TETRAPHASE PHARMACEUTICALS INC

FORM 10-K
(Annual Report)

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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, 2013

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: 001-34655

TETRAPHASE PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

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

480 Arsenal Street, Suite 110
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 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 Market at the close of business on June 28, 2013, was $119,444,895. 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 February 28, 2014: 25,790,396

Documents incorporated by reference:

Portions of our definitive proxy statement for our 2014 annual meeting of stockholders are incorporated by reference into Part III of this annual report on Form 10-K.

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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 subsidiary, and "our board of directors" refers to the board of directors of Tetraphase Pharmaceuticals, Inc.

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," "project," "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. Our lead product candidate, eravacycline, is a fully synthetic tetracycline derivative that we are developing as a broad-spectrum intravenous and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant Gram-negative infections. We initiated a Phase 3 clinical trial of eravacycline with intravenous administration for the treatment of complicated intra-abdominal infections, or cIAI, during the third quarter of 2013. We also initiated and are currently screening patients for a second Phase 3 clinical trial of eravacycline for the treatment of complicated urinary tract infections, or cUTI, with intravenous-to-oral step-down therapy, during the first quarter of 2014. We expect to have top-line data from the Phase 3 cIAI clinical trial in the first quarter of 2015, data from a lead-in portion of the Phase 3 cUTI clinical trial in mid-2014 and top-line data from the Phase 3 cUTI clinical trial in mid-2015. 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, we expect that positive results from these two Phase 3 clinical trials would be sufficient to support submission of a new drug application, or NDA, for eravacycline in the treatment of cIAI and cUTI. If we complete the Phase 3 clinical trials of eravacycline when we anticipate and the trials are successful, we expect to submit an NDA to the FDA in the second half of 2015 and a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, in the first half of 2016.

In our Phase 2 clinical trial of eravacycline monotherapy for the treatment of cIAI, eravacycline administered intravenously and dosed once or twice per day demonstrated a favorable safety and tolerability profile and a high cure rate, including against multidrug-resistant Gram-negative, Gram-positive and anaerobic 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* , the species of Gram-negative bacteria that killed seven patients at the Clinical Center of the National Institutes of Health in 2012. Multidrug-resistant *Klebsiella pneumoniae* is one of the carbapenem-resistant *Enterobacteriaceae* listed as an urgent threat by the Centers for Disease Control and Prevention, or CDC, in a September 2013 report. Gram-negative bacteria that are resistant to all 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 intravenous-to-oral step-down 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. The FDA has designated the intravenous formulation of eravacycline as a qualified infectious disease product, making it eligible for fast track designation and priority review by the FDA as well as an additional five years of U.S. market exclusivity if eravacycline receives marketing approval from the FDA.

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.

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 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. 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. We own exclusive worldwide rights to these compounds and our technology.

We have designed our 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-spectrum coverage of multidrug-resistant infections, including multidrug-resistant Gram-negative infections. Our program is consistent with the draft guidance issued by the FDA for drug development for cIAI and cUTI. The cIAI guidance indicates that, for companies developing a drug for cIAI and an additional indication caused by similar bacterial pathogens, such as cUTI, a single trial in cIAI and a single trial in that additional indication could be sufficient to provide evidence of effectiveness in both indications.

In the third quarter of 2013, we initiated a global, multi-center, randomized, double-blind, double-dummy Phase 3 clinical trial to assess the efficacy, safety and pharmacokinetics of eravacycline compared to ertapenem in patients with cIAI. We plan to enroll 536 patients in the trial at approximately 100 clinical sites worldwide. These patients will be randomized into two arms on a 1:1 basis. Patients in the eravacycline arm will receive 1.0 mg/kg of eravacycline administered intravenously twice per day. Patients in the ertapenem arm will receive 1.0 g of ertapenem administered intravenously once per day. We have designed the trial as a non-inferiority study. The primary endpoint of the trial is clinical response at the test-of-cure visit in the microbiological intent-to-treat, or micro-ITT, patient population in the trial. The micro-ITT population consists of all randomized patients in the trial who have baseline bacterial pathogens that cause cIAI and against which the dosed eravacycline has antibacterial activity.

In the first quarter of 2014, we initiated and are currently screening patients for a two-part, multi-center, randomized, double-blind clinical trial to assess the efficacy and safety of eravacycline compared with levofloxacin in the treatment of cUTI. We plan to enroll 120 patients in the lead-in portion of the trial. These patients will be randomized into three arms on a 1:1:1 basis receiving 1.5 mg/kg of eravacycline intravenously every 24 hours followed by 200 mg of eravacycline orally every 12 hours, 1.5 mg/kg of eravacycline intravenously every 24 hours followed by 250 mg of eravacycline orally every 12 hours or 750 mg of levofloxacin intravenously every 24 hours followed by 750 mg of levofloxacin orally every 24 hours. Following treatment of the 120 patients, we plan to evaluate primary efficacy, safety and tolerability endpoints to determine the dose regimen for eravacycline to be studied in the second portion of the trial. We then plan to enroll 720 patients who will be randomized on a 1:1 basis to receive the selected dose regimen of eravacycline or the levofloxacin dose regimen. We have designed the second portion of the trial as a non-inferiority study. The primary endpoint of the second portion of the trial is clinical and microbiological response in the micro-ITT population approximately seven days after completion of treatment.

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 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, which we refer to as the BARDA Contract. These awards also include a contract for up to $36 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, a preclinical compound that we are developing for respiratory diseases caused by bacterial biothreat pathogens, which we refer to as the NIAID Contract. 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 $39.8 million reflecting the portion of the BARDA Contract funding that may be paid to us for our activities, and up to approximately $13.3 million reflecting the portion of the NIAID Contract funding that may be paid to us for our activities. The BARDA Contract includes funding for some of the activities that we would otherwise be required to fund on our own in connection with any NDA filing for eravacycline.

In addition to eravacycline and TP-271, we are pursuing the discovery and development of additional antibiotics to target unmet medical needs, including multidrug-resistant Gram-negative bacteria. Any efforts by us with respect to these programs will be subject to the availability of resources not allocated to our development of 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 have completed a Phase 2 clinical trial of the intravenous formulation of eravacycline in patients with cIAI. We are conducting two global Phase 3 clinical trials of eravacycline, one for the treatment of cIAI, which we initiated in the third quarter of 2013, and one for the treatment of cUTI, which we initiated and are currently screening patients for in the first quarter of 2014. We expect to have top-line data from the Phase 3 cIAI clinical trial in the first quarter of 2015, data from the lead-in portion of the Phase 3 cUTI clinical trial in mid-2014 and top-line data from the Phase 3 cUTI clinical trial in mid-2015. If we complete the Phase 3 clinical trials of eravacycline when we anticipate and the trials are successful, we expect to submit an NDA to the FDA in the second half of 2015 and an MAA to the EMA in the first half of 2016.
- ***Establish one or more collaborations for the development and commercialization of eravacycline outside the United States.*** We intend to seek to enter into one or more collaborations for the development and commercialization of eravacycline outside the United States.
- ***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 broad-spectrum coverage of multidrug-resistant Gram-negative bacteria and other multidrug-resistant bacteria, with the potential for intravenous-to-oral step-down, 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 hospital-acquired bacterial pneumonias and other serious and life-threatening infections following our development of eravacycline for the treatment of cIAI and cUTI. 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.*** 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. According to IMS Health, in 2011, approximately $41 billion was spent on antibiotic drugs worldwide, of which almost $9 billion was spent in the United States. The widespread use of antibiotics has resulted in a rapid increase in bacterial infections that are resistant to multiple antibacterial agents. For example, the bacterial pathogen *Klebsiella pneumoniae* is responsible for roughly 14% of Gram-negative infections in hospital intensive care units. Multidrug-resistant *Klebsiella pneumoniae* are typically treated with the carbapenem class of antibiotics. However, in recent years, strains resistant to carbapenem antibiotics have emerged and markedly increased the threat posed by *Klebsiella pneumoniae* , as infections caused by carbapenem-resistant strains have few treatment options.

As a result of the increasing prevalence of such multidrug-resistant bacteria, some antibiotics targeting these bacteria have been highly successful commercially. These include:

- linezolid, an intravenously and orally administered antibiotic marketed by Pfizer as Zyvox, which had worldwide sales in 2012 of $1.3 billion;
- levofloxacin, an intravenously and orally administered antibiotic marketed by Ortho-McNeil and Johnson & Johnson as Levaquin, which had worldwide sales in 2012 of $75 million, down from worldwide sales of $1.4 billion in 2010 after losing U.S. market exclusivity in June 2011;
- meropenem, an intravenously administered antibiotic marketed by AstraZeneca as Merrem, which had worldwide sales in 2012 of $396 million, down from worldwide sales of $817 million in 2010 after losing U.S. market exclusivity in June 2010; and
- daptomycin, an intravenously administered antibiotic marketed by Cubist Pharmaceuticals, Inc. as Cubicin, which had worldwide sales in 2012 of $860 million.

Bacterial infections are caused by a variety of different types of bacteria and the infections they cause can range from mild to serious, life threatening infections requiring immediate treatment. Bacteria are broadly categorized as Gram-positive, Gram-negative, atypical or anaerobic. Gram-positive bacteria possess a single membrane and a thick cell wall and turn dark-blue or violet when subjected to a laboratory staining method known as Gram's method. Common causes of Gram-positive bacterial infections include species of *Staphylococcus* , such as methicillin-resistant *Staph aureus* , or MRSA, *Streptococcus* and *Enterococcus* . Gram-negative bacteria have two membranes with a thin cell wall and, when subjected to Gram's method of staining, lose the stain or are decolorized. According to The New England Journal of Medicine, the most common cause of Gram-negative infection is *Escherichia coli* , or *E. coli* . Less prevalent Gram-negative bacteria strains include species of *Acinetobacter* , *Klebsiella* and *Pseudomonas* . Atypical bacteria, such as *Mycoplasma* species, have modified cell walls and are neither Gram-positive nor Gram-negative. Anaerobic bacteria, such as *Bacteroides* species, either cannot grow in the presence of oxygen or do not require oxygen to grow and are classified as either Gram-positive or Gram-negative.

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.

