating or managing government-funded contracts. CUBRC serves as the prime

contractor under the BARDA Contract, the NIAID Grant and the NIAID Contract, primarily carrying out a program management and administrative role with additional responsibility for the management of preclinical studies. We serve as lead technical expert on all aspects of these awards and also serve as a subcontractor responsible for management of chemistry, manufacturing and control activities and clinical studies. We derive all of our revenue under these collaborations through subcontracts with, and a subaward from, CUBRC, with the flow of funds following the respective activities being conducted by us and by CUBRC.

- In connection with the BARDA Contract, in February 2012, we entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on May 10, 2018 under which we may receive funding of up to approximately $41.6 million, reflecting the portion of the BARDA Contract funding that may be paid to us for our activities.
- In connection with the NIAID Contract, in October 2011, we entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on December 31, 2018 under which we may receive funding of up to approximately $15.1 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities.
- In connection with the NIAID Grant, in November 2011, CUBRC awarded us a no-fee subaward which currently expires on May 31, 2017 under which we may receive funding of up to approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to us for our activities.

Although the BARDA Contract and our subcontract with CUBRC under the BARDA Contract have terms which currently expire on May 10, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is up to $41.6 million from the initial contract date through May 10, 2018, of which $32.4 million had been received through December 31, 2016.

Similarly, although the NIAID Contract and our subcontract with CUBRC under the NIAID Contract have terms which currently expire on December 31, 2018, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond December 31, 2018. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subcontract with respect to the NIAID Contract is up to $15.1 million, from the initial contract date through December 31, 2018, of which $10.4 million had been received through December 31, 2016. In addition, although the NIAID Grant and our subaward from CUBRC have terms which currently expire on May 31, 2017, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond May 31, 2017. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subaward with respect to the NIAID Grant is $0.9 million from the initial grant date through May 31, 2017, of which $0.8 million had been received through December 31, 2016.

We have no products approved for sale. Other than the government funding described above, we do not expect to receive any revenue from any product candidates that we develop, including eravacycline, until we obtain regulatory approval and commercialize such products or until we potentially enter into collaborative agreements with third parties for the development and commercialization of such product candidates. We continue to pursue government funding for other preclinical and clinical programs. If our development efforts for any of our product candidates result in clinical success and regulatory approval, or collaboration agreements with third parties, we may generate revenue from those product candidates.

We expect that our revenue will be less than our expenses for the foreseeable future and that we will experience increasing losses as we continue our development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. Even if we are able to generate revenue from the sale of one or more products, we may not become profitable.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the research and development of our preclinical and clinical candidates, and include:

- personnel-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations, and consultants that provide preclinical, clinical, regulatory and manufacturing services;
- payments made under our license agreement with Harvard University;
- the cost of acquiring, developing and manufacturing clinical trial materials and lab supplies;

- facility, depreciation and other expenses, which include direct and allocated expenses for rent, maintenance of our facilities, insurance and other supplies; and
- costs associated with preclinical, regulatory and medical affair activities.

We expense research and development costs to operations as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors.

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and laboratory supplies, to each program based on the personnel resources allocated to such program. Expenses related to facilities, consulting, travel, conferences, stock-based compensation and depreciation are not allocated to a program and are separately classified as other research and development expenses. The following table identifies research and development expenses on a program-specific basis for our product candidates for the years ended December 31, 2016, 2015 and 2014:

	Year Ended December 31,		
	2016	2015	2014
	(in thousands)		
Eravacycline	$37,430	$48,368	$46,595
BARDA Contract	2,394	10,280	6,782
NIAID Contract and NIAID Grant	1,870	890	2,149
TP-6076	5,517	3,232	1,219
Other development programs	2,196	619	-
Other research and development	14,357	10,379	5,187
Total research and development	$63,764	$73,768	$61,932

Research and development activities are central to our business model. 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.

As of December 31, 2016, we had incurred an aggregate of $180.8 million in research and development expenses related to the development of eravacycline, and $31.1 million in research and development expenses related to the development of eravacycline that were funded under the BARDA Contract. We expect that our research and development expenses will increase as we continue development of eravacycline, incur nonclinical, regulatory and drug manufacturing costs in support of NDA-related activities, pursue development of eravacycline for additional indications, advance our other product candidates and satisfy our obligations under our license agreement with Harvard University.

Because of the numerous risks and uncertainties associated with product development, however, we cannot determine with certainty the duration and completion costs of current or future clinical trials of eravacycline or our other product candidates. We may never succeed in achieving regulatory approval for eravacycline or any of our other product candidates. The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors, including the uncertainties of future clinical and preclinical studies, uncertainties in clinical trial enrollment rate and significant and changing government regulation. In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial

viability.

We have licensed our proprietary chemistry technology from Harvard University on an exclusive worldwide basis under a license agreement that we entered into in August 2006. Under our license agreement, we have paid Harvard an aggregate of $4.4 million in upfront license fees and development milestone payments. We have also issued 31,379 shares of our common stock to Harvard under the license agreement. In addition, we have agreed to make payments to Harvard upon the achievement of specified future development and regulatory milestones totaling up to $15.1 million for each licensed product candidate ($3.1 million of which has already been paid with respect to eravacycline), and to pay tiered royalties in the single digits based on annual worldwide net sales, if any, of licensed products, our affiliates and our sublicensees. We are also obligated to pay Harvard a specified share of non-royalty sublicensing revenues that we receive from sublicensees for the grant of sublicenses under the license and to reimburse Harvard for specified patent prosecution and maintenance costs. The next milestone payment due under the license agreement with respect to eravacycline would be a $3.0 million payment upon acceptance of an NDA filing to the FDA.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, including salaries and related costs such as benefits and stock-based compensation for personnel in executive, finance, operational, corporate communications, marketing and human resource functions. Other significant general and administrative expenses include professional fees for legal, patent, auditing and tax services, consulting, and facility costs not otherwise included in research and development expenses.

We anticipate that our general and administrative expenses will increase for a number of reasons, including:

- support of the anticipated expansion of our research and development activities as we continue the development of our product candidates;
- expansion of infrastructure, including increases in personnel-related costs, consulting, legal, and accounting costs, and directors and officers insurance premiums; and
- if and when we believe a regulatory approval of our first product candidate appears likely, anticipated increases in our personnel-related and consulting costs as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of our product candidates.

Interest Income

Interest income consists of interest earned on our cash and cash equivalents. The primary objective of our investment policy is capital preservation.

Interest Expense

Interest expense from prior periods consisted primarily of interest accrued on our outstanding indebtedness and non-cash interest related to the amortization of debt discount costs associated with our term loan facility with Silicon Valley Bank and Oxford Finance. We repaid the remaining indebtedness under the term loan facility on March 31, 2015 and, accordingly, will not incur any more interest expense under the term loan facility.

Other Income

Other income for the years ended December 31, 2016, 2015 and 2014 was de minimis.

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued clinical expenses, and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we and our management believe 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 from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this annual report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

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Revenue Recognition

We have derived all of our revenue to date from our subcontracts with CUBRC under the BARDA Contract and the NIAID Contract and our subaward under the NIAID Grant. We recognize revenue under these best-efforts, cost-reimbursable and cost-plus-fixed-fee subcontracts and subaward as we perform services under the subcontracts and subaward so long as a subcontract and subaward has been executed and the fees for these services are fixed or determinable, legally billable and reasonably assured of collection. Recognized amounts reflect our partial performance under the subcontracts and subaward and equal direct and indirect costs incurred plus fixed fees, where applicable. We do not recognize revenue under these arrangements for amounts related to contract periods where funding is not yet committed as amounts above committed funding thresholds would not be considered fixed or determinable or reasonably assured of collection. Revenues and expenses under these arrangements are presented gross on our statements of operations and comprehensive loss as we have determined we are the primary obligor under these arrangements relative to the research and development services we perform as lead technical expert.

Revenue under our subcontracts under both the NIAID Contract and the BARDA Contract are earned under a cost-plus-fixed-fee arrangement in which we are reimbursed for direct costs incurred plus allowable indirect costs and a fixed-fee earned. Billings under these contracts are based on approved provisional indirect billing rates, which permit recovery of fringe benefits, allowable overhead and general and administrative expenses and a fixed fee.

Revenue under our subaward under the NIAID Grant is earned under a cost-reimbursable arrangement in which we are reimbursed for direct costs incurred plus allowable indirect costs. Billings under the NIAID Grant are based on approved provisional indirect billing rates, which permit recovery of fringe benefits and allowable general and administrative expenses.

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed for us and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our 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 fees paid to:

- contract research organizations in connection with the conduct of our clinical trials;
- contract manufacturing organizations with respect to the manufacture of drug supply for clinical trials and manufacture of drug substance and finished product; and
- vendors and consultants in connection with preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services completed and efforts expended pursuant to contracts with multiple contract research organizations that conduct and manage clinical studies 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. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we

do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

Stock-Based Compensation

We apply the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, Compensation-Stock Compensation, or ASC 718, to account for all stock-based compensation. We recognize compensation costs related to stock options and restricted stock units granted to employees based on the estimated fair value of the awards on the date of grant. Stock compensation related to non-employee awards is remeasured at each reporting period until the awards are vested.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their grant date for awards granted to employees and as of their measurement date for awards granted to non-employees. For awards granted to employees, we recognize stock-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. For awards granted to non-employees, we recognize stock-based compensation expense over the requisite service period using the accelerated attribution method. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the fair value of our common stock on the grant date for the period prior to our initial public offering, or IPO, the expected term of our stock options, the risk free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Because there had been no public market for our common stock prior to our IPO, we believe that we have insufficient data from our limited public trading history to appropriately utilize company-specific historical and implied volatility information. Accordingly, we utilize data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the biopharmaceutical industry with similar characteristics as us, including stage of product development and therapeutic focus. We use the simplified method as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, Share-Based Payment as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. For non-employee grants, we use an expected term equal to the remaining contractual term of the award. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention of paying cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of measurement for instruments with a similar expected term.

Under ASC 718, we are also required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest. We have performed an historical analysis of option awards that were forfeited prior to vesting and recorded total stock option expense that reflected this estimated forfeiture rate. ASC 718 requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Results of Operations

Comparison of Years Ended December 31, 2016 and 2015

The following tables summarize the results of our operations for each of the years ended December 31, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2016	2015		
	(in thousands)			
Revenues	$5,145	$11,686	$(6,541)	(56)%
Operating expenses:				
Research and development	63,764	73,768	(10,004)	(14)%
General and administrative	19,211	20,916	(1,705)	(8)%

Total operating expenses	82,975	94,684	(11,709)	(12)%
Loss from operations	(77,830)	(82,998)	5,168	(6)%
Interest income	350	42	308	733 %
Interest expense	-	(231)	231	(100)%
Other (expense) income	-	(2)	2	(100)%
Net loss	$(77,480)	$(83,189)	$5,709	(7)%

Revenue from U.S. Government Contracts and Grants

The following table sets forth our contract and grant revenue for the years ended December 31, 2016 and 2015:

	Years Ended December 31,		Increase/	
Revenue	2016	2015	(decrease)	%
	(in thousands)			
BARDA Contract	$2,879	$10,773	$ (7,894)	(73)%
NIAID Contract	2,164	756	1,408	186%
NIAID Grant	102	157	(55)	(35)%
	$5,145	$11,686	$ (6,541)	(56)%

Contract and grant revenue was $5.1 million for the year ended December 31, 2016 compared to $11.7 million for the year ended December 31, 2015, a decrease of $6.6 million, or 56%. This decrease was primarily due to a changes in the timing and scope of activities under our subcontract with respect to the BARDA Contract conducted during the year ended December 31, 2016 as compared to the year ended December 31, 2015, offset in part by the timing and scope of activities under our subcontract with respect to the NIAID Contract.

Research and Development Expenses

Research and development expenses were $63.8 million for the year ended December 31, 2016 compared to $73.8 million for the year ended December 31, 2015, a decrease of approximately $10.0 million, or 14%. This trend was primarily due to a decrease in clinical trial costs associated with the completion of IGNITE2 of $16.4 million offset in part by costs associated with the start of IGNITE3 and IGNITE4 of $11.8 million, a decrease in certain pre-clinical registration activities for eravacycline of $4.1 million, and a decrease in drug manufacturing costs under our BARDA sub-contract of $3.8 million. These decreases were offset in part by an increase in personnel-related costs of $1.8 million due to additional headcount and an increase in stock-based compensation expense of $0.8 million resulting from additional headcount and our annual stock option awards and restricted stock units granted to employees during the first quarter of 2016.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2016 were $19.2 million compared to $20.9 million for the year ended December 31, 2015, a decrease of $1.7 million, or 8%. This decrease was primarily due to a decrease of $2.3 million in market research and pre-commercialization expenses. This decrease was offset by an increase in stock-based compensation expense of $0.8 million primarily due a non-employee stock-based compensation credit during 2015 and an increase in legal fees of $0.5 million.

Interest Income

Interest income for the year ended December 31, 2016 was $0.3 million compared to $42,000 for the year ended December 31, 2015, driven by implementation of a new cash sweep account and improved overall yields on our money market funds.

Interest Expense

There was no interest expense for the year ended December 31, 2016 compared to interest of $0.2 million for the year ended December 31, 2015. The decrease in interest expense reflected the payoff of indebtedness under our term loan facility with Silicon Valley Bank and Oxford Finance on March 31, 2015.

Other Income

Other income for the years ended December 31, 2016 and 2015 was de minimis.

Comparison of Years Ended December 31, 2015 and 2014

The following tables summarize the results of our operations for each of the years ended December 31, 2015 and 2014, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2015	2014		
	(in thousands)			
Revenues	$11,686	$9,098	$2,588	28 %
Operating expenses:				
Research and development	73,768	61,932	11,836	19 %
General and administrative	20,916	12,932	7,984	62 %
Total operating expenses	94,684	74,864	19,820	26 %
Loss from operations	(82,998)	(65,766)	(17,232)	26 %
Interest income	42	17	25	147 %
Interest expense	(231)	(1,017)	786	(77)%
Other income	(2)	24	(26)	(108)%
Net loss	$(83,189)	$(66,742)	$(16,447)	25 %

Revenue from U.S. Government Contracts and Grants

The following table sets forth our contract and grant revenue for the years ended December 31, 2015 and 2014:

	Years Ended December 31,		Increase/ (decrease)	%
Revenue	2015	2014		
	(in thousands)			
BARDA Contract	$10,773	$6,886	$ 3,887	56 %
NIAID Contract	756	2,077	(1,321)	(64)%
NIAID Grant	157	135	22	16 %
	$11,686	$9,098	$ 2,588	28 %

Contract and grant revenue was $11.7 million for the year ended December 31, 2015 compared to $9.1 million for the year ended December 31, 2014, an increase of $2.6 million, or 28%. This increase was primarily due to the scope and timing of activities under our BARDA subcontract conducted during the year ended December 31, 2015 versus the prior year, offset in part by a decrease in activities under our NIAID subcontract.

Research and Development Expenses

Research and development expenses were $73.8 million for the year ended December 31, 2015 compared to $61.9 million for the year ended December 31, 2014, an increase of approximately $11.8 million, or 19%. This increase was primarily due to higher drug manufacturing and nonclinical costs of $7.4 million in support of our NDA-related and pre-commercialization activities for eravacycline; an increase of $4.9 million primarily related to our eravacycline program, consisting of an increase in costs associated with additional personnel of $1.9 million, medical affairs of $1.9 million, regulatory activities of $0.9 million, and consulting of $0.3 million; an increase in stock-based compensation expense of $4.1 million resulting from additional headcount and our annual stock option awards granted to employees during the quarter ended March 31, 2015; an increase of $2.8 million in drug manufacturing and clinical costs under our government programs; an increase of $2.4 million related to certain preclinical activities for pipeline programs; and an increase in rent and utilities of $0.7 million related to our additional facilities occupied during 2015. These increases were offset in part by a decrease of $11.7 million of clinical trial costs related to our phase 3 clinical program of eravacycline.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2015 were $20.9 million compared to $12.9 million for the year ended December 31, 2014, an increase of $8.0 million, or 62%. This increase was primarily due to an increase of $3.4 million in consulting costs related to pre-commercialization activities for eravacycline; an increase in stock-based compensation expense of $2.3 million resulting from additional headcount to support pre-commercialization activities for eravacycline and general corporate

activities and our annual stock option awards granted to employees during the quarter ended March 31, 2015; and increased personnel-related costs of $1.7 million in connection with additional headcount.

Interest Income

Interest income for the years ended December 31, 2015 and December 31, 2014 was de minimis.

Interest Expense

Interest expense for the year ended December 31, 2015 was $0.2 million compared to $1.0 million for the year ended December 31, 2014, a decrease of $0.8 million or 77%. The decrease in interest expense resulted from the payoff of indebtedness under our term loan facility with Silicon Valley Bank and Oxford Finance on March 31, 2015.

Other Income

Other income for the years ended December 31, 2015 and 2014 was de minimis.

Liquidity and Capital Resources

We have incurred losses since our inception and anticipate that we will continue to incur losses for at least the next several years. We expect that our research and development and general and administrative expenses will continue to increase and, as a result, we will need additional capital to fund our operations, which we may obtain from additional financings, research funding, collaborations, contract and grant revenue or other sources.

Since our inception, we have funded our operations principally through the receipt of funds from public offerings and private placements of equity securities, debt financings and contract research funding and research grants from the United States government. As of December 31, 2016, we had cash and cash equivalents of approximately $142.1 million. We invest cash in excess of immediate requirements in accordance with our investment policy, primarily with a view to liquidity and capital preservation. As of December 31, 2016, our funds were held in cash and money market funds.

On October 22, 2014, we completed the sale of 4,542,500 shares of common stock in a follow-on public offering at a price to the public of $19.00 per share, which number of shares includes the underwriters' exercise in full of their option to purchase additional shares. This offering resulted in net proceeds to us of $80.8 million after deducting underwriting discounts and commissions of $5.2 million and offering costs of $0.4 million.

On March 17, 2015, we completed the sale of 4,945,000 shares of common stock in a follow-on public offering at a price to the public of $35.00 per share, which number of shares includes the underwriters' exercise in full of their option to purchase additional shares. This offering resulted in net proceeds to us of $162.2 million after deducting underwriting discounts and commissions of $10.4 million and offering costs of $0.5 million.

On January 17, 2017, we entered into a Controlled Equity Offering Sales Agreement, or Sales Agreement, with Cantor Fitzgerald & Co., as sales agent, or Cantor. In accordance with the terms of the Agreement, we may offer and sell through Cantor, from time to time, shares of our common stock up to an aggregate offering price of $40,000,000.

Under the Sales Agreement, Cantor may sell shares of our common stock by methods deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on The NASDAQ Global Select Market or on any other existing trading market for our common stock.

We are not obligated to make any sales of shares of our common stock under the Sales Agreement. We or Cantor may suspend or terminate the offering of shares of our common stock upon notice to the other party and subject to other conditions. We will pay Cantor a commission rate equal to 3.0% of the gross proceeds per share sold. No shares have been sold to date via this facility.

The following table summarizes our sources and uses of cash for each of the periods set forth below:

	Years Ended December 31,		
	2016	2015	2014
	(in thousands)		
Net cash used in operating activities	$(63,766)	$(76,707)	$(57,623)
Net cash used in investing activities	(393)	(838)	(191)
Net cash provided by financing activities	333	162,415	76,144
Net increase (decrease) in cash and cash equivalents	$(63,826)	$84,870	$18,330

During the years ended December 31, 2016, 2015 and 2014, our operating activities used net cash of $63.8 million, $76.7 million and $57.6 million, respectively. Net cash used by operating activities for the year ended December 31, 2016 decreased by $12.9 million compared to the year ended December 31, 2015. The decrease is primarily due a net decrease in expenses related to our eravacycline Phase 3 clinical studies and lower drug manufacturing and nonclinical costs in support of our NDA-related and pre-commercialization activities for eravacycline. Net cash used in operating activities for the year ended December 31, 2015 increased by $19.1 million compared to the year ended December 31, 2014. The increase was primarily due to an increase in clinical expenses related to IGNITE2 and an increase in drug manufacturing and nonclinical costs in support of our NDA-related and pre-commercialization activities for eravacycline.

During the years ended December 31, 2016, 2015 and 2014, our investing activities used net cash of $0.4 million, $0.8 million and $0.2 million, respectively. The net cash used in investing activities during these periods resulted from purchases of property, plant and equipment to facilitate our increased research and development activities and increased headcount.