Many strains of bacteria have mutated over time and have developed resistance to existing drugs, resulting in infections that are increasingly serious or more difficult to treat. These drug-resistant pathogens have become a

growing menace to all people, regardless of age, gender or socioeconomic background. They endanger people in affluent, industrial societies like the United States, as well as in less-developed nations. Gram-positive bacteria that have developed resistance to existing drugs include:

- *Streptococcus pneumoniae* that cause pneumonia, ear infections, bloodstream infections and meningitis;
- *Staphylococcus aureus* that cause skin, bone, lung and bloodstream infections; and
- *Enterococci* that are responsible for infections transmitted in healthcare settings.

Gram-negative bacteria that have developed resistance to existing drugs include:

- *Escherichia coli* that cause urinary tract, skin and bloodstream infections;
- *Salmonella* and *Escherichia coli* that cause foodborne infections; and
- *Acinetobacter baumannii* , *Pseudomonas aeruginosa* and *Klebsiella* spp. that are responsible for infections transmitted in healthcare settings.

Broad-spectrum antibiotics are used to treat major hospital infections such as cIAI, cUTI, acute bacterial skin and skin structure infections, or ABSSSI, and acute bacterial pneumonias. Based on an analysis of data from a variety of industry sources, we estimate that the number of patients treated with antibiotics in hospitals in the United States in a year include approximately 1.7 million cIAI patients, 4.0 million cUTI patients and 8.0 million ABSSSI and acute bacterial pneumonia patients. Of these patients, we believe that approximately 45% of cIAI patients, 25% of cUTI patients and 15% of ABSSSI and acute bacterial pneumonia patients have infections caused at least in part by multidrug-resistant Gram-negative bacteria.

According to a September 2013 report of the CDC, each year in the United States, at least two million people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a direct result of these antibiotic-resistant infections, with 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 already overburdened 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. In addition, the CDC reported that, 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* .

As such, at present, there is an acute need for new drugs to treat multidrug-resistant Gram-negative bacteria. Currently approved products, such as Merrem and Levaquin, are becoming increasingly ineffective against Gram-negative bacteria due to increasing resistance, limiting patients' treatment options, particularly for patients with multidrug-resistant infections, and few new therapeutic agents 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. This resistance was confirmed by the SENTRY Antimicrobial Surveillance Program which evaluated *Enterobacteriaceae* and *Acinetobacter* spp., two Gram-negative species of bacteria, from 31 U.S. medical centers from 2005 to 2009. Specifically, the SENTRY Program found that, with respect to the *Enterobacteriaceae* family of bacteria, 6.8% of the *Escherichia coli* strains studied and 15.4% of the *Klebsiella* spp. strains studied exhibited an extended-spectrum beta lactamase, or ESBL, phenotype, and that 22.2% of *Enterobacter* spp. strains studies were ceftazidime-resistant. ESBLs are enzymes present in certain multidrug-resistant bacteria that destroy classes of beta lactam antibiotics, such as penicillins, cephalosporins and

carbapenems. In addition, *Klebsiella pneumoniae* carbapenemase-, or KPC-, producing bacteria have emerged as a highly drug resistant Gram-negative bacteria associated with mortality rates ranging from 32% to 48%, as compared to 9% to 17% for strains of *Klebsiella pneumoniae* that are not carbapenem-resistant.

As a further example of the seriousness of the threat of Gram-negative bacteria resistant to all available antibacterial agents, in 2012, the national media including *The New York Times* , *The Wall Street Journal* and *The Washington Post* reported that the Clinical Center of the National Institutes of Health had an outbreak of Gram-negative *Klebsiella pneumoniae* bacteria strains that were resistant to all available antibiotics that resulted in seven deaths. In addition, there have been numerous reports that physicians have resorted to prescribing colistin to treat Gram-negative bacterial infections resistant to all other drugs. Colistin was discovered in 1949 and has not been widely used for decades because of serious toxicities, including nephrotoxicity. In our Phase 2 cIAI clinical trial, eravacycline dosed intravenously once or twice per day as a monotherapy was effective against infections caused by multidrug-resistant *Klebsiella pneumoniae* .

The growing issue of antibiotic-resistant bacterial infections has been widely recognized as an increasingly urgent public health threat, including by the World Health Organization, the CDC and the Infectious Disease Society of America, or IDSA. In April 2011, the IDSA issued a report warning that unless significant measures are taken to increase the pipeline of new antibiotics active against drug resistant bacteria, people will start to die from common, formerly treatable infections, and medical interventions such as surgery, chemotherapy, organ transplantation and care of premature infants will become increasingly risky. In the pre-antibiotic era before penicillin began to be available in 1942, patients frequently died from what subsequently became easily cured infections. The important need for new treatment options for serious bacterial infections was further highlighted by the passage in July 2012 of the Generating Antibiotic Incentives Now 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 2012, the FDA announced the formation of an internal task force to support the development of new antibacterial drugs, which they called “a critical public healthcare goal and a priority for the agency.”

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 afford to be too limited in the spectrum of bacteria covered by antibiotics when initially treating a patient for a serious infection that has not yet been definitively identified. Frequently used products, such as Zyvox and Cubicin, are limited to Gram-positive 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 Levaquin, piperacillin/tazobactam, which is marketed by Pfizer as Zosyn, carbapenems, such as Merrem, and imipenem/cilastatin, which is marketed by Merck as Primaxin, 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 two, 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 or have recently concluded clinical development to

cover a broad spectrum of bacteria, including Gram-negative bacteria, or solely to address Gram-negative bacteria, are being developed to be used 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.

Lack of Oral Dosage Forms to Permit Step-Down Therapy. When a patient comes to the emergency room or hospital for treatment of a serious infection, the patient initially receives intravenous treatment, which allows the drug to be delivered more rapidly and in a larger dose than oral treatment. Once the infection begins to respond to treatment and the patient is stabilized, depending on the infection, hospitals and physicians generally seek to minimize in-hospital treatment and, if possible, discharge patients from the hospital in order to reduce costs, avoid hospital-acquired infections, and improve the patients' quality of life. Upon discharge, physicians typically prefer to prescribe step-down treatment with an oral formulation of the same antibiotic. A step-down to oral treatment allows for more convenient and cost-effective out-patient treatment, with the oral antibiotic providing enhanced patient comfort and mobility and avoiding the risk of infection from the intravenous catheter. In addition, the use of the same antibiotic allows the physician to avoid switching the patient from the antibiotic that has proven effective during intravenous administration to a different antibiotic that may be less effective and carries the risk of new or different side effects. Many of the antibiotics that are most commonly used as first-line empiric monotherapies are only available in an intravenous formulation. Very few of the antibiotics that cover or are focused on the treatment of Gram-negative bacteria have oral dosage forms.

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 spectrum 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;
- A favorable safety and tolerability profile; and
- Availability in both intravenous dosage and 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 a broad-spectrum intravenous and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant Gram-negative bacteria. We developed eravacycline using our proprietary chemistry technology. We believe our fully synthetic process will enable us to have a cost of manufacturing that is sufficiently low to enable us to sell eravacycline, when and if approved, for a cost that is similar to other hospital-based antibiotics. Our patent strategy to broadly protect eravacycline includes the filing of patent applications directed towards the composition of matter of eravacycline as well as our proprietary chemistry technology, which we used to create eravacycline. We own exclusive worldwide rights for the development and commercialization of eravacycline.

In 2012, we completed a successful Phase 2 clinical trial of eravacycline with intravenous administration for the treatment of patients with cIAI. We initiated a Phase 3 clinical trial of eravacycline with intravenous administration for the treatment of cIAI in the third quarter of 2013 and subsequently initiated and are currently screening patients for a second Phase 3 clinical trial of eravacycline for the treatment of cUTI with intravenous-to-oral step-down therapy during the first quarter of 2014. We expect to have top-line data from the Phase 3 cIAI clinical trial in the first quarter of 2015, data from the lead-in portion of the Phase 3 cUTI clinical trial in mid-2014 and top-line data from the Phase 3 cUTI clinical trial in mid-2015. If we complete the Phase 3 clinical trials of eravacycline when we anticipate and the trials are successful, we expect to submit an NDA to the FDA in the second half of 2015 and an MAA to the EMA in the first half of 2016.

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 tetracycline 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 spectrum 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 intravenous-to-oral step-down 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, 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.

Based on *in vitro* studies we have completed, we believe that eravacycline shares a similar potency profile with carbapenems except that it more broadly covers Gram-positive pathogens like MRSA and *enterococci*, is active against carbapenem-resistant Gram-negative bacteria and, unlike carbapenems like Primaxin and Merrem, is not active against *Pseudomanas aeruginosa* . Eravacycline has 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, such as hospital-acquired bacterial pneumonias.

- **Broad-spectrum activity against a wide variety of multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria.** In our Phase 2 clinical trial of the intravenous 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 *E. coli* ; ESBL-producing *Klebsiella pneumoniae* ; *Acinetobacter baumannii* ; Gram-positive bacteria, including MRSA and vancomycin-resistant *enterococcus* , or VRE; and anaerobic pathogens. As a result of this broad-spectrum coverage, we believe that eravacycline has the potential to be used as a first-line empiric monotherapy for the treatment of cIAI, cUTI, hospital-acquired bacterial pneumonias 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 more than 350 subjects in the Phase 1 and Phase 2 clinical trials that we have conducted. In these trials, eravacycline demonstrated a favorable safety and tolerability profile. In our Phase 2 clinical trial of eravacycline, no patients suffered any serious adverse events, and safety and tolerability were comparable to ertapenem, the control therapy in the trial. In addition, in the Phase 2 clinical trial, the rate at which gastrointestinal adverse events such as nausea and vomiting that occurred in the eravacycline arms was comparable to the rate of such events in the ertapenem arm of the trial.
- **Convenient dosing regimen.** In our Phase 2 clinical trial we 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 intravenous-to-oral step-down.** In addition to the intravenous formulation of eravacycline, we are also developing an oral formulation of eravacycline. If successful, this oral formulation would enable patients who begin intravenous 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 intravenous and oral administration and the oral step-down may reduce the length of a patient's hospital stay and the overall cost of care.

Clinical Experience

We have studied intravenous and oral formulations of eravacycline in 377 subjects in ten completed clinical trials from October 2009 to December 2013.