During the years ended December 31, 2016, 2015 and 2014 our net cash provided by financing activities was $0.3 million, $162.4 million and $76.1 million, respectively. The net cash provided by financing activities during the year ended December 31, 2016 primarily reflected proceeds from the issuance of stock under our stock plans. The net cash provided by financing activities during the year ended December 31, 2015 was primarily related to proceeds from our March 2015 follow-on public offering of $162.2 million, as well as proceeds from the exercise of stock options of $4.9 million, offset in part by repayment of the remaining indebtedness under our term loan facility with Silicon Valley Bank and Oxford Finance of $4.6 million. The net cash provided by financing activities during the year ended December 31, 2014 was primarily related to proceeds from our follow-on public offering of $80.8 million, as well as proceeds from the exercise of stock options of $1.5 million, offset in part by principal payments on our loans payable of $6.1 million.

Operating Capital Requirements

We expect to incur increasing operating losses for at least the next several years as we continue development of eravacycline, seek marketing approval for eravacycline, manufacture drug product for our clinical and pre-clinical trials, conduct pre-commercialization and launch-related activities for eravacycline, conduct our phase 1 clinical trial of TP-271in healthy volunteers, and our phase 1 clinical trial of TP-6076 in healthy volunteers and satisfy our obligations under our license agreement with Harvard University. We may not be able to complete the development and initiate commercialization of eravacycline or our other product candidates if, among other things, our preclinical

research and clinical trials are not successful, our manufacturing efforts are not successful, the FDA or the EMA does not approve eravacycline or our other product candidates when we expect, or at all, or funding under the NIAID Contract, the NIAID Grant or the BARDA Contract is discontinued.

We believe that our available funds will be sufficient to support our operations into the second half of 2018, which we believe would allow us to obtain results from IGNITE4 and file the NDA for IV eravacycline for the treatment of cIAI. We do not believe these funds will be sufficient, however, to enable us to commercially launch eravacycline, complete IGNITE3 or submit an sNDA for IV eravacycline for the treatment of cUTI. As a result, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

We have based our projections of operating capital requirements on assumptions that may prove to be incorrect and we may use all of our available capital resources sooner than we expect. Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical products, we are unable to estimate the exact amount of our operating capital requirements. Our future funding requirements will depend on many factors, including, but not limited to:

- the timing and costs of our clinical development program for eravacycline;
- manufacturing costs related to regulatory filings and anticipated commercial launch;

- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our other product candidates and potential product candidates;
- the amount of funding that we receive under our subcontracts under the BARDA Contract and the NIAID Contract and under our subaward under the NIAID Grant, and the activities funded under the BARDA Contract, the NIAID Contract and the NIAID Grant;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for eravacycline and other product candidates if we receive marketing approval, including the timing and costs of establishing product sales, marketing, distribution and manufacturing capabilities;
- revenue received from commercial sales of eravacycline, subject to receipt of marketing approval;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay to Harvard pursuant to our license agreement;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

We expect that we will need to obtain substantial additional funding in order to commercialize eravacycline. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, the ownership interests of our existing stockholders may be materially diluted and the terms of these securities could include liquidation or other preferences that could adversely affect the rights of our existing stockholders. In addition, debt financing, if available, would result in increased fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. If we are unable to raise capital when needed or on attractive terms, we could be forced to significantly delay, scale back or discontinue the development or commercialization of eravacycline or other product candidates, seek collaborators at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available, and relinquish or license, potentially on unfavorable terms, our rights to eravacycline or other product candidates that we otherwise would seek to develop or commercialize ourselves.

Contractual Obligations and Commitments

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2016:

	Payment due by period				
Contractual Obligations	Total	Less than 1 Year	1 -3 Years	3-5 Years	More than 5 Years
	(in thousands)				
Operating leases (1)	$5,103	$1,701	$3,402	$ -	$ -
Harvard milestone payment (2)	4,750	-	4,750	-	-
Total contractual cash obligations	$9,853	$1,701	$8,152	$ -	$ -

(1) On June 18, 2015, we amended our existing operating lease to expand our leased premises under that lease to a total of 37,438 square feet, and we also extended our lease term through November 30, 2019. In third quarter of 2016, we entered into a sublease with respect to a portion of our principal facilities, which consist of office, research and laboratory space located at 480 Arsenal Way, Watertown, Massachusetts, with an unrelated third party. The term of the sublease expires in November 2019, with the sublessee obligated to pay rent to us that approximates the rent we are currently paying to our landlord with respect to such portion of the facility.

(2) Consists of milestone payments that would become due to Harvard of (i) $3.0 million upon acceptance by the FDA of an NDA filing for eravacycline and (ii) $1.8 million upon acceptance by the EMA of our MAA filing for eravacycline. We cannot determine the exact timing of payment of these milestones, or if they would ever become due at all.

We are contractually obligated under our license agreement with Harvard University to make payments to Harvard upon the achievement of specified future development and regulatory milestones totaling up to $15.1 million for each licensed product candidate ($3.1 million of which has already been paid with respect to eravacycline), and to pay tiered royalties in the single digits based on annual worldwide net sales, if any, of licensed products by us, our affiliates and sublicensees. We are also obligated to pay Harvard a specified share of non-royalty sublicensing revenue that we receive from sublicensees for the grant of sublicenses under the license and to reimburse Harvard for specified patent prosecution and maintenance costs. Many of these potential payments are contingent upon the occurrence of certain future events and, given the nature of those events, it is unclear when, if ever, we may be required to pay such amounts or what the total amount of such payments will be. Except for the milestone payments referenced in the contractual obligations table and described in the footnote above, the table does not include any other potential milestone or royalty payments to Harvard.

We have employment agreements with certain employees which require the funding of a specific level of payments, if certain events, such as a change in control or termination without cause, occur.

In the course of normal business operations, we also have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. We can elect to discontinue the work under these agreements at any time. We could also enter into additional collaborative research, contract research, manufacturing, and supplier agreements in the future, which may require up-front payments and even long-term commitments of cash.

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 under applicable SEC rules.

ITEM 7A. Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our cash equivalents are classified as available-for-sale and consisted of money market funds at December 31, 2016 and 2015. The investments in these financial instruments are made in accordance with an investment policy approved by our board of directors which specifies the categories, allocations and ratings of securities we may consider for investment. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Some of the financial instruments that we invest in could be subject to market risk. This means that a change in prevailing interest rates may cause the value of the instruments to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value of that security will probably decline. To minimize this risk, we intend to maintain a portfolio which may include cash, cash equivalents and investment securities available-for-sale in a variety of securities which may include money market funds, government and non-government debt securities and commercial paper, all with various maturity dates. Based on our current investment portfolio, we do not believe that our results of operations or our financial condition would be materially impacted by an immediate change of 10% in interest rates.

We do not hold or issue derivatives, derivative commodity instruments or other financial instruments for speculative trading purposes. Further, we do not believe our cash equivalents and investment securities have significant risk of default or illiquidity. We made this determination based on discussions with our investment advisors and a review of our holdings. While we believe our cash equivalents and investment securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. All of our investments are recorded at fair value.

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ITEM 8. Financial Statements and Supplementary Data

TETRAPHASE PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of

Tetraphase Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Tetraphase Pharmaceuticals, Inc. (the Company) as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2016. 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as 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 Tetraphase Pharmaceuticals, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Tetraphase Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated March 13, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts

March 13, 2017

Tetraphase Pharmaceuticals, Inc.

Consolidated Balance Sheets

(In thousands, except par value amounts)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$142,086	$205,912
Accounts receivable	1,789	4,151
Prepaid expenses and other current assets	6,582	3,705
Total current assets	150,457	213,768
Property and equipment, net	1,054	943
Restricted cash	199	199
Other assets	-	7
Total assets	$151,710	$214,917
Liabilities and stockholders’ equity		
Current liabilities:		
Accounts payable	$2,555	$2,857
Accrued expenses	7,685	6,931
Deferred revenue	1,255	909
Total current liabilities	11,495	10,697
Other long term liabilities	162	165
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, par value $0.001 per share; 5,000 shares authorized; no shares issued and outstanding	-	-
Common stock, par value $0.001 per share; 125,000 shares authorized; 36,942 and 36,585 shares issued and outstanding at December 31, 2016 and 2015, respectively	37	37
Additional paid-in capital	487,148	473,670
Accumulated deficit	(347,132)	(269,652)
Total stockholders’ equity	140,053	204,055
Total liabilities and stockholders’ equity	$151,710	$214,917

See accompanying notes to consolidated financial statements.

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Tetraphase Pharmaceuticals, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except per share data)

	Year Ended December 31,		
	2016	2015	2014
Revenues	$5,145	$11,686	$9,098
Operating expenses:			
Research and development	63,764	73,768	61,932
General and administrative	19,211	20,916	12,932
Total operating expenses	82,975	94,684	74,864
Loss from operations	(77,830)	(82,998)	(65,766)
Other income (expense):			
Interest income	350	42	17
Interest expense	-	(231)	(1,017)
Other income (expense)	-	(2)	24
Other income (expense), net	350	(191)	(976)
Net loss	$(77,480)	$(83,189)	$(66,742)
Net loss per share-basic and diluted	$(2.11)	$(2.36)	$(2.49)
Weighted-average number of common shares used in net loss per share-basic and diluted	36,704	35,261	26,807
Comprehensive loss	$(77,480)	$(83,189)	$(66,742)

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity

(In thousands)

	Common Shares	Shares Amount	Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance at December 31, 2013	25,629	$ 26	$ 207,503	$ (119,721)	$ 87,808
Exercise of stock options	563	—	1,421	—	1,421
Issuance of common stock from initial public offering (net of underwriters discounts and issuance costs of $7,391)	4,543	5	80,761	—	80,766
Reclassification of warrants for common stock	8	—	83	—	83
Issuance of common stock from warrant exercise	63	—	—	—	—
Stock-based compensation expense	—	—	5,230	—	5,230
Net loss	—	—	—	(66,742)	(66,742)
Balance at December 31, 2014	30,806	31	294,998	(186,463)	108,566
Exercise of stock options	818	1	4,671	—	4,672
Issuance of common stock from follow-on public offering (net of underwriters discounts and issuance costs of $10,924)	4,945	5	162,146	—	162,151
Shares issued in connection with employee stock purchase plan	16	—	239	—	239
Stock-based compensation expense	—	—	11,616	—	11,616
Net loss	—	—	—	(83,189)	(83,189)
Balance at December 31, 2015	36,585	37	473,670	(269,652)	204,055
Exercise of stock options and vesting of restricted stock units	298	—	146	—	146
Shares issued in connection with employee stock purchase plan	59	—	187	—	187
Stock-based compensation expense	—	—	13,145	—	13,145
Net loss	—	—	—	(77,480)	(77,480)
Balance at December 31, 2016	36,942	$ 37	$ 487,148	$ (347,132)	$ 140,053

See accompanying notes to consolidated financial statements.

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Tetraphase Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,		
	2016	2015	2014
Operating activities			
Net loss	$(77,480)	$(83,189)	$(66,742)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation and amortization	282	193	124
Amortization of deferred financing costs and debt discount	—	94	226
Accretion of final interest payment on term loans	—	45	115
Stock-based compensation expense	13,145	11,616	5,230
Loss from disposal of property and equipment	—	2	2
Changes in operating assets and liabilities:			
Accounts receivable	2,362	(693)	(1,752)
Prepaid expenses and other assets	(2,870)	(1,514)	(1,199)
Accounts payable	(302)	(1,249)	2,224
Accrued expenses and other liabilities	751	(2,663)	3,983
Deferred revenue	346	651	166
Net cash used in operating activities	(63,766)	(76,707)	(57,623)
Investing activities			
Purchases of property and equipment	(393)	(838)	(191)
Net cash used in investing activities	(393)	(838)	(191)
Financing activities			
Proceeds from sale of common stock, net of underwriter discounts and issuance costs	—	162,151	80,766
Repayment of term loan payable	—	(4,646)	(6,126)
Proceeds from issuance of stock under stock plans	333	4,910	1,504
Net cash provided by financing activities	333	162,415	76,144
Net increase (decrease) in cash and cash equivalents	(63,826)	84,870	18,330
Cash and cash equivalents at beginning of period	205,912	121,042	102,712
Cash and cash equivalents at end of period	$142,086	$205,912	$121,042
Supplemental cash flow information			
Cash paid for interest	$-	$363	$945

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

(1) Organization and Operations

The Company

Tetraphase Pharmaceuticals, Inc. (the "Company") is a clinical-stage biopharmaceutical company using its proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. The Company is using its proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. The Company is developing its lead product candidate, eravacycline, a fully synthetic fluorocycline, as an intravenous, or IV, and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant, or MDR, Gram-negative infections.

The Company is conducting a global phase 3 clinical program for eravacycline called IGNITE (Investigating Gram-Negative Infections Treated with Eravacycline). The Company is also pursuing the discovery and development of additional antibiotics that target unmet medical needs, including multidrug-resistant Gram-negative bacteria.

The Company is conducting IGNITE4, a phase 3 randomized, double-blind, double-dummy, multicenter, prospective study that is designed to assess the efficacy, safety and pharmacokinetics of twice-daily eravacycline compared with meropenem for the treatment of cIAI. Consistent with draft guidance issued by the United States Food and Drug Administration, or FDA, with respect to the development of antibiotics for cIAI and the Company's discussions with the FDA, the Company expects that positive results from its phase 3 clinical trials (IGNITE1 and IGNITE4) would be sufficient to support submission of a new drug application for eravacycline for the treatment of cIAI. The Company expects to report top-line results from IGNITE4 as early as the fourth quarter of 2017.

During the second half of 2017, the Company plans to submit a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for IV eravacycline for the treatment of cIAI. The Company expects the MAA submission will be supported by data from IGNITE1, its completed phase 3 clinical trial, which evaluated the efficacy and safety of twice-daily IV eravacycline for the treatment of cIAI. In this study, eravacycline was well tolerated, and met the primary endpoint of statistical non-inferiority compared to ertapenem, the control therapy for the trial.

In January 2017, the Company initiated IGNITE3, a randomized, double-blind, phase 3 clinical trial evaluating the efficacy and safety of once-daily IV eravacycline compared to ertapenem, the control therapy in this trial, for the treatment of complicated urinary tract infections, or cUTI.

In parallel with the clinical trials using IV eravacycline, the Company is continuing its development program for an oral formulation of eravacycline. The Company recently completed phase 1 clinical testing in which the administration of oral eravacycline to patients in the fasted state resulted in increased drug exposure. Further clinical tests designed to evaluate other important variables are currently ongoing, with the goal of optimizing the oral eravacycline dosing regimen. The Company expects to provide an update with top-line findings from this testing and potential next steps during the third quarter of 2017.

In January 2016, the Company initiated a phase 1 clinical trial of the IV formulation of TP-271, a fully synthetic fluorocycline being developed for respiratory disease caused by bacterial biothreat pathogens, in healthy volunteers. In addition to eravacycline and TP-271, the Company is pursuing the development of TP-6076, a fully synthetic fluorocycline, as a lead candidate under its second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria, and in July 2016 initiated a phase 1 clinical trial of the IV formulation of TP-6076 in healthy volunteers.

The Company is devoting substantially all of its efforts to product research and development, market development, and raising capital. The Company is subject to a number of risks similar to those of other life science companies in a similar stage of development, including rapid technological change, dependence on key individuals, competition from other companies, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability, the need for development of commercially viable products, regulatory approval of products, uncertainty of market acceptance of products, and the need to obtain additional financing to fund the development of its product candidates. The Company has not completed development of any product candidate and has devoted substantially all of its financial resources and efforts to research and development, including preclinical and clinical development. The Company expects to continue to incur significant expenses and increasing operating losses for at least the next several years, and expects to require additional financial resources to advance its product candidates. Based upon

current plans, the Company projects that current cash resources will enable it to fund operations for at least twelve months beyond the filing date of the financial statements.

The Company has incurred annual net operating losses in every year since its inception. As of December 31, 2016, the Company had incurred losses since inception of $347.1 million. The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities, debt financings and funding from the United States government.

There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. The failure of the Company to obtain sufficient funds on acceptable terms when needed could have a material adverse effect on the Company's business, results of operations and financial condition.

(2) Summary of Significant Accounting Policies

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing its proprietary chemistry technology to create novel antibiotics for serious and life-threatening infections, including multidrug-resistant infections.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles ("GAAP") requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue and expenses, and related disclosures. On an ongoing basis, the Company's management evaluates its estimates, including estimates related to clinical trial accruals, stock-based compensation expense, contract and grant revenues, and expenses. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents and restricted cash. The Company maintains its cash and cash equivalent balances in the form of cash and money market accounts with financial institutions that management believes are creditworthy. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimize its exposure to concentration of credit risk. The Company has no financial instruments with off-balance-sheet risk of loss.

Principles of Consolidation

The condensed consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents at December 31, 2016 and 2015 consisted of cash and money market funds.

Fair Value Measurements

The Company's financial instruments consist principally of cash and cash equivalents, accounts receivable, accounts payable, and accrued liabilities. Fair value measurements are classified and disclosed in one of the following three categories:

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

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

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.

Financial instruments measured at fair value as of December 31, 2016 and 2015 are classified below based on the three fair value hierarchy tiers described above (in thousands):

		Fair Value Measurements at Reporting Date Using		
	Balance	Level 1	Level 2	Level 3
December 31, 2016				
Cash and money market funds	$142,086	$142,086	$ —	$ —
December 31, 2015				
Cash and money market funds	$205,912	$205,912	$ —	$ —

The Company measures cash equivalents at fair value on a recurring basis. The fair value of cash equivalents is determined based on “Level 1” inputs, which consist of quoted prices in active markets for identical assets.

Accounts Receivable

Accounts receivable at December 31, 2016 and 2015 represent amounts due from CUBRC Inc. (“CUBRC”), an independent, not for profit, research corporation that specializes in U.S. government-based contracts under the Company’s subcontracts under the National Institutes of Health’s (“NIH”) National Institute of Allergy and Infectious Diseases (“NIAID”) division contract awarded for the development of TP-271 (“NIAID Contract”) and the Biomedical Advanced Research and Development Authority (“BARDA”), an agency of the U.S. Department of Health and Human Services, contract awarded for the development of eravacycline as a potential countermeasure for the treatment of disease caused by bacterial biothreat pathogens (“BARDA Contract”) and under the Company’s subaward under a separate grant from the NIAID (“NIAID Grant”) (each, Note 3). The Company’s practice is to bill the prime contractor, CUBRC, amounts for which the Company has been invoiced by third parties in the case of contract research or subcontractor costs or for internal costs incurred. Expenses directly associated with the Company’s NIAID and BARDA Contracts and NIAID Grant that have been accrued at the end of the reporting period are not billed to the prime contractor until third-party invoices have been received or until internal costs have been paid. Unbilled accounts receivable, included in accounts receivable in the accompanying balance sheets, were $0.4 million and $2.2 million at December 31, 2016 and 2015, respectively.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation and amortization are recognized using the straight-line method over the estimated useful lives of the respective assets, which is generally three to five years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful economic lives of the related assets.

Restricted Cash

At December 31, 2016 and 2015, the Company had $199,000 in restricted cash deposits with a bank, of which $159,000 is collateral for a letter of credit issued to the landlord of the Company's leased facility. If the Company defaults on its rental obligations, $159,000 will be payable to the landlord. In addition, the Company has $40,000 in restricted cash to secure the Company's corporate credit card issued through the same bank.

Revenue Recognition

The Company's revenue is derived from its subcontracts with CUBRC under the BARDA Contract and the NIAID Contract and its subaward under the NIAID Grant (Note 3). The Company recognizes revenue under these best-efforts, cost-reimbursable and cost-plus-fixed-fee subcontracts and subaward as the Company performs services under the subcontracts and subaward so long as a subcontract and subaward has been executed and the fees for these services are fixed or determinable, legally billable and reasonably assured of collection. Recognized amounts reflect the Company's partial performance under the subcontracts and subaward and equal direct and indirect costs incurred plus fixed fees, where applicable. The Company does not recognize revenue under these arrangements for amounts related to contract periods where funding is not yet committed as amounts above committed funding thresholds would not be considered fixed or determinable or reasonably assured of collection. Revenues and expenses under these arrangements are presented gross on the condensed consolidated statements of operations and comprehensive loss as the Company has determined it is the primary obligor under these arrangements relative to the research and development services it performs as lead technical expert.