Phase 1 clinical trials of intravenous formulation

From 2009 to 2010, we studied the intravenous formulation of eravacycline in a Phase 1 single ascending dose, or SAD, clinical trial and a Phase 1 multiple ascending dose, or MAD, clinical trial. These trials were designed to evaluate the safety and tolerability of single escalating doses and multiple escalating doses of

eravacycline. 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 vomiting were observed at the higher dose levels in the Phase 1 clinical trials.

In 2009, we conducted the Phase 1 single ascending dose clinical trial of the intravenous formulation of eravacycline in 56 healthy subjects at a single clinical site in the United States. In the trial, subjects received a single 30-minute intravenous infusion of either placebo or eravacycline at doses of 0.10, 0.25, 0.50, 1.00, 1.50, 2.00 or 3.00 mg/kg. In each dose group of eight patients, six patients received eravacycline and two patients received placebo. The most common adverse events reported were nausea and vomiting. All adverse events were mild to moderate in intensity.

In 2010, we conducted the Phase 1 multiple ascending dose clinical trial of the intravenous formulation of eravacycline in 32 healthy subjects at a single clinical site in the United States. In the trial, subjects received 30-minute intravenous infusions of either placebo or eravacycline at doses of 0.50 or 1.50 mg/kg once daily for 10 days, 60-minute intravenous infusions of either placebo or eravacycline at a dose of 1.50 mg/kg once daily for 10 days or 60-minute intravenous infusions of either placebo or eravacycline at a dose of 1.00 mg/kg twice daily for 10 days. In each cohort of eight patients, six patients received treatment and two patients received placebo. The most common adverse events were associated with the infusion site. All adverse events were mild to moderate in intensity.

In the Phase 1 MAD clinical trial, we also measured levels of eravacycline in urine in patients who had received eravacycline to assess the potential for treatment of cUTI. A summary of the results of those measurements, which were taken following the final dose on the last day of treatment, is shown in the table below. These data show that renal excretion is not the primary route of elimination for eravacycline. We believe that the levels of eravacycline in urine support the development of eravacycline as a potential first-line therapy in patients with cUTI.

Eravacycline Levels in Urine

MAD Dose Group (mg/kg)	Day 10 Urine Concentration in ng/mL (%CV)	
	0-8 Hours	8-24 Hours
0.5 every 24 hours infused in 30 minutes	4,576.7(57.9)	2,250.0(31.1)
1.5 every 24 hours infused in 60 minutes	13,316.7(25.7)	5,565.0(39.2)
1.0 every 12 hours infused in 60 minutes	25,060.0(21.1)	9,230.0(26.1)

CV refers to the coefficient of variability, a statistical measure of the dispersion of a probability distribution.

The most recent tetracycline-based antibiotic to be approved for marketing by the FDA is tigecycline, which was approved in 2005 and is marketed by Pfizer under the name Tygacil. We have not conducted a head-to-head comparison of eravacycline and tigecycline in a clinical trial, but have compared the published data from Pfizer's Phase 1 clinical trials of tigecycline to the data from our Phase 1 clinical trials of eravacycline. Based on this comparison, eravacycline demonstrated better gastrointestinal tolerability than tigecycline while also achieving higher blood levels with higher area under the curve, or AUC, than tigecycline. AUC is a measure of total exposure to a drug over a period of time. Specifically, with respect to tolerability, all subjects in Pfizer's Phase 1 clinical trials of tigecycline that were treated with 75mg or 100mg of tigecycline every 12 hours experienced unacceptable rates and severity of nausea and emesis resulting in early termination of all subjects in both dosing groups. In the eravacycline Phase 1 MAD clinical trial, one of the six subjects in the 1.00 mg/kg every 12 hours dosing group discontinued the study drug because of nausea. The other subjects all tolerated the full 10 days of dosing. At the same time, the AUC_{0-12} for the 1.00 mg/kg every 12 hours dose in the eravacycline Phase 1 MAD clinical trial was 6344 ng*h/mL (19.9% CV), while the AUC_{0-12} for tigecycline administered at a higher dose (100 mg every 12 hours) was 4980 ng*h/mL (19% CV). While we believe this comparison to tigecycline's

previously published Phase 1 data, and the other comparisons we make in this annual report on Form 10-K to tigecycline's previously published clinical trial data, are useful in evaluating eravacycline's clinical trial results, the fact that we have not conducted a head-to-head study and that the tigecycline trials were conducted under different protocols at different sites and at different times than our trials may limit the value or reliability of any such comparison.

In 2013, we conducted a Phase 1 cardiac repolarization clinical trial of the intravenous formulation of eravacycline in 53 healthy volunteers. We observed no clinically significant effects of eravacycline on electrical activity in the heart in this clinical trial. As part of the development program for eravacycline, we have also initiated a required Phase 1 clinical trial to investigate the pharmacokinetics of eravacycline in 18 subjects with hepatic insufficiency and initiated a required Phase 1 clinical trial to investigate the pharmacokinetics of eravacycline in six subjects with renal insufficiency.

Phase 2 clinical trial of intravenous 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 intravenous 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:

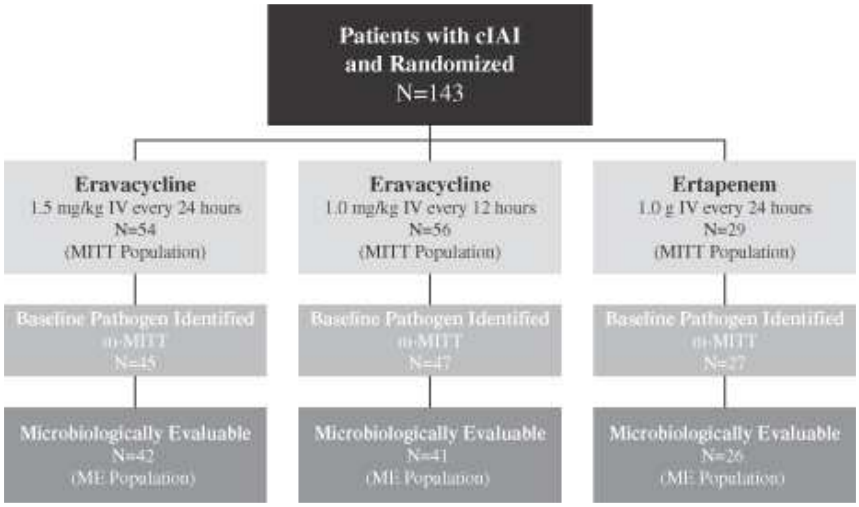
- an arm in which patients received 1.5 mg/kg of eravacycline administered intravenously once per day;
- an arm in which patients received 1.0 mg/kg of eravacycline administered intravenously twice per day; and
- a control arm in which patients received 1.0 g of ertapenem administered intravenously once 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 test-of-cure, or 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.

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 m-MITT, patients. Of the 119 m-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 m-MITT patients as the microbiologically evaluable, or ME, patients. The 10 m-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 study, 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. Included as one of the secondary endpoints in the trial was clinical response at the follow-up visit in the m-MITT population.

A diagram summarizing the trial design follows:

Eravacycline Phase 2 Trial Design



The baseline demographics of the patients in each arm of the trial are summarized in the table below. As shown in the table, 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.

Eravacycline Phase 2 Trial Patient Demographics

Parameter	Eravacycline (1.5 mg/kg every 24 hours) N=56	Eravacycline (1.0 mg/kg every 12 hours) N=57	Ertapenem (1.0 g every 24 hours) N=30
Mean Age (y) [Standard Deviation]	43.6 [18.4]	42.1 [17.2]	41.8 [17.6]
Mean Weight (kg) [Standard Deviation]	68.1 [13.2]	70.0 [14.4]	68.8 [16.2]
Male (%)	38 (67.9)%	43 (75.4)%	22 (73.3)%
Caucasian (%)	40 (71.4)%	37 (64.9)%	21 (70.0)%
APACHE Score			
Mean [Standard Deviation]	8.2 [3.9]	6.0 [3.8]	6.1 [2.7]
<10 (%)	41 (74.6)%	48 (84.2)%	28 (96.6)%
10-15 (%)	13 (23.6)%	8 (14.0)%	1
>15	1	1	—

The following table summarizes the diseases underlying the MITT patients' infections, which were being treated with the antibiotics in the trial.

Eravacycline Phase 2 Trial MITT Population Diseases

Intra-Operative Diagnosis	Eravacycline (1.5mg/kg every 24 hours) N=54	Eravacycline (1.0mg/kg every 12 hours) N=56	Ertapenem (1.0g every 24 hours) N=29
Complicated Appendicitis	29	31	15
Other	25	25	14
Perforation of Intestine	5	5	1
Complicated Diverticulitis	—	2	—
Gastric/Duodenal Perforation	13	12	8
Complicated Cholecystitis	3	4	3
Other (Abscess/Peritonitis)	4	2	2

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 of eravacycline intravenously once per day; 5.6 days for the patients receiving 1.0 mg/kg of eravacycline intravenously twice per day; and 6.0 days for the patients receiving 1.0 g of ertapenem intravenously once per day.