Revenue under the Company's subcontracts with respect to the BARDA Contract and NIAID Contract is earned under a cost-plus-fixed-fee contract through which the Company is reimbursed for direct costs incurred plus allowable indirect costs and a fixed fee earned. Billings under the Company's subcontracts under the BARDA Contract and NIAID Contract are based on approved provisional indirect billing rates that permit recovery of allowable fringe benefits, overhead and general and administrative expenses and a fixed fee.

Revenue under the Company's subaward with respect to the NIAID Grant is earned under a cost-reimbursable contract through which the Company is reimbursed for direct costs incurred plus allowable indirect costs. Billings under the Company's subaward under the NIAID Grant are based on approved provisional indirect billing rates that permit recovery of allowable fringe benefits and general and administrative expenses.

Research and Development Expenses

Research and development costs are charged to expense as incurred and include, but are not limited to:

- personnel-related expenses, including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that provide preclinical, clinical, regulatory and manufacturing services;
- payments made under the Company's license agreement with Harvard University;
- the cost of acquiring, developing and manufacturing clinical trial materials and lab supplies;
- facility, depreciation and other expenses, which include direct and allocated expenses for rent, maintenance of the Company's facilities, insurance and other supplies; and
- costs associated with preclinical, regulatory and medical affair activities.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development. In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

Comprehensive Loss

Comprehensive loss consists of net income or loss and changes in equity during a period from transactions and other events and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss for all periods presented.

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 difference between the financial reporting and the tax reporting basis of assets and liabilities and are measured using the enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized. The Company has evaluated available evidence and concluded that the Company may not realize the benefit of its deferred tax assets; therefore a valuation allowance has been established for the full amount of the deferred tax assets. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense.

Stock-Based Compensation

The Company determines equity-based compensation at the grant date using the Black-Scholes option pricing model to estimate fair value for employee equity awards. The Company recognizes the value of the award that is ultimately expected to vest as an expense on a straight-line basis over the requisite service period using the estimated fair market value of the stock. Any changes to the estimated forfeiture rates are accounted for prospectively. The Company records stock-based compensation expense for share-based payments issued to non-employees based on the fair value of the awards using the Black-Scholes option pricing model. Share-based payments issued to non-employees are revalued at each reporting period and as the equity instruments vest and are recognized as expense using the accelerated attribution method over the related service period.

Going Concern Assessment

Accounting Standards Update ("ASU") No. 2014-15, Presentation of Financial Statements - Going Concern, requires management to evaluate the company's ability to continue as a going concern one year beyond the filing date of the given financial statements. This evaluation requires management to perform two steps. First, management must evaluate whether there are conditions and events that raise substantial doubt about the entity's ability to continue as a going concern. Second, if management concludes that substantial doubt is raised, management is required to consider whether it has plans in place to alleviate that doubt. Disclosures in the notes to the financial statements are required if management concludes that substantial doubt exists or that its plans alleviate the substantial doubt that was raised.

Based on a detailed cash forecast incorporating current development activities and related spending plans, the Company expects its cash to last more than one year beyond the date that the financial statements were issued. Based on this analysis, no additional disclosures were required.

Recent Accounting Pronouncements Issued

In May 2014, the Financial Accounting Standard Board ("FASB") issued ASU No. 2014-09, Revenue from Contracts with Customers (Topic 606), which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. In August 2015, the FASB issued ASU No. 2015-14, Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date, which delayed the effective date of the new standard from January 1, 2017 to January 1, 2018. The FASB also agreed to allow entities to choose to adopt the standard as of the original effective date. FASB has subsequently issued ASU 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net); ASU 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing; ASU 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow- Scope Improvements and Practical Expedients; and ASU 2016-20, Technical

Corrections and Improvements to Topic 606, Revenue from Contracts with Customers. The Company is currently evaluating the potential impact that these updates may have on its financial position, results of operations and cash flows.

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842). The new standard requires that all lessees recognize the assets and liabilities that arise from leases on the balance sheet and disclose qualitative and quantitative information about its leasing arrangements. The new standard will be effective for the Company on January 1, 2019. The Company is currently evaluating the potential impact that this standard may have on its financial position, results of operations and cash flows.

In March 2016, the FASB issued ASU 2016-09, Improvements to Employee Share-Based Payment Accounting (“ASU 2016-09”). ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, forfeiture rates, and classification on the statement of cash flows. This guidance will be effective for annual reporting periods beginning after December 15, 2016, including interim periods within

those annual reporting periods, and early adoption is permitted. The Company adopted this ASU as of January 1, 2017. The adoption of this standard is expected to impact income tax footnote disclosures and stock compensation expense. Upon adoption of the standard, the Company expects to make a policy election to realize forfeitures as they occur. The Company expects to record a cumulative-effect adjustment to (1) increase additional paid-in capital and accumulated deficit as a result of recognizing forfeitures as they occur, and (2) increase the deferred tax asset, with an offsetting increase to the valuation allowance upon adoption.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments ("ASU 2016-15"). This new standard provides guidance to ensure consistency in how transactions are reflected in the statement of cash flows. ASU 2016-15 will be effective for the Company on January 1, 2018. The Company is currently evaluating the potential impact that this standard may have on its statements of cash flows.

In November 2016, the FASB issued ASU 2016-16, Intra-Entity Transfers of Assets Other Than Inventory ("ASU 2016-16"). ASU 2016-16 requires companies to account for the income tax effects of intercompany transfers of assets other than inventory (e.g., intangible assets) when the transfer occurs. ASU 2016-16 will be effective for the Company beginning January 1, 2018. The Company is currently evaluating the potential impact that this standard may have on its financial position, statements of operations and cash flows.

In November 2016, the FASB issued ASU 2016-18, Restricted Cash ("ASU 2016-18"). ASU 2016-18 clarifies how entities should present restricted cash and restricted cash equivalents in the statement of cash flows. The guidance will be applied retrospectively and will be effective for the Company beginning January 1, 2018. The Company is currently evaluating the potential impact that this standard may have on its financial position, statements of operations and cash flows.

Subsequent Events

On January 17, 2017, the Company entered into a Controlled Equity Offering Sales Agreement (the "Agreement"), with Cantor Fitzgerald & Co., as sales agent ("Cantor"). In accordance with the terms of Agreement, the Company may offer and sell through Cantor, from time to time, shares of its common stock up to an aggregate offering price of $40,000,000.

Under the Agreement, Cantor may sell shares of the Company's common stock by methods deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on The NASDAQ Global Select Market or on any other existing trading market for the Company's common stock.

The Company is not obligated to make any sales of shares of its common stock under the Agreement. The Company or Cantor may suspend or terminate the offering of shares of the Company's common stock upon notice to the other party and subject to other conditions. The Company will pay Cantor a commission rate equal to 3.0% of the gross proceeds per share sold. No shares have been sold to date via this facility.

Net Loss per Common Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of Common Stock outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, warrants, stock options, and restricted stock units are considered to be common stock equivalents and are only included in the calculation of

diluted net loss per share when their effect is dilutive.

The amounts in the table below were excluded from the calculation of diluted weighted-average shares outstanding, prior to the use of the treasury stock method, due to their anti-dilutive effect:

	Year Ended December 31,		
	2016	2015	2014
Warrants	1,103	1,103	1,103
Outstanding stock options	4,066,411	3,833,806	3,409,497
Unvested restricted stock units	254,378	308,875	-
Total	4,321,892	4,143,784	3,410,600

(3) Significant Agreements and Contracts

License Agreement

In August 2006, the Company entered into a license agreement for certain intellectual property with Harvard University (the "University"). Under the license agreement, as of December 31, 2016, the Company has paid the University an aggregate of $4.4 million in upfront license fees and development milestone payments, and has issued 31,379 shares of common stock to the University.

For each product covered by the license agreement, the Company is obligated to make certain payments totaling up to approximately $15.1 million upon achievement of certain development and regulatory milestones and to pay additional royalties on net sales of such product. In January 2007 and April 2010, the Company and the University amended the license agreement to include certain additional intellectual property. The Company paid an additional $25,000 to the University with each amendment. In February 2011, the license agreement was further amended to include additional intellectual property in the license granted by the University without the payment of any additional consideration.

Government Grant and Contracts

BARDA Contract for Eravacycline

The Company has received funding for its lead product candidate, eravacycline, under an award from BARDA. In January 2012, BARDA awarded a five-year contract that provides for up to a total of $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. The funding under the BARDA Contract is also being used for the development, manufacturing and clinical evaluation of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria.

In connection with the BARDA Contract, in February 2012, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on May 10, 2018 under which the Company may receive funding of up to approximately $41.6 million, reflecting the portion of the BARDA Contract funding that may be paid to the Company for its activities.

Although the BARDA Contract and the Company's subcontract with CUBRC under the BARDA Contract have terms which currently expire on May 10, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from Congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to the Company. Committed funding from CUBRC under the Company's BARDA subcontract is up to $41.6 million through May 10, 2018, the current contract end date, as a result of the exercise of several options by BARDA under the BARDA Contract. Total funds of $32.4 million had been received by the Company through December 31, 2016 under this contract. During the years ended December 31, 2016, 2015 and 2014, the Company recognized revenue of $2.9 million, $10.8 million and $6.9 million, respectively, from the Company's subcontract under the BARDA Contract.

NIAID Grant and Contract for TP-271

The Company has received funding for its preclinical compound TP-271 under two awards from NIAID for the development, manufacturing, and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired

bacterial pneumonia:

- the NIAID Grant awarded in July 2011 that provides up to a total of approximately $2.9 million over five years; and
- the NIAID Contract awarded in September 2011 that provides up to a total of approximately $35.8 million in funding over five years.

In connection with the NIAID Grant, in November 2011, CUBRC awarded the Company a no-fee subaward of approximately $0.9 million, reflecting the portion of the NIAID Grant funding that may be paid to the Company for its activities.

In connection with the NIAID Contract, in October 2011, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on December 31, 2018 under which the Company may receive funding of up to approximately $15.1 million, reflecting the portion of the NIAID Contract funding that may be paid to the Company for its activities.