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 m-MITT patients were confirmed to be multidrug-resistant as a result of being ESBL-positive and/or carbapenem-resistant. The table below summarizes the pathogens isolated from the m-MITT patients enrolled in the Phase 2 clinical trial, of which 60.4% were members of the *Enterobacteriaceae* family. m-MITT patients in the trial were infected with an average of 1.8 pathogens:

Eravacycline Phase 2 Trial m-MITT Population Pathogens

	Total Pathogens	Eravacycline (1.5 mg/kg every 24 hours)	Eravacycline (1.0 mg/kg every 12 hours)	Ertapenem (1.0 g every 24 hours)
Gram-negative aerobic pathogens				
Escherichia coli	94	40	37	17
Klebsiella pneumoniae	14	8	4	2
Klebsiella oxytoca	7	2	4	1
Pseudomonas aeruginosa	8	5	3	—
Acinetobacter baumannii complex	4	1	1	2
Acinetobacter spp.	1	—	—	1
Comamonas testosteroni	2	—	2	—
Proteus mirabilis	2	1	—	1
Aeromonas spp.	1	—	—	1
Citrobacter braakii	1	1	—	—
Citrobacter freundii	1	—	1	—
Enterobacter cloacae	2	—	2	—
Morganella morganii	4	1	—	3
Pantoea spp.	1	—	—	1
Providencia rustigianii	1	—	1	—
Stenotrophomonas maltophilia	1	—	1	—
Total	144	59	56	29
Gram-positive aerobic pathogens				
Streptococcus spp.	16	5	6	5
Streptococcus anginosus	4	2	1	1
Enterococcus faecalis	8	2	2	4
Enterococcus faecium	3	1	1	1
Enterococcus avium	4	2	1	1
Enterococcus gallinarum	1	—	—	1
Staphylococcus spp.	5	1	3	1
Staphylococcus aureus	7	1	4	2
Bacillus spp.	1	—	—	1
Leuconostoc spp.	1	—	1	—
Total	50	14	19	17
Anaerobic pathogens				
Bacteroides fragilis	5	1	1	3
Bacteroides vulgatus	2	2	—	—
Bacteroides ovatus	1	—	—	1
Bacteroides thetaiotaomicron	1	—	1	—
Bacteroides ureolyticus	3	—	3	—
Clostridium spp.	4	—	4	—
Bifidobacterium spp.	1	—	1	—
Gemella morbillorum	1	1	—	—
Total	18	4	10	4

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 vomiting occurred at modest 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. The table below shows the adverse events experienced by patients in the trial that were assessed by the investigator as possibly related to the study drugs.

Eravacycline Phase 2 Trial Study-Drug Adverse Events

Adverse Event (≥ 1 occurrence)	Eravacycline (1.5 mg/kg every 24 hours) N=53 [a]	Eravacycline (1.0 mg/kg every 12 hours) N=56	Ertapenem (1.0 g every 24 hours) N=30 [a]
Any TEAE	2 (3.8)%	3 (5.4)%	3 (10.0)%
Nausea	—	2 (3.6)%	1 (3.3)%
Vomiting	1 (1.9)%	1 (1.8)%	—
Elevated amylase	—	—	1 (3.3)%
Elevated lipase	—	—	1 (3.3)%
Thrombophlebitis (associated with infusion sites)	—	1 (1.8)%	—

[a] For the analysis of safety and tolerability, one of the MITT patients in the arm of the trial receiving 1.5 mg/kg of eravacycline intravenously once per day was reclassified into the ertapenem arm of the trial as a result of having, in error, received the ertapenem dosing instead of eravacycline.

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.

Eravacycline Phase 2 Trial Pharmacokinetic Results

Parameter		Eravacycline (1.5 mg/kg every 24 hours) N=48	Eravacycline (1.0 mg/kg every 12 hours) N=51
C_{max}			
	Mean (ng/mL)	**1,445.6**	**952.6**
	%CV	80.8%	79.8%
AUC_{0-12}			
	Mean (ng*h/mL)	**4,349.9**	**3,240.7**
	%CV	50.2%	53.5%

The table above summarizes selected pharmacokinetic parameters that we obtained from the pharmacokinetic sampling. C_{max} refers to the maximum observed peak plasma concentration.

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. For the patients receiving 1.5 mg/kg of eravacycline intravenously once per day we estimated that the AUC over the 24 hours following dosing would be 5220 ng*h/mL. For the patients receiving 1.0 mg/kg of eravacycline intravenously twice per day, we estimated that the AUC over the 24 hours following dosing would be at least 6480 ng*h/mL. We calculated this latter figure by doubling the AUC over the 12 hours following dosing shown in the table above due to twice daily dosing in this arm of the trial. These estimated AUCs for eravacycline over the 24 hours following dosing are higher than the AUC over the 24 hours following dosing in the Phase 3 clinical trial data included in tigecycline's product label. We believe that these higher estimated AUCs for eravacycline as compared to tigecycline combined with the better tolerability indicated for eravacycline in our Phase 2 clinical trial, is supportive of eravacycline's potential to treat multidrug-resistant Gram-negative and other bacteria.

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. Results of the trials demonstrated that an oral formulation of eravacycline could achieve drug levels equivalent to those in the patients that received intravenous infusions of 1.5 mg/kg of eravacycline once per day in our Phase 2 cIAI clinical trial, levels that were effective in treating patients in our Phase 2 cIAI clinical trial. In the oral clinical trials, we utilized simple formulations. For the SAD oral trial, we formulated eravacycline in liquid solution of 5% dextrose in water, commonly referred to as D5W. For the MAD oral clinical trials, we formulated eravacycline in a simple capsule.

As part of the completed Phase 1 clinical trials referred to above, 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.

In 2010, we conducted a Phase 1 single ascending dose clinical trial of an oral formulation of eravacycline in 28 healthy subjects in a single-center, placebo-controlled, double-blind clinical trial. In the trial, subjects received eravacycline reconstituted in a solution of D5W at doses of 50mg, 100mg, 200mg and 300mg or placebo. In each dose group of eight patients, six patients received eravacycline and two patients received placebo. The most common adverse event reported was nausea. All adverse events were mild to moderate in intensity.

In 2011, we conducted a Phase 1 multiple ascending dose clinical trial of an oral formulation of eravacycline in 58 healthy subjects in a single-center, placebo-controlled, double-blind clinical trial. In the trial, subjects received eravacycline capsules at doses of 50mg, 100mg, 200mg and 300mg or placebo. In each dose group of eight patients, six patients received eravacycline and two patients received placebo. The most common adverse events reported were nausea and vomiting. All adverse events were mild to moderate in intensity. Doses of 100mg provided twice daily and 300mg provided once daily were well tolerated. A single daily dose of 400mg was not tolerated due to gastrointestinal-related adverse events. We also measured pharmacokinetic parameters for eravacycline.

In 2013, we conducted a second Phase 1 multiple ascending dose clinical trial of an oral formulation of eravacycline in 36 healthy subjects in a single-center, placebo-controlled, double-blind clinical trial. In the trial, subjects received eravacycline capsules at doses of up to 250mg provided two or three times daily or placebo. In each dose group of eight patients, six patients received eravacycline and two patients received placebo. The most common adverse events reported were nausea and vomiting. All adverse events were mild to moderate in intensity. We also measured pharmacokinetic parameters for eravacycline. Doses of 200mg and 250mg provided twice daily were well tolerated, with key pharmacokinetic parameters summarized in the table below.

Eravacycline Oral MAD Pharmacokinetic Results

Parameter	Eravacycline (200 mg every 12 hours)	Eravacycline (250 mg every 12 hours)
C_{max}		
Day 7 Mean (ng/mL) %CV	261 47%	398 14%
AUC_{0-24}		
Day 7 Mean (ng*h/mL) % CV	4520[a] 43%	6200[a] 17%

[a] Reflects two doses administered in the 24 hour period.

We carried out extensive modeling of the intravenous and oral pharmacokinetic data from our clinical trials of eravacycline in order to establish an oral step-down dose following intravenous administration. Based on our modeling results of eravacycline, we believe that a twice daily dose of either 200mg or 250mg of oral eravacycline will achieve plasma exposure levels equivalent to those resulting from daily administration of the intravenous formulation of eravacycline at 1.5 mg/kg and that a twice per day oral dosage form of eravacycline

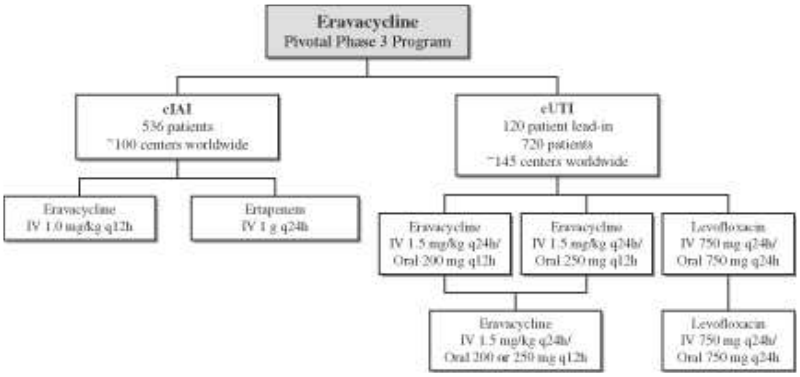
can be developed to permit oral step-down treatment of serious infections. As these twice daily oral doses of 200mg and 250mg were safe and well tolerated in the second Phase 1 MAD clinical trial, we plan to evaluate these doses in our Phase 3 clinical trial of eravacycline with intravenous-to-oral step-down therapy for the treatment of cUTI.

Phase 3 Clinical Program

We have designed our 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-spectrum coverage of multidrug-resistant infections, including multidrug-resistant Gram-negative infections. Our program is consistent with the draft guidance issued by the FDA for drug development for cIAI and cUTI. The cIAI guidance indicates that, for companies developing a drug for cIAI and an additional indication caused by similar bacterial pathogens, such as cUTI, a single trial in cIAI and a single trial in that additional indication could be sufficient to provide evidence of effectiveness in both indications. We believe that prior to the issuance of this guidance, a company that was developing a drug for cIAI and an additional indication would have been required to conduct two Phase 3 clinical trials of the drug for the treatment of cIAI, enrolling 500 to 600 patients in each trial, and additional Phase 3 clinical trials of the drug for the treatment of the additional indication, even where cIAI and the additional indication were caused by similar bacterial pathogens. We believe that the opportunity provided by the draft guidance to submit an NDA package for two indications on the basis of only two Phase 3 clinical trials makes the process of developing and seeking approval of drugs for cIAI and a second indication more cost-effective. The trials can be conducted at the same time, and because the patient populations are different for the two trials, patient enrollment could be faster.

A diagram summarizing the trial design follows:

Eravacycline Phase 3 Program Design



Phase 3 cIAI Clinical Trial

In the third quarter of 2013, we initiated a global, multi-center, randomized, double-blind, double-dummy Phase 3 clinical trial to assess the efficacy, safety and pharmacokinetics of eravacycline compared to ertapenem in patients with cIAI. We plan to enroll 536 patients in the trial at approximately 100 clinical sites worldwide. These patients are being randomized into two arms on a 1:1 basis. Patients in the eravacycline arm receive 1.0 mg/kg of eravacycline administered intravenously twice per day. Patients in the ertapenem arm receive 1.0 g of ertapenem administered intravenously once per day.

Investigators will obtain baseline intra-abdominal cultures at the time of operation and treat patients for a minimum of four days and a maximum of 14 days and until symptoms of cIAI are resolved. A test-of-cure visit will take place 25 to 31 days after the initial dose of treatment and a final or follow-up visit will occur 38 to 50 days after the initial dose of treatment.

We have designed the trial as a non-inferiority study. The primary endpoint of the trial is clinical response at the test-of-cure visit in the microbiological intent-to-treat, or micro-ITT, patient population in the trial. The micro-ITT population consists of all randomized patients in the trial who have baseline bacterial pathogens that cause cIAI and against which the dosed eravacycline has antibacterial activity. In order to achieve the primary endpoint, eravacycline would need to demonstrate non-inferiority as compared to ertapenem within a margin of no more than 10%. Secondary endpoints include clinical response at the end-of-treatment, test-of-cure and follow-up visits in the intent-to-treat population, the clinically evaluable population, the micro-ITT population and the microbiologically evaluable, or ME, population. In the trial, we also plan to study microbiologic response at the end-of-treatment and test-of-cure 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 draft 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 microbiological intent-to-treat 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. The draft guidance defined this population as all randomized patients who have baseline bacterial pathogens that cause cIAI and against which the investigational drug has antibacterial activity.

Phase 3 cUTI Clinical Trial

In the first quarter of 2014, we initiated and are currently screening patients for a two-part, multi-center, randomized, double-blind Phase 3 clinical trial to assess the efficacy and safety of eravacycline compared with levofloxacin in the treatment of cUTI. We plan to enroll 120 patients in the lead-in portion of the trial. These patients will be randomized into three arms on a 1:1:1 basis:

- an arm in which patients will receive 1.5 mg/kg of eravacycline intravenously every 24 hours followed by 200 mg of eravacycline orally every 12 hours;
- an arm in which patients will receive 1.5 mg/kg of eravacycline intravenously every 24 hours followed by 250 mg of eravacycline orally every 12 hours; and
- an arm in which patients will receive 750 mg of levofloxacin intravenously every 24 hours followed by 750 mg of levofloxacin orally every 24 hours.

Following treatment of the 120 patients, we plan to evaluate primary efficacy, safety and tolerability endpoints to determine the dose regimen for eravacycline to be studied in the second portion of the trial.

In the second portion of the trial, we plan to enroll 720 patients who will be randomized on a 1:1 basis to receive the selected dose regimen of eravacycline or the levofloxacin dose regimen. We have designed the second portion of the trial as a non-inferiority study and the primary endpoint is clinical and microbiological response in the micro-ITT population approximately seven days after completion of treatment. In order to achieve the primary endpoint, eravacycline would need to demonstrate non-inferiority as compared to levofloxacin within a margin of no more than 10%.

Regulatory Filing Timeline

We expect to have top-line data from the Phase 3 cIAI clinical trial in the first quarter of 2015, data from the lead-in portion of the Phase 3 cUTI clinical trial in mid-2014 and top-line data from the Phase 3 cUTI clinical trial in mid-2015. If we complete the Phase 3 clinical trials of eravacycline when we anticipate and the trials are

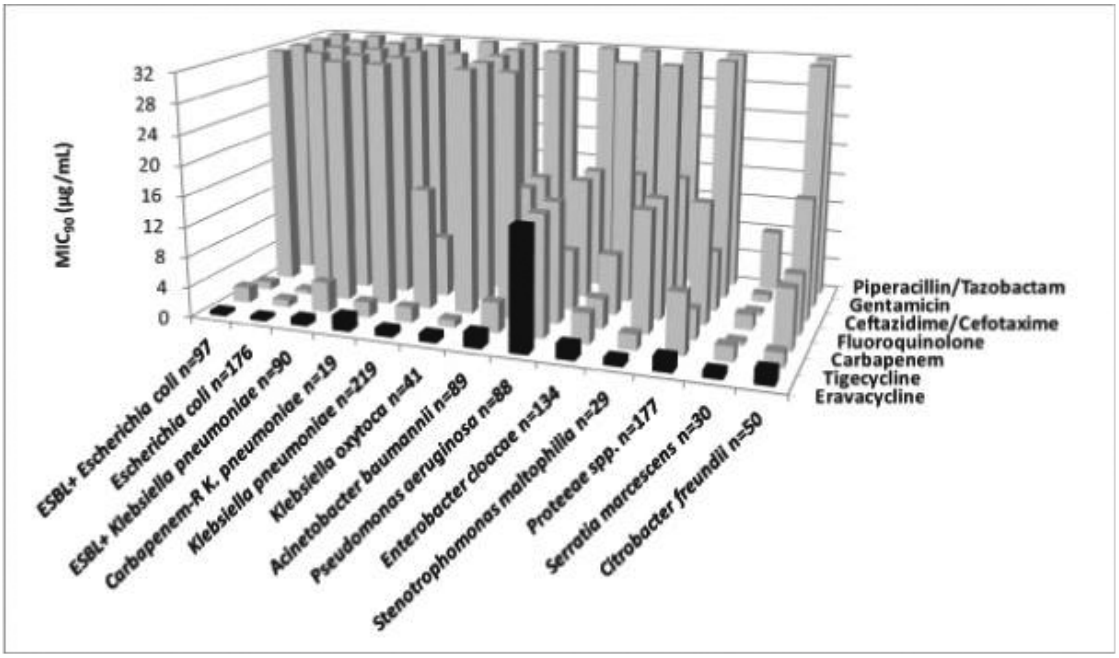
successful, we expect to submit an NDA to the FDA in the second half of 2015 and an MAA to the EMA in the first half of 2016. Our goal is to develop eravacycline to be the drug of choice for first-line empiric treatment of a wide variety of serious and life-threatening infections.

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 table 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 1,059 Gram-negative isolates. 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 table 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.

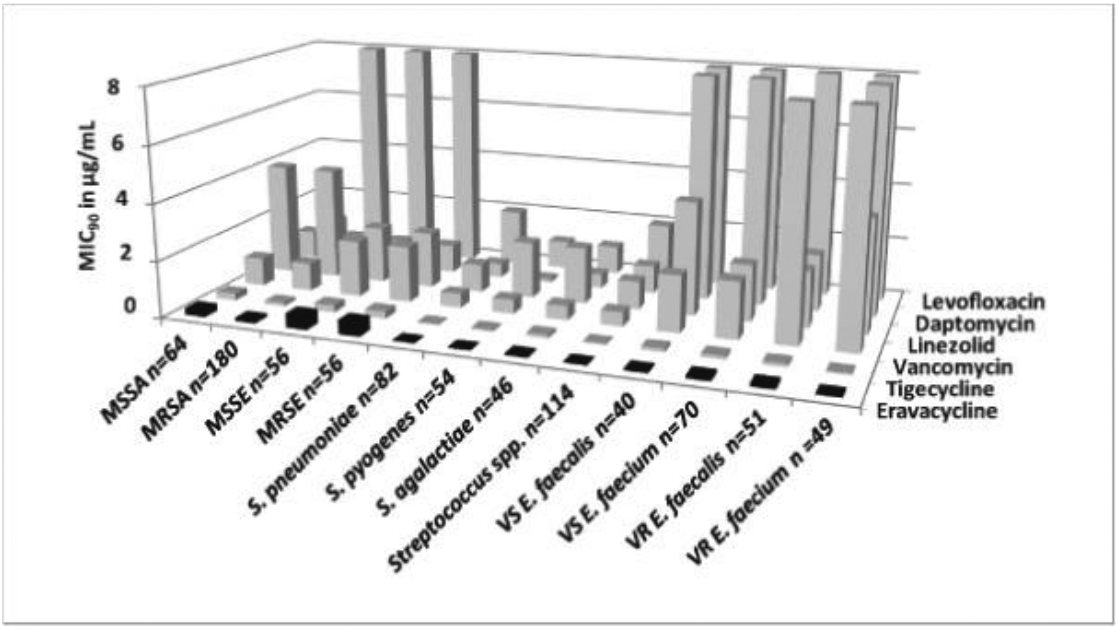


As shown in the table, eravacycline demonstrated potent, broad-spectrum Gram-negative antibacterial activity. In the majority of instances, the MIC_{90} of eravacycline was equivalent to or lower than the MIC_{90} values of the other antibiotics studied for each bacterium. Key observations from these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

- Eravacycline had MIC_{90} values of under 2 µg/mL against clinical isolates of *E. cloacae, A. baumannii, K. pneumoniae* , *i* ncluding ESBL-producing and carbapenem-resistant isolates, *C. freundii, S. maltophilia, M. morganii, P. vulgaris, P. stuartii,* and *K. oxytoca* .
- Eravacycline was twice as potent as the next most active comparator, tigecycline, against *A. baumannii* in a panel that was 44% resistant to carbapenems, 53% resistant to tetracyclines and 64% resistant to fluoroquinolones.
- Eravacycline was four 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.
- Isolates of *Proteus mirabilis* , one of the *proteeae* species included in the table above, were two times more susceptible to eravacycline (MIC_{90} of 4 µg/mL) than to tigecycline.
- *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).

In Vitro Activity Against Gram-positive Bacteria

The table 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 762 Gram-positive isolates. The bacteria selected for evaluation were chosen because they are commonly found in serious hospital infections.