Although the NIAID Contract and the Company's subcontract with CUBRC under the NIAID Contract have terms which currently expire on December 31, 2018, and the Company's subaward under the NIAID Grant has a term which currently expires on May 31, 2017, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond the respective expiration dates. To the extent that NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to the Company. As of December 31, 2016, committed funding from CUBRC under the Company's subcontract with respect to the NIAID Contract is $15.1 million, of which $10.4 million had been received through December 31, 2016. Committed funding from CUBRC under the Company's subaward with respect to the NIAID Grant is $0.9 million, of which $0.8 million had been received through December 31, 2016.

During the years ended December 31, 2016, 2015 and 2014, the Company recognized revenue of $2.2 million, $0.8 million, and $2.1 million, respectively, from the Company's subcontract under the NIAID Contract. During the years ended December 31, 2016, 2015 and 2014, the Company recognized revenue of $102,000, $157,000 and $135,000, respectively, from the Company's subaward under the NIAID Grant.

(4) Property and Equipment

Property and equipment at December 31, 2016 and 2015 consisted of the following (in thousands):

	Estimated Useful Life	December 31,	
	In Years	2016	2015
Laboratory equipment	5	$2,358	$2,087
Furniture and fixtures	5	509	484
Office and computer equipment	3	232	159
Leasehold improvements		915	891
Property and equipment, gross		4,014	3,621
Less accumulated depreciation and amortization		(2,960)	(2,678)
Property and equipment, net		$1,054	$943

Depreciation and amortization expense for the years ended December 31, 2016, 2015 and 2014 was $282,000, $193,000 and $124,000, respectively.

(5) Accrued Expenses

Accrued expenses at December 31, 2016 and 2015 consisted of the following (in thousands):

	December 31, 2016	December 31, 2015
Drug supply and development	$ 2,698	$ 2,971
Salaries and benefits	2,498	1,856
Clinical trial related	1,129	677
Professional fees	965	684
Preclinical	163	303
Other	232	440
Total	$ 7,685	$ 6,931

(6) Long-Term Debt

In May 2011, the Company executed a Loan and Security Agreement with Silicon Valley Bank and Oxford Finance (the “Term Loan”), which originally provided for up to $8.0 million of funding, to be made available in two tranches. The Term Loan was paid in full on March 31, 2015.

In December 2012, the Company amended the Term Loan (the “2012 Term Loan”) to provide for up to an additional $9.2 million in funding, to be made available in two tranches. On March 31, 2015, the Company repaid the 2012 Term Loan. As a result, no indebtedness remains outstanding under either the Term Loan or the 2012 Term Loan.

(7) Warrants

In May 2011, December 2012 and February 2013, the Company issued warrants to purchase an aggregate of 2,987,164 shares of Series C Preferred Stock in connection with the Term Loan and the 2012 Term Loan (Note 6).

Upon completion of the Company's IPO, the warrants became exercisable for an aggregate of 103,004 shares of the Company's common stock.

On June 23, 2014, Silicon Valley Bank exercised its warrants under the Term Loan and 2012 Term Loan described above pursuant to the cashless exercise feature of the warrants. In connection with the exercise of the warrants the Company issued an aggregate of 23,720 shares of the Company's common stock to Silicon Valley Bank. Warrants held by Silicon Valley Bank to purchase an aggregate of 27,782 shares of common stock were cancelled as payment for the aggregate exercise price of the warrants.

On December 13, 2014, Oxford Finance exercised its warrants under the Term Loan and 2012 Term Loan described above pursuant to the cashless exercise feature of the warrants. In connection with the exercise of the warrants, the Company issued an aggregate 39,337 shares of the Company's common stock to Oxford Finance. Warrants to purchase an aggregate of 12,165 shares of common stock were cancelled as payment for the aggregate exercise price of the warrants.

(8) Stockholders' Equity

2014 Follow-on Public Offering

In October 2014, the Company sold 4,542,500 shares of common stock in a follow-on public offering at a price to the public of $19.00 per share, resulting in net proceeds to the Company of $80.8 million after deducting underwriting discounts and commissions of $5.2 million and offering costs of $0.4 million.

2015 Follow-on Public Offering

In March 2015, the Company sold 4,945,000 shares of common stock in a follow-on public offering at a price to the public of $35.00 per share, resulting in net proceeds to the Company of $162.2 million after deducting underwriting discounts and commissions of $10.4 million and offering costs of $0.5 million.

(9) Stock-based Compensation

In February 2013, the Company's board of directors and stockholders approved, effective upon the closing of the IPO, the 2013 Stock Incentive Plan (the "2013 Plan"). Under the 2013 Plan, the Company may grant incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards for the purchase of that number of shares of Common Stock equal to the sum of (i) 1,688,777 shares of Common Stock, (ii) 258,265 shares of Common Stock that were reserved for issuance under the 2006 Plan that remained available for issuance under the 2006 Plan upon the closing of the IPO, (iii) any shares of Common Stock subject to awards under the 2006 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 2013 Plan is subject to automatic annual increases, to be added on January 1 of each year from January 1, 2014 through and including January 1, 2023, equal to the number of shares that is the lesser of (a) 3,000,000, (b) 4% of the then outstanding shares of Common Stock or (c) an amount determined by the Company's board of directors. In January 2014, the number of shares authorized for issuance under the 2013 Plan increased by 1,025,171 shares. In January 2015, the number of shares authorized for issuance under the 2013 Plan increased by 1,232,232 shares. In January 2016, the number of shares authorized for issuance under the 2013 Plan increased by 1,463,391 shares. As of December 31, 2016, 1,354,464 shares were available for future issuance under the 2013 Plan. In January 2017, the number of shares authorized for issuance under the 2013 Plan increased by 1,477,677 shares.

Terms of stock award agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2013 Plan. Options granted by the Company typically vest over a four year period. Certain of the options are subject to acceleration of vesting in the event of certain change of control transactions. The options are exercisable from the date of grant for a period of ten years. For options granted prior to the Company's IPO, the exercise price equaled the estimated fair value of the Common Stock as determined by the board of directors on the date of grant. For options granted subsequent to the Company's IPO, the exercise price equaled the closing price of the Company's stock on the NASDAQ Global Select Market on the date of grant.

Stock option activity at December 31, 2016 and changes during the year then ended are presented in the table and narrative below (in thousands, except share and per share data):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Options outstanding at December 31, 2015	3,833,806	$ 22.72	7.80	$ 5,439
Granted	1,343,825	7.53		
Exercised	(93,447)	1.57		
Canceled	(1,017,773)	21.78		
Options outstanding at December 31, 2016	4,066,411	$ 18.42	7.62	$ 687
Options vested or expected to vest at December 31, 2016 (1)	3,798,989	$ 18.41	7.54	$ 680
Options exercisable at December 31, 2016	2,051,692	$ 16.96	6.78	$ 650

(1) This represents the number of vested options as of December 31, 2016, plus the number of unvested options that the Company estimated as of December 31, 2016 would vest, based on the unvested options at December 31, 2016, as adjusted for the estimated forfeiture rate.

The aggregate intrinsic value in the table above represents the difference between the Company's closing common stock price on the last trading day during the year ended December 31, 2016 and the exercise price of the options, multiplied by the number of in-the-money options. The total intrinsic value of options exercised in the years ended December 31, 2016, 2015, and 2014 was $0.3 million, $27.0 million and $8.1 million, respectively. As of December 31, 2016, there was $18.4 million of total unrecognized stock-based compensation cost related to employee and non-employee unvested stock options granted under the 2006 Plan and the 2013 Plan. Total unrecognized compensation cost will be adjusted for future forfeitures. The Company expects to recognize that cost over a remaining weighted-average period of 2.3 years.

Since the Company completed its IPO on March 25, 2013, it has not had sufficient historical data to support a calculation of volatility and expected life. As such, the Company has used a weighted-average volatility considering the Company's own volatility and the volatilities of a representative group of publicly traded companies. For purposes of identifying similar entities, the Company selected a group of publicly traded life science/biotechnology companies based on their disease focus, stage of development, number of compounds in clinical trials and number of years as a publicly-traded company. The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant, commensurate with the expected life assumption. The expected life of stock options granted represents the weighted-average period of time that stock options granted are expected to be outstanding determined using the simplified method for employee grants. For non-employee grants, the expected life is equal to the remaining contractual term. The expected life is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population.

The Company estimates the fair value of each employee and director stock option award on the grant date using the Black-Scholes option-pricing model based on the following assumptions:

	Year Ended December 31,		
	2016	2015	2014
Volatility factor	85.77-87.82%	87.82-95.34%	53.41-58.13%
Expected life (in years)	5.31-6.11	5.31-6.11	5.31-6.11
Risk-free interest rate	1.25%-2.10%	1.50%-1.94%	1.71%-2.13%
Dividend yield	0%	0%	0%

Compensation cost for stock options and restricted stock units granted to employees is based on the estimated grant-date fair value and is recognized over the vesting period of the applicable option on a straight-line basis. Stock-based compensation expense related to stock options and restricted stock units granted to employees was $13.2 million, $12.6 million, and $4.0 million during the years ended December 31, 2016, 2015, and 2014, respectively. The amount of stock-based compensation expense recognized during a period is based on the value of the portion of the awards that the Company determines are expected to vest. Forfeitures are required to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term “forfeitures” is distinct from “cancellations” and represents only the unvested portion of the surrendered option. The Company re-evaluates this analysis quarterly, and adjusts the forfeiture rate as necessary. Ultimately, the actual expense recognized over the vesting period will only be for those options that vest.

Using the Black-Scholes option-pricing model, the weighted-average grant date fair values of options granted to employees for the years ended December 31, 2016, 2015 and 2014 was $7.53, $22.78 and $7.54, respectively.

Stock-based compensation expense recognized in the Company’s consolidated statements of operations during the periods presented was as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Research and development	$6,661	$5,906	$1,845
General and administrative	6,484	5,710	3,385
Total (includes employee and non-employee stock compensation)	$13,145	$11,616	$5,230

Stock Option Grants to Non-employees

During the year ended December 31, 2014, the Company granted nonqualified options to purchase 110,000 shares of common stock to non-employee consultants, with an average exercise price of $12.56 per share. During the years ended December 31, 2016 and 2015, respectively, 25,000 and 75,000 stock options to non-employee consultants were canceled. There were no stock options granted to non-employee consultants during the years ended December 31, 2016 and 2015. The Company initially valued these options using the Black-Scholes option-pricing model and revalues the options at each reporting period and as the equity instruments vest and are recognized as expense using the accelerated attribution method over the related service period. The re-measurement of these non-employee stock options resulted in a reversal of expense of $12,000 and $1.0 million, for the years ended December 31, 2016 and 2015, respectively and resulted in expense of $1.2 million for the year ended December 31, 2014. Stock-based compensation expense for the year ended December 31, 2016 was estimated using the Black-Scholes option pricing model with the following assumptions: risk-free interest rate of 1.22%; dividend rate of 0%; expected volatility of 88.83%; and an expected term of 8.0 years. Stock-based compensation expense for the year ended December 31, 2015 was estimated using the Black-Scholes option pricing model with the following assumptions: risk-free interest rate of 2.17%; dividend rate of 0%; expected volatility of 86.02%; and an expected term of 8.6 years.