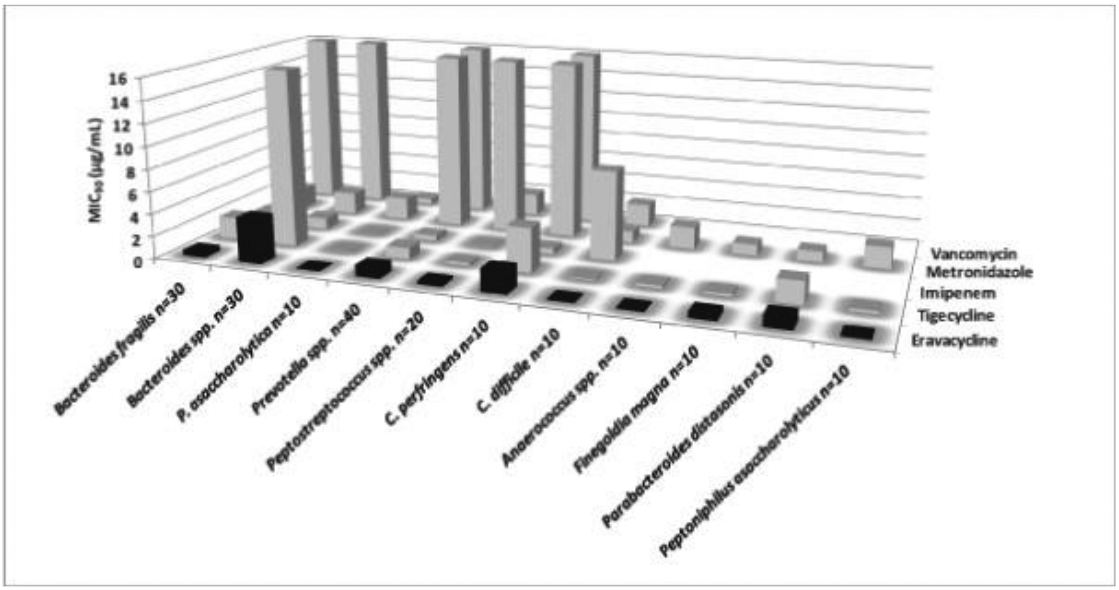


Eravacycline demonstrated excellent *in vitro* potency against methicillin-susceptible and resistant *Staphylococcus aureus* and *Staphylococcus epidermidis* , vancomycin-susceptible and resistant *Enterococcus*

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 180 MRSA isolates tested.

In Vitro Activity Against Anaerobic Bacteria

The table 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 190 anaerobic isolates. 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 Gram-positive and Gram-negative anaerobes; and
- 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.

Other Indications

Subject to obtaining additional financing, we intend to pursue development of eravacycline for the treatment of additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections following our development of eravacycline for the treatment of cIAI and cUTI.

We are also developing eravacycline as a potential empiric countermeasure for the treatment of disease caused by bacterial biothreat pathogens under funding from BARDA. In January 2012, BARDA awarded a five-year contract that provides a total of up to $67 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. 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.

We are collaborating with CUBRC because when we initially determined to seek government funding we recognized that we did not have any expertise in bidding for, or the administration and management of, government-funded contracts. CUBRC serves 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 responsible for management of chemistry, manufacturing and control activities and clinical studies.

In connection with the BARDA Contract, in February 2012, we entered into with CUBRC a five-year cost-plus-fixed-fee subcontract under which we may receive funding of up to approximately $39.8 million, reflecting the portion of the BARDA funding that may be paid to us for our activities.

Although the BARDA Contract, and our subcontract with CUBRC under the BARDA Contract, have five-year terms, 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 $15.7 million from the initial contract date through April 30, 2015, of which $11.7 million had been received through December 31, 2013. If BARDA continues to support the program under the contract for the full five-year term, we believe BARDA funding for this program will be sufficient to provide the funds to advance eravacycline through enabling studies for an NDA, evaluation of efficacy in non-pivotal murine and non-human primate models challenged with biothreat pathogens and a Phase 2 clinical trial for the treatment of community-acquired bacterial pneumonia, commonly referred to as CABP.

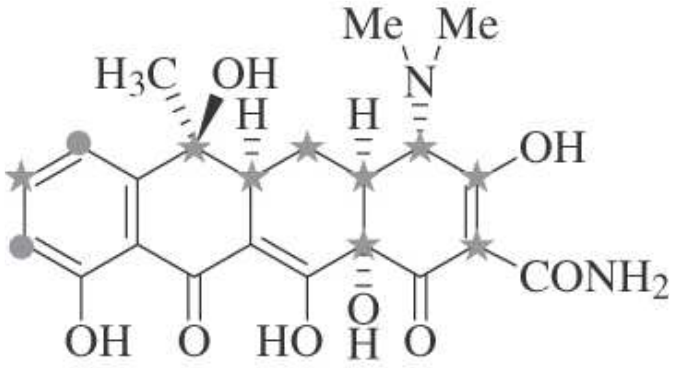
Technology Platform

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.

Other 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 started third quarter of 2013
	cUTI (IV/oral)	Phase 3 started first quarter of 2014
	Pneumonia (IV)	Phase 1
TP-271	Bacterial biothreats	IND-enabling studies ongoing
Gram - negative Program	Multidrug-resistant Gram-negative infections	Preclinical

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. Given our progress on TP-271, we expect to submit an investigational new drug application with the FDA for TP-271 by the end of 2014.

Funding for TP-271 is covered by two awards from NIAID. The first award is a grant awarded in July 2011 that provides up to approximately $2.8 million in funding over five years, 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 over five years. 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.

We are collaborating with CUBRC because when we initially determined to seek government funding we recognized that we did not have any expertise in bidding for, or the administration and management of, government-funded contracts. CUBRC serves as the prime contractor under the NIAID awards, primarily carrying out a program management and administrative role, though also with responsibility for the management of certain preclinical studies under the NIAID Contract. We serve as lead technical experts on all aspects of the NIAID Grant and NIAID Contract and serve as a subcontractor responsible for management of chemistry, manufacturing and control activities and clinical studies.

In connection with the NIAID Contract, in October 2011, we entered into a five-year cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $13.3 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 55-month, no-fee subaward of approximately $980,000 reflecting the portion of the NIAID Grant funding that may be paid to us for our activities.

Although the NIAID Contract and our subcontract with CUBRC under the NIAID Contract have five-year terms, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond September 30, 2016. 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 $7.5 million, of which $4.4 million had been received through December 31, 2013. In addition, although the NIAID Grant has a term of five years and our subaward from CUBRC has a term of 55 months, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond May 31, 2016. 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 $0.7 million from the initial grant date through May 31, 2016, of which $0.5 million had been received through December 31, 2013. If NIAID continues to support the program for the full term, we believe NIAID funding for our TP-271 program will provide funding sufficient to advance TP-271 through IND-enabling studies, determination of efficacy in non-pivotal murine and non-human primate models challenged with biothreat pathogens, filing intravenous and oral INDs and performing Phase 1 single and multiple-ascending dose clinical trials.

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 have identified a lead preclinical candidate from these compounds and expect to advance this compound into preclinical studies during the second half of 2014.

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 a broad-spectrum intravenous 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.

If we complete our Phase 3 clinical trials of eravacycline when we anticipate and the trials are successful, we expect to submit an NDA to the FDA in the second half of 2015 and an MAA to the EMA in the first half of 2016. Our current plan is to develop and commercialize eravacycline outside the United States with collaborators.

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. As a result, we believe that our use of synthetic process will enable us to have a cost of manufacturing for our product candidates that is sufficiently low to enable us to sell our product candidates, when and if approved, for a cost that is similar to other hospital-based antibiotics.

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 28, 2014, we owned two U.S. patents, six foreign patents, seven pending U.S. patent applications, one pending international application filed under the Patent Cooperation Treaty and 46 pending foreign patent applications in Europe and 17 other jurisdictions. In addition we have exclusively licensed from Harvard University rights under seven U.S. patents, 12 foreign patents, three pending U.S. patent applications and 24 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 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 use of eravacycline and other fluorocyclines, such as TP-271, pending in the United States, Europe, Japan and other countries. Patents specific to the composition and use of eravacycline have been granted in Europe, Australia, Mexico, New Zealand and Singapore. The granted patents have an expiration date of August 7, 2029, as will any patents that may issue from the pending applications absent any term extensions or adjustments that may be available. Any patents that may issue from these pending applications will have an expiration date no earlier than 2031.

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, as well as 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.

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, or PMA, 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.

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, we have paid Harvard an aggregate of $3.8 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

Our program to develop eravacycline for the treatment of disease caused by bacterial biothreat pathogens is funded by BARDA through a five-year contract that provides a total of up to $67 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 broad-spectrum 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. In connection with the BARDA Contract, in February 2012, we entered into a five-year cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $39.8 million, reflecting the portion of the BARDA funding that may be paid to us for our activities.

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 provides up to approximately $2.8 million in funding over five years, and the NIAID Contract, a separate a five-year contract that provides up to $35.8 million in funding that NIAID awarded to CUBRC in October 2011. The NIAID Contract contemplates 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 five-year cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $13.3 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 55-month, no-fee subaward of approximately $980,000 reflecting the portion of the NIAID Grant funding that may be paid to us for our activities.

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 September 30, 2016 in the case of the NIAID Contract and May 31, 2016 in the case of the NIAID Grant, 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.

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 substantially 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. Our potential competitors' drugs may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render our product candidates obsolete or non-competitive before we can recover the expenses of their development and commercialization. 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 capability for intravenous-to-oral step-down, price, availability of reimbursement from governmental and other third-party payers and susceptibility to drug resistance.

We are developing eravacycline as a broad-spectrum intravenous and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant Gram-negative 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 as Primaxin, tigecycline, which is marketed by Pfizer as Tygacil, levofloxacin, which is marketed by Ortho-McNeil and Johnson & Johnson as Levaquin, and piperacillin/tazobactam, which is marketed by Pfizer as Zosyn, as well as antibiotics currently in Phase 3 development, including ceftazidime/avibactam, which is being developed by Forest Laboratories Inc. and AstraZeneca, cefalozine/tazobactam, which is being developed by Cubist, and plazomicin, which is being developed by Achaogen, Inc. We also expect that eravacycline, if approved, would compete with future generic versions of currently marketed antibiotics.

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

- broad-spectrum activity against a wide variety of multidrug-resistant Gram-negative, Gram-positive and anaerobic bacteria;
- lower probability of drug resistance;
- a favorable safety and tolerability profile;
- a convenient dosing regimen; and
- potentially, convenient intravenous-to-oral step-down.

Recent Changes in the Regulatory Landscape

The FDA's Anti-Infective Drugs Division 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 they perceive 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 2012, the FDA published a draft guidance entitled "Guidance for Industry Complicated Urinary Tract Infections: Developing Drugs for Treatment" and in September 2012, it published a draft guidance entitled "Guidance for Industry Complicated Intra-Abdominal Infections: Developing Drugs for Treatment." The purpose of these guidelines was to address any uncertainties regarding what the FDA expected from sponsors and clinical trials for the indications of cUTI and cIAI. The FDA asked sponsors to include additional measurements in their evaluation of efficacy that the FDA believes are more objective and less susceptible to interpretation by investigators.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with 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 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 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. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each

institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, 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 limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population.