Restricted Stock Units

The restricted stock activity for the year ended December 31, 2016 is as follows:

	Shares	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2015	308,875	$ 7.81
Granted	296,680	8.47
Cancelled	(146,177)	8.00
Vested/Released	(205,000)	7.81
Unvested at December 31, 2016	254,378	$ 8.47

As of December 31, 2016, there was $1.2 million of total unrecognized stock-based compensation expense related to restricted stock units granted under the Plan. The expense is expected to be recognized over a weighted-average period of 2.0 years.

(10) Employee Stock Purchase Plan

On February 27, 2014, upon the recommendation of the Company's compensation committee, the Company's board of directors adopted, subject to stockholder approval, the 2014 Employee Stock Purchase Plan (the "ESPP") pursuant to which the Company may sell up to an aggregate of 300,000 shares of Common Stock. The ESPP was approved by the Company's stockholders on June 12, 2014. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each period during the term of the ESPP. The offering periods are six months each from August to November and from November to May of each calendar year. Pursuant to the ESPP, the Company sold a total of 58,702 shares of common stock during the year ended December 31, 2016 under the ESPP at purchase prices of $2.95, and $3.32, respectively, which represented 85% of the closing price of the Company's common stock on May 13, 2016, and November 14, 2016, respectively. Pursuant to the ESPP, the Company sold a total of 16,422 shares of common stock during the year ended December 31, 2015 under the ESPP at purchase prices of $19.29, and $9.30, respectively, which represented 85% of the closing price of the Company's common stock on May 14, 2015, and November 14, 2015, respectively. Pursuant to the ESPP, the Company sold a total of 8,394 shares of common stock during the year ended December 31, 2014 at a purchase price of $9.88, which represented 85% of the closing price of the Company's common stock on August 15, 2014. The Company records stock-based compensation expense under the ESPP based on the fair value of the purchase rights using the Black-Scholes option pricing model. The total stock-based compensation expense recorded as a result of the ESPP was $158,000, $156,000, and $46,000 during the years ended December 31, 2016, 2015 and 2014, respectively.

(11) Income Taxes

The Company accounts for income taxes under ASC 740, Accounting for Income Taxes. Deferred income tax assets and liabilities are determined based upon differences between financial reporting and 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.

Loss before income tax (benefit) provision consists of the following (in thousands):

	Year ended December 31,		
	2016	2015	2014
United States	$(62,536)	$(64,037)	$(66,742)
Foreign	(14,944)	(19,152)	—
Total loss before income taxes	$(77,480)	$(83,189)	$(66,742)

For the years ended December 31, 2016, 2015 and 2014 the Company did not have a current or deferred income tax expense or benefit.

A reconciliation of the Federal statutory tax rate of 34% to the Company's effective income tax rate follows:

	Year ended

	December 31,		
	2016	2015	2014
Statutory tax rate	(34.00)%	(34.00)%	(34.00)%
State taxes, net of Federal benefits	(4.19)%	(4.02)%	(5.28)%
Permanent differences	1.19 %	0.71 %	0.61 %
Credits	(1.47)%	(1.65)%	(2.34)%
Change in valuation allowance	29.78 %	30.74 %	39.87 %
Foreign rate differential	6.56 %	7.03 %	—
Other	2.13 %	1.19 %	1.14 %
Effective tax rate	— %	— %	— %

As of December 31, 2016 the Company had federal net operating loss carryforwards of approximately $275.8 million and state net operating loss carryforwards of $242.3 million, which are available to reduce future taxable income. The federal net operating loss carryforwards exclude approximately $26.9 million of deductions related to the exercise of stock options. This amount represents an excess tax benefit and has not been included in the gross deferred tax asset reflected for net operating losses. The Company will adopt ASU 2016-09, Improvements to Employee Share-Based Payment Accounting, during the quarter ended March 31, 2017, upon which the net operating loss carryforward deferred tax assets will be increased by the excess tax benefits with a corresponding increase to the

Company's valuation allowance. The Company does not believe that the adoption of ASU 2016-09 will have a material impact to the Company's income statement, balance sheet, or retained earnings.

The Company also had federal tax credits of $6.2 million and state tax credits of $2.2 million, which may be used to offset future tax liabilities. The net operating loss (NOL) and tax credit carryforwards will expire at various dates through 2036. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not, as yet, conducted a study of research and development ("R&D") credit carryforwards. This study may result in an adjustment to the Company's R&D credit carryforwards.

The principal components of the Company's deferred tax assets are as follows (in thousands):

	Year ended December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carry forwards	$106,560	$86,880
Equity-based compensation	6,937	4,636
Other temporary differences	1,235	1,280
Research and development credit and carry forwards	7,682	6,543
Deferred tax assets	122,414	99,339
Less valuation allowance	(122,414)	(99,339)
Net deferred tax assets	$—	$—

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported, if based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2016 and 2015, respectively, because the Company's management has determined that is it more likely than not that these assets will not be realized. The $23.1 million increase in the valuation allowance in 2016 primarily relates to the net loss incurred by the Company.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statement by prescribing the minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return. The Company had gross tax-effected unrecognized tax benefits of $1.0 million and $0.8 million at December 31, 2016 and 2015, respectively. Unrecognized tax benefits represent tax positions for which reserves have been established. A full valuation allowance has been provided against the Company's deferred tax assets, so that the effect of any unrecognized tax benefits would simply be to reduce the gross amount of the deferred tax asset and the corresponding valuation allowance. The Company anticipates that the amount of unrecognized tax benefits recorded will not change in the next twelve months.

As of December 31, 2016 and 2015, the Company had no accrued interest or penalties related to uncertain tax positions.

The aggregate changes in gross unrecognized tax benefits during the years ended December 31, 2015, 2014, and 2013 were as follows (in thousands):

	Year ended December 31,		
	2016	2015	2014
Balance at beginning of year	$822	—	—
Increases for tax positions taken during current period	145	249	—
Increases for tax positions taken in prior periods	—	573	—
Decreases for tax positions taken during current period	—	—	—
Decreases for tax positions taken in prior periods	—	—	—
Balance at end of year	$967	$822	—

The Company is currently open to examination under the statute of limitations by the Internal Revenue Service and state jurisdictions for the tax years ended 2013 through 2015. Carryforward tax attributes generated in years past may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

(12) Commitments and Contingencies

Lease Commitments

On March 24, 2015, the Company amended its existing operating lease to expand its existing premises by an additional 13,711 square feet of office and laboratory space for a total of 29,610 square feet. The effective date of this amendment was April 1, 2015. On March 31, 2015, the Company canceled an existing sublease entered into in September 2014 covering 15,174 square feet of office and laboratory space.

On June 18, 2015, the Company further amended its existing operating lease to expand its leased premises by an additional 7,828 square feet of office and laboratory space for a total of 37,438 square feet. The lease for the additional office and laboratory space was effective as of August 1, 2015. In connection with the amendment, the lease term was extended from November 30, 2016 to November 30, 2019.

In the third quarter of 2016, the Company entered into a sublease with respect to a portion of its principal facilities with an unrelated third party. The term of the sublease expires in November 2019, with the sublessee obligated to pay rent to the Company that approximates the rent the Company is currently paying to its landlord with respect to such portion of its facility.

As of December 31, 2016, the aggregate minimum future rent payments under the lease agreement, net of the sublease agreement, are as follows (in thousands):

	December 31, 2016
2017	1,701
2018	1,752
2019	1,650
Total minimum lease payments	$ 5,103

The Company recorded $1.6 million, $1.7 million and $1.0 million in rent expense for the years ended December 31, 2016, 2015 and 2014, respectively.

Litigation

In January 2016 and March 2016, two securities class action lawsuits were filed against the Company, its chief executive officer, its former chief operating officer and its former chief financial officer in the United States District Court for the District of Massachusetts. In May 2016, the court consolidated the two lawsuits and appointed lead plaintiffs and lead counsel. The lead plaintiffs filed a consolidated amended complaint in July 2016 and filed a second consolidated amended complaint in August 2016. The second amended complaint is brought on behalf of an alleged class of those who purchased the Company's common stock between March 5, 2015 and September 8, 2015, and alleges claims arising under Sections 10 and 20 of the Securities Exchange Act of 1934, as amended. Each complaint generally alleges that the defendants violated the federal securities laws by, among other things, making material misstatements or omissions concerning IGNITE2. The complaint seeks, among other relief, unspecified compensatory damages, attorneys' fees, and costs. In October 2016, defendants filed a motion to dismiss the second amended complaint in its entirety, which plaintiffs have opposed. That motion is pending. The Company believes it has valid defenses against these claims, and will engage in a vigorous defense of such litigation.

In addition, in May 2016, Donald Britton filed a shareholder derivative complaint against the Company's chief executive officer, its former chief operating officer, its former chief financial officer, all the members of the Company's current board of directors, a former board member, and against the Company as nominal defendant, in Massachusetts Superior Court (Suffolk County). The complaint generally alleges that the individual defendants breached fiduciary duties owed to the Company and its shareholders by disseminating materially false and misleading statements to the market concerning IGNITE2. The complaint purports to assert derivative claims against the individual defendants for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, and waste of corporate assets, and seeks to recover on behalf of the Company for any liability the Company incurs as a result of the individual defendants' alleged misconduct. The complaint seeks declaratory, equitable and monetary relief, an

unspecified amount of damages, with interest, and attorney's fees and costs. In August 2016, this action was dismissed by the Massachusetts Superior Court without prejudice due to plaintiff's failure to perfect service of process in a timely manner.

In the Company's opinion, it is not possible to predict the final outcome of these proceedings, nor is any potential liability estimable at this time.

(13) Employee Benefit Plan

In 2007, the Company established the Tetraphase Pharmaceuticals, Inc. 401(k) Plan (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. During 2014, the Company began to make matching contributions of 50% of the first 6% of employee contributions. The Company made matching contributions of $311,000, $261,000, and $84,000 for the years ended December 31, 2016, 2015, and 2014, respectively.

(14) Quarterly Results (Unaudited)

	Three Months Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(in thousands, except per share data) (unaudited)			
Revenue	$1,962	$1,243	$850	$1,090
Operating expenses	18,776	18,505	22,048	23,646
Loss from operations	(16,814)	(17,262)	(21,198)	(22,556)
Other income (expense), net	73	94	88	95
Net loss	$(16,741)	$(17,168)	$(21,110)	$(22,461)
Net loss per share—basic and diluted	$(0.46)	$(0.47)	$(0.58)	$(0.61)

	Three Months Ended			
	March 31, 2015	June 30, 2015	September 30, 2015	December 31, 2015
	(in thousands, except per share data) (unaudited)			
Revenue	$3,016	$3,343	$2,856	$2,471
Operating expenses	23,776	29,396	20,909	20,603
Loss from operations	(20,760)	(26,053)	(18,053)	(18,132)

Other expense, net	(226)	10	9	16
Net loss	$(20,986)	$(26,043)	$(18,044)	$(18,116)
Net loss per share—basic and diluted	$(0.66)	$(0.72)	$(0.49)	$(0.50)

ITEM 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

ITEM 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Vice President of Finance, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2016. In designing and evaluating our disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Vice President of Finance concluded that as of December 31, 2016, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer

by others, particularly during the period in which this annual report on Form 10-K was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

The certifications of our principal executive officer and principal financial officer attached as Exhibits 31.1 and 31.2 to this report include, in paragraph 4 of such certifications, information concerning our disclosure controls and procedures and internal controls over financial reporting.

Internal Control Over Financial Reporting

(a) Management's Report on Internal Control Over Financial Reporting

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

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

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013 framework) (COSO). Based on its assessment, management believes that, as of December 31, 2016, our internal control over financial reporting is effective at the reasonable assurance level.

Ernst and Young LLP, our independent registered public accounting firm has audited the consolidated financial statements included in this Annual Report on Form 10-K and, as part of the audit, has issued a report on the effectiveness of our internal control over financial reporting as of December 31, 2016, which report is included herein.

(b) Report of Independent Registered Public Accounting Firm on Internal Control over Financial Reporting

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of

Tetraphase Pharmaceuticals, Inc.

We have audited Tetraphase Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Tetraphase Pharmaceuticals, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

In our opinion, Tetraphase Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2016 of Tetraphase Pharmaceuticals, Inc. and our report dated March 13, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young

Boston, Massachusetts

March 13, 2017

(c) Changes in Internal Control Over Financial Accounting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2016 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 10 will be contained in the sections entitled “Election of Directors” and “Section 16(a) Beneficial Ownership Reporting Compliance” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item concerning our code of ethics is set forth in the section entitled “Code of Business Conduct and Ethics” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item relating to executive officers is set forth in the section entitled “Executive Officers” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 11. Executive Compensation

The information required by this Item 11 will be contained in the sections entitled “Executive and Director Compensation,” “Compensation Committee Interlocks and Insider Participation” and “Compensation Committee Report” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item 12 will be contained in the sections entitled “Ownership of Our Common Stock” and “Executive and Director Compensation—Equity Compensation Plan Information” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 13. Certain Relationships and Related Person Transactions, and Director Independence

The information required by this Item 13 will be contained in the sections entitled “Certain Relationships and Related Person Transactions” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein.

ITEM 14. Principal Accounting Fees and Services

The information required by this Item 14 will be contained in the section entitled “Corporate Governance—Principal Accountant Fees and Services” appearing in the definitive proxy statement we will file in connection with our 2017 Annual Meeting of Stockholders and is incorporated by reference herein.

PART IV

ITEM 15. Exhibits and Financial Statement Schedules

(a) Documents filed as part of Form 10-K.

(1) Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

(3) Exhibits

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

ITEM 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

TETRAPHASE PHARMACEUTICALS, INC.

Date: March 13, 2017 By: /s/ Guy Macdonald
Guy Macdonald

President & Chief Executive Officer

(Principal Executive Officer)

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

Signature	Title	Date
/s/ Guy Macdonald Guy Macdonald	Director, President and Chief Executive Officer (Principal Executive Officer)	March 13, 2017
/s/ Christopher Watt Christopher Watt	Senior Vice President, Finance (Principal Financial and Accounting Officer)	March 13, 2017
/s/ L. Patrick Gage L. Patrick Gage, Ph.D.	Chairman	March 13, 2017
/s/ Garen Bohlin Garen Bohlin	Director	March 13, 2017
/s/ Jeffrey A. Chodakewitz Jeffrey A. Chodakewitz	Director	March 13, 2017
/s/ John G. Freund John G. Freund	Director	March 13, 2017
/s/ Geraldine Henwood Geraldine Henwood	Director	March 13, 2017
/s/ Nancy Wysenski Nancy Wysenski	Director	March 13, 2017

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EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference from Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number
3.1	Restated Certificate of Incorporation of the Registrant	10-Q	001-35837	5/13/13	3.1
3.2	Amended and Restated Bylaws of the Registrant	10-Q	001-35837	5/13/13	3.2
4.1	Specimen certificate evidencing shares of common stock	S-1/A	333-186574	3/5/13	4.1
10.1#	2006 Stock Incentive Plan, as amended	S-1	333-186574	2/11/13	10.5
10.2#	Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan	S-1	333-186574	2/11/13	10.6
10.3#	Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan	S-1	333-186574	2/11/13	10.7
10.4#	2013 Stock Incentive Plan	S-1/A	333-186574	3/5/13	10.8
10.5#	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-186574	3/5/13	10.9
10.6#	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-186574	3/5/13	10.10
10.7*	Form of Restricted Stock Agreement under 2013 Incentive Plan				
10.8#	2014 Employee Stock Purchase Plan	10-Q	001-35837	8/12/14	10.1
10.9#	Form of Nonstatutory Option Agreement for Inducement Grants	10-Q	001-35837	5/7/2015	10.3
10.10#	Offer letter, dated as of December 4, 2007, by and between the Registrant and Guy Macdonald, as amended	S-1	333-186574	2/11/13	10.11
10.11#	Second Amendment to Offer Letter, dated as of March 5, 2014, by and between the Registrant and Guy Macdonald	10-Q	001-35837	5/12/14	10.2
10.12#*	Offer letter, dated as of June 11, 2015, by and between the Registrant and Jacques Dumas, as amended				

10.13#	Offer letter, dated as of December 22, 2010, by and between the Registrant and Patrick T. Horn	S-1	333-186574	2/11/13	10.13
10.14#	Amendment to Offer Letter, dated March 5, 2014, by and between the Registrant and Patrick Horn	10-Q	001-35837	5/12/14	10.4
10.15#	Offer letter, dated as of February 16, 2015, by and between the Registrant and Maria Stahl	10-Q	001-35837	5/7/15	10.2

Exhibit Number	Description	Incorporated by Reference from Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number
10.16#	Offer letter, dated as of June 19, 2015, by and between the Registrant and Christopher Watt	10-K	001-35837	3/25/16	10.17
10.17#	Form of Indemnification Agreement entered into between the Registrant and each of its directors and executive officers	S-1/A	333-186574	3/5/13	10.27
10.18	Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended on September 9, 2011, March 15, 2012, September 18, 2012, November 20, 2013, March 24, 2015 and June 18, 2015	10-Q	001-35837	8/6/15	10.1
10.19	Amendment, dated September 4, 2014, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended	10-Q	001-35837	11/10/14	10.1
10.20	Amendment, dated March 24, 2015, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended.	10-Q	001-35837	5/7/2015	10.1
10.21	Amendment, dated June 18, 2015, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended.	10-Q	001-35837	8/6/2015	10.1
10.22†	License Agreement, dated as of August 3, 2006, by and between the Registrant and the President and Fellows of Harvard College, as amended	S-1	333-186574	2/11/13	10.20
10.23†	Subcontract Agreement, dated as of February 1, 2012, by and between the Registrant and CUBRC, Inc.	S-1	333-186574	2/11/13	10.21
10.24†	Subcontract Agreement, dated as of September 30, 2011, by and between the Registrant and CUBRC, Inc.	S-1	333-186574	2/11/13	10.22
10.25	Second Amended and Restated Registration Rights Agreement, dated as of May 14, 2010, as amended	S-1	333-186574	2/11/13	10.1
10.26	Warrant to purchase shares of Series A Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank expiring on September 27, 2017	S-1	333-186574	2/11/13	10.2
10.27		S-1	333-186574	2/11/13	10.18

	Loan and Security Agreement, dated as of May 16, 2011, among the Registrant, Tetraphase Securities Corporation, Silicon Valley Bank and Oxford Finance LLC				
10.28	First Amendment to Loan and Security Agreement, dated December 20, 2012, by and among the Registrant, Tetraphase Securities Corporation, Silicon Valley Bank and Oxford Finance LLC	S-1	333-186574	2/11/13	10.23
10.29	Consent and Second Amendment to Loan and Security Agreement, dated December 1, 2014, by and among the Registrant, Tetraphase Securities Corporation, Silicon Valley Bank, Oxford Finance LLC, the other Lenders named therein, and Silicon Valley Bank, as agent for the Lenders	10-K	001-35837	3/6/15	10.26

Exhibit Number	Description	Incorporated by Reference from Registrant's Form	File No.	Date Filed with the SEC	Exhibit Number
10.30	Consent and Third Amendment to Loan and Security Agreement, dated December 18, 2014, by and among the Registrant, Tetraphase Securities Corporation, Silicon Valley Bank, Oxford Finance LLC, the other Lenders named therein, and Silicon Valley Bank, as agent for the Lenders	10-K	001-35837	3/6/15	10.27
21.1*	Subsidiaries of the Registrant				
23.1*	Consent of Ernst & Young LLP				
31.1*	Chief Executive Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
31.2*	Principal Financial Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
32.1*	Chief Executive Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
32.2*	Principal Financial Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
101.INS*	XBRL Instance Document				
101.SCH*	XBRL Taxonomy Extension Schema Document				
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document				
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document				

* Filed herewith.
# Indicates management contract or compensatory plan or arrangement.
† Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.