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. 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. 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.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, 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 qualified infectious disease product under the recently enacted Generating Antibiotic Incentives Now, or 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. We have requested fast track designation for eravacycline and are awaiting a response from the FDA.

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

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

Moreover, under the provisions of the 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.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

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

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Exclusivity and Approval of Competing Products

Hatch-Waxman Exclusivity

Market and data exclusivity provisions under the FDCA can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. We believe that 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 intravenous formulation of eravacycline for cUTI and cIAI in July 2013 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 licensing, 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, which 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.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered and reimbursed 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 reducing coverage and reimbursement amounts for medical products and services. Additionally, 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 United States, a number of recent legislative reform measures have been passed to contain healthcare reimbursement for pharmaceuticals, including drugs such as our product candidates. For example, the 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 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 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 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, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

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

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

Facilities

Our headquarters are located in Watertown, Massachusetts, where we occupy approximately 23,728 square feet of office and laboratory space. The term of the lease expires on July 31, 2015.

Employees

As of February 28, 2014, we had 46 full-time employees, 33 of whom were primarily engaged in research and development activities. A total of 20 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.

Executive Officers

The following table lists the positions, names and ages of our executive officers as of February 28, 2014:

Executive Officers

Guy Macdonald	54	President and Chief Executive Officer, Director
David C. Lubner	49	Senior Vice President and Chief Financial Officer
Patrick T. Horn, M.D., Ph.D.	59	Chief Medical Officer
J. Craig Thompson	47	Chief Operating Officer
Joyce Sutcliffe, Ph.D.	62	Senior Vice President, Biology

Guy Macdonald has served as our President and Chief Executive Officer and a member of our board of directors since January 2008. From August 2003 until January 2008, Mr. Macdonald served as Executive Vice President, Operations, of Idenix Pharmaceuticals, Inc., a biopharmaceutical company. Prior to joining Idenix, he served in various positions at Merck & Co., Inc., a pharmaceutical company, from 1981 to 2003, most recently serving as the Vice President for Anti-Infective and Hospital Products. Mr. Macdonald currently serves as Chairman of the board of directors of Spring Bank Pharmaceuticals, Inc., a privately held company. Mr. Macdonald received an Honours Degree in biochemistry from Dundee University in Dundee, Scotland.

David C. Lubner has served as our Senior Vice President and Chief Financial Officer since October 2010 and from our inception in 2006 until October 2010 he served on a part-time basis as our Senior Vice President and Chief Operating Officer. Mr. Lubner also served as Chief Financial Officer of Mediphase Venture Partners, a venture capital firm, from 2006 until October 2010. From 1999 to 2005, he served as Vice President and Chief Financial Officer at PharMetrics, Inc., a pharmacy and medical claims data informatics company, until its acquisition by IMS Health in 2005. Prior to joining PharMetrics, Mr. Lubner served as Vice President and Chief Financial Officer of ProScript, Inc., a biotechnology company, from 1996 to 1999. Mr. Lubner is a member of the American Institute of CPAs and is a certified public accountant in the Commonwealth of Massachusetts. Mr. Lubner received a B.S. in business administration from Northeastern University and an M.S. in Taxation from Bentley University.

Patrick T. Horn, M.D., Ph.D. has served as our Chief Medical Officer since January 2011. From September 2007 until December 2010, he served as Vice President, Clinical & Medical Affairs at Dyax Corporation, a biopharmaceutical company. Prior to joining Dyax, Dr. Horn served in various positions at Abbott Laboratories, a pharmaceutical company, from 2001 to 2006, most recently serving as Medical Director, Head of Clinical Pharmacology. Dr. Horn received a B.S. in Chemistry from the University of Illinois, doctorate in the Pharmacological and Physiological Sciences from the University of Chicago and an M.D. from the University of Chicago, Pritzker School of Medicine.

J. Craig Thompson has served as our Chief Operating Officer since February 2014. From January 2011 to December 2013, Mr. Thompson served as Chief Commercial Officer with Trius Therapeutics, Inc. From 2003 to December 2010, Mr. Thompson served in various global and U.S. commercial roles with Pfizer Inc., most recently as Vice President of Marketing for Pfizer's Specialty Care Business Unit. From 1992 to 2003, Mr. Thompson served in positions of increasing responsibility at Merck & Co., Inc., where he most notably worked on the commercial planning and marketing activities for the company's anti-infectives as well as on major cardiovascular brands. Mr. Thompson holds a Bachelor's degree in Commerce from McMaster University and an MBA from the University of Notre Dame.

Joyce Sutcliffe, Ph.D. has served as our Senior Vice President, Biology, since May 2009. From October 2007 until May 2009, Dr. Sutcliffe served as Vice President, Research at NanoBio Corporation, a biopharmaceutical company. From September 2001 until September 2007, Dr. Sutcliffe served as Chief Research Scientist and Vice President, Biology at Rib-X Pharmaceuticals, Inc., a biopharmaceutical company. Prior to joining Rib-X Pharmaceuticals, she held various positions at Pfizer, Inc., a pharmaceutical company, for 16 years. Dr. Sutcliffe received a B.S. in zoology from the University of Florida and a Ph.D. in microbiology from the University of Florida, Gainesville, and has held postdoctoral positions at the University of Massachusetts Medical School and the National Institutes of Health.

Available Information

We file reports and other information with the SEC 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. 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 Street, Suite 110, 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 is subject to numerous 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. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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 $29.6 million for the year ended December 31, 2013, $15.1 million for the year ended December 31, 2012 and $21.6 million for the year ended December 31, 2011. As of December 31, 2013, we had a deficit accumulated during the development stage of $119.7 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 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 increasing 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 substantially as we continue our ongoing Phase 3 clinical trials of our lead product candidate, eravacycline, for the treatment of patients with complicated intra-abdominal infections, or cIAI, and for the treatment of patients with complicated urinary tract infections, or cUTI, seek marketing approval for eravacycline, pursue development of eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections, advance our other product candidates 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 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 clinical, quality control and scientific 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 and successfully completing Phase 3 clinical trials of eravacycline;
- 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 United States Food and Drug Administration, or FDA, or the European Medicines Agency, or EMA, to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development 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 substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We expect that our expenses will increase substantially as we continue our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI, and for the treatment of cUTI, seek marketing approval for eravacycline, pursue development of eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections, advance our other product candidates and satisfy our obligations under our license agreement with Harvard University. We expect that the total external costs of our ongoing Phase 3 clinical trial of eravacycline for the treatment of cIAI and for the treatment of cUTI will be approximately $55.0-$60.0 million. If we obtain marketing approval for eravacycline or any other product candidate that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing.

We believe that our existing cash and cash equivalents will enable us to fund our current operating plan and capital expenditure requirements into the first quarter of 2016. We believe that our available funds will be sufficient to enable us to obtain top-line data from our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI and for the treatment of cUTI and to submit a new drug application, or NDA, to the FDA for eravacycline. We expect that these funds will not, however, be sufficient to enable us to commercially launch eravacycline. 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. 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.

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 our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI and for the treatment of cUTI;

- the timing and costs of developing eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections;
- 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 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 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 costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue received from commercial sales of eravacycline;
- the terms and timing of any future collaborations, licensing 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;
- the costs of operating as a public company; 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 five-year terms, 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 $15.7 million from the initial contract date through April 30, 2015, of which $11.7 million had been received through December 31, 2013.

Similarly, although the NIAID contract and our subcontract with CUBRC under the NIAID contract have five-year terms, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond September 30, 2016. 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 $7.5 million, of which $4.4 million had been received through December 31, 2013. In addition, although the NIAID grant has a term of five years and our subaward from CUBRC has a term of 55 months, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond May 31, 2016. 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 $0.7 million from the initial grant date through May 31, 2016, of which $0.5 million had been received through December 31, 2013.

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 actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business. For example, our debt facility with Silicon Valley Bank and Oxford Finance contains restrictive covenants that, subject to certain exceptions, prohibit us from transferring all or any part of our business or property, changing our business, liquidating or dissolving, merging with or acquiring another entity, entering into a transaction that will result in a change of control, incurring additional indebtedness, creating any lien on our property, paying dividends, entering into material transactions with affiliates, changing key management or adding new offices or business locations. Future debt securities or other financing arrangements could contain similar or more restrictive negative covenants. 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 successfully complete a large-scale, pivotal clinical trial, 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. 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 completion of clinical trials;
- 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;
- launch of commercial sales 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, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections, 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 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 our Phase 2 trial in cIAI, we may nonetheless fail to achieve success in our pivotal Phase 3 program for eravacycline. We have not previously conducted a clinical trial to evaluate eravacycline in treating cUTI and have not tested any oral formulation of eravacycline in any clinical trial designed to evaluate its therapeutic efficacy in any indication. Moreover, the primary endpoint we are using for our ongoing Phase 3 clinical trial of eravacycline for the treatment of cIAI differs from the primary endpoint we successfully achieved in our Phase 2 trial in cIAI. The primary endpoint of this Phase 3

clinical trial is clinical response in the microbiological intent-to-treat patient population, which includes all randomized patients who have baseline bacterial pathogens that cause cIAI and against which the dosed eravacycline has antibacterial activity, at the test-of-cure visit 25 to 31 days after the initial dose of treatment. Our Phase 2 primary endpoint was clinical response at the test-of-cure visit that took place ten to 14 days after the last dose of the drug was administered (approximately 16 to 21 days after randomization) in microbiologically evaluable patients, a narrower patient population. Clinical response was defined as complete resolution or significant improvement of signs or symptoms of infection with no further systemic antibiotic treatment required.

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. 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 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 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 our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI and for the treatment of cUTI 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 vomiting. 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 postmarket 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 step-down 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 and publications, 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 have no experience in the sales, 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 inability 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 eravacycline or any other 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 multidrug-resistant infections that we would expect would compete with eravacycline, including meropenem, which is marketed by AstraZeneca as Merrem, imipenem/cilastatin, which is marketed by Merck as Primaxin, tigecycline, which is marketed by Pfizer as Tygacil, levofloxacin, which is marketed by Ortho-McNeil and Johnson & Johnson as Levaquin, and piperacillin/tazobactam, which is marketed by Pfizer 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 in clinical development by third parties to treat multidrug-resistant infections, including ceftazidime/avibactam, which is being developed by Forest Laboratories Inc. and AstraZeneca, cefalozine/tazobactam, which is being developed by Cubist, and plazomicin, which is being developed by Achaogen, Inc. If our competitors obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapidly than we do, it 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, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller 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 Generating Antibiotics Incentives Now Act, or 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 licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we 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 eravacycline, 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.

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 outside the United States.

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 for eravacycline and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. 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 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:

- manufacturing delays 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;
- 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. 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 and may impose requirements that increase the costs of commercialization and production of product candidates developed under those government-funded programs.

Our development of eravacycline for the treatment of disease caused by bacterial biothreat pathogens is currently being funded through a subcontract with funding from BARDA. In addition, our development of TP-271 is being funded through a subcontract and grant subaward with funding 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 powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason;
- reduce or modify the government's obligations under such agreements without the consent of the other party;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor 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;
- suspend or debar the contractor or grantee from doing future business with the government;
- 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. These requirements include, for example:

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

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.

As a U.S. government contractor, we are subject to financial audits and other reviews by the U.S. government of our costs and performance on their contracts, as well as our accounting and general business practices related to these contracts. Based on the results of its audits, the government may adjust our contract-related costs and fees, including allocated indirect costs. Although adjustments arising from government audits and reviews have not had a material adverse effect on our financial condition or results of operations in the past, we cannot be certain that future audits and reviews will not have those effects.

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 be 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.

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 products candidates, including 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, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. 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 registered our trademarks. Failure to secure those registrations could adversely affect our business.

We have not yet registered our trademarks in the United States or other countries. 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 not yet registered trademarks for any of our product candidates in any jurisdiction. When we file trademark applications for our product candidates those applications 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.

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, 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. 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 other 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. 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.

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, 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;
- 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 or withdraw marketing approvals;
- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions or impose civil 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 false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements 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.

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 2012, 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 Guy Macdonald, our President and Chief Executive Officer, Patrick T. Horn, our Chief Medical Officer, David C. Lubner, our Senior Vice President and Chief Financial Officer, J. Craig Thompson, our Chief Operating Officer, and Joyce Sutcliffe, our Senior Vice President, Biology, 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.

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.

If foreign approvals are obtained, we will be subject to additional risks in conducting business in international markets.

Even if we are able to obtain approval for commercialization of a product candidate in a foreign country, we will be subject to additional risks related to international business operations, 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.

These and other risks may materially adversely affect our ability to attain or sustain revenue from international markets.

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. 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 success of existing or new competitive products or technologies;
- the timing of clinical trials of eravacycline and any other product candidate;
- results of clinical trials of eravacycline and any other product candidate;

- failure or discontinuation of any of our development programs;
- 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.

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

Although we have listed our common stock on The NASDAQ Global 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 are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years following our initial public offering in March 2013. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We are currently incurring and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a newly public company we are incurring, and, particularly after we are no longer an "emerging growth company," we expect that we will incur further, 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 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 will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors.

We are currently evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an annual report on Form 10-K with the Securities and Exchange Commission. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over

financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are currently engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan 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. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, 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 debt facility with Silicon Valley Bank and Oxford Finance preclude 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.

Our executive officers and directors, and their affiliates, if they choose to act together, have the ability to significantly influence all matters submitted to stockholders for approval.

As of February 28, 2014, our executive officers and directors, and stockholders affiliated with our executive officers and directors, beneficially owned in the aggregate shares representing approximately 17% of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and/or the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

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 23,728 square feet of office, research and laboratory space located at 480 Arsenal Street, Watertown, Massachusetts. The leases covering this space expire on July 31, 2015. We believe that our existing facilities are sufficient for our current needs for the foreseeable future.

ITEM 3. Legal Proceedings

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

ITEM 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Price Information

Our common stock began trading on the NASDAQ Global 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 Market:

	High	Low
2013		
First Quarter from and after March 20, 2013	$ 7.50	$6.62
Second Quarter	$ 9.66	$7.00
Third Quarter	$11.77	$7.04
Fourth Quarter	$13.89	$9.85

Holders

At February 28, 2014, there were approximately 11 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 and our ability to pay cash dividends is currently prohibited by the terms of our debt financing arrangements. 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.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of common stock issued, and options and warrants granted, by us during 2013 that were not registered under the Securities Act of 1933, as amended. Included is the consideration, if any, we received for such shares, options and warrants and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed. No underwriters were involved in any such issuances.

(a) Stock Option Grants:

Between January 1, 2013 and June 14, 2013, we granted options to purchase an aggregate of 1,250,940 shares of common stock, with exercise prices ranging from $7.07 to $8.75 per share, to employees and directors pursuant to our 2013 Stock Incentive Plan. Between January 1, 2013 and June 14, 2013, we issued an aggregate of 6,178 shares of common stock upon the exercise of options for aggregate consideration of $9,765.

The stock options and the common stock issuable upon the exercise of such options as described in this paragraph (a) were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

(b) Warrant Grants:

On February 28, 2013, in connection with the our borrowing of $3.0 million under our Loan and Security Agreement with Silicon Valley Bank and Oxford Finance, an existing warrant to purchase Series C preferred stock that we issued to Silicon Valley Bank on December 20, 2012 became exercisable for an additional 233,372 shares of Series C preferred stock at a price of $0.2571 per share and we simultaneously issued an additional warrant to purchase 233,372 shares of Series C preferred stock at a price of $0.2571 per share to Oxford Finance.

The securities described in this paragraph (b) were issued in reliance upon the exemption from the registration requirements of the Securities Act set forth in Section 4(a)(2) under the Securities Act promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required.

All of the securities described in paragraphs (a) and (b) are deemed restricted securities for purposes of the Securities Act. All of the certificates representing such securities included appropriate legends setting forth that the securities have not been registered and the applicable restrictions on transfer.

Use Of Proceeds

We effected the initial public offering, or IPO, of our common stock through a Registration Statement on Form S-1 (File No. 333-186574) that was declared effective by the Securities and Exchange Commission on March 19, 2013. On March 25, 2013, we completed the sale of 10,714,286 shares of common stock in our IPO at a price to the public of $7.00 per share, resulting in net proceeds to us of $68.0 million after deducting underwriting discounts and commissions of $4.4 million and offering costs of $2.5 million. In addition, we granted the underwriters a 30-day option to purchase up to 1,607,143 additional shares of common stock at the IPO price to cover over allotments, if any. On April 12, 2013, we completed the additional sale of 797,792 shares of common stock under this option at a price to the public of $7.00 per share, resulting in net proceeds to us of $5.2 million after deducting underwriting discounts and commissions of $0.4 million. The offering commenced on March 19, 2013 and terminated before the sale of all of the securities registered in the offering. Barclays Capital Inc. and BMO Capital Markets Corp. acted as joint book-running managers for the offering and Stifel, Nicolaus & Company, Incorporated, JMP Securities LLC and Needham & Company, LLC acted as co-managers of the offering. There were no selling stockholders in the offering.

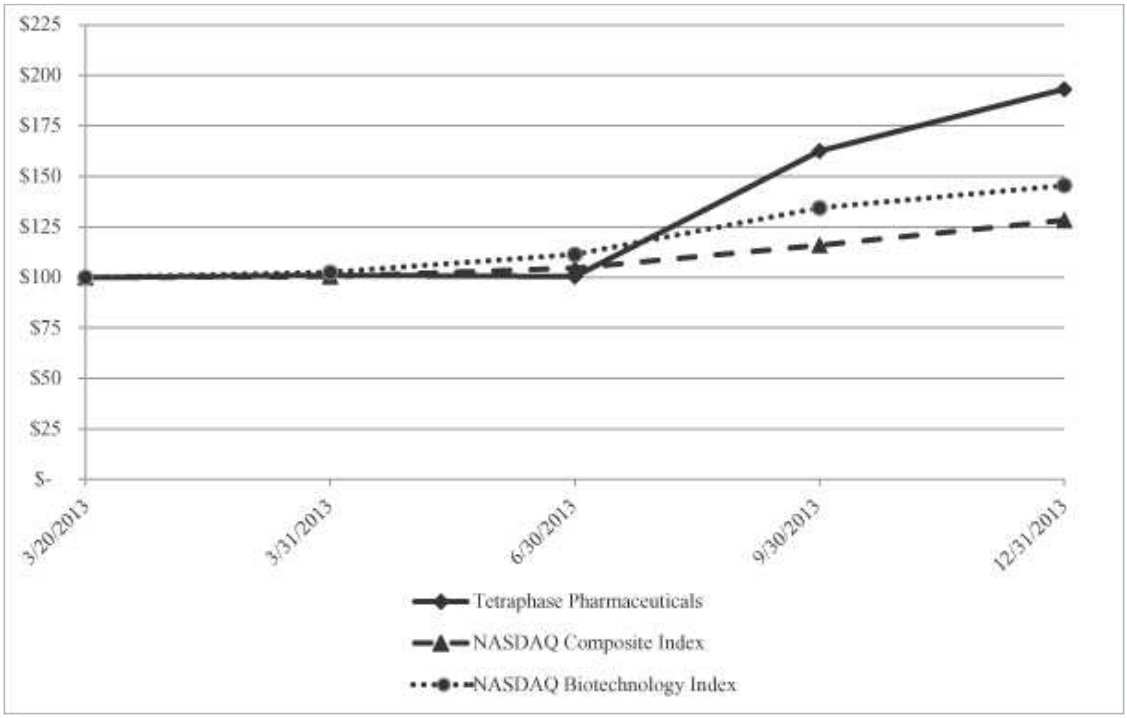
The aggregate net offering proceeds to us, after deducting underwriting discounts and offering expenses, were approximately $73.2 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

As of December 31, 2013, we estimate that we have used approximately $18.9 million of the net proceeds from the IPO to fund the clinical development of eravacycline and for working capital and other general corporate purposes. We hold the unused proceeds from the offering in cash and money market funds. There has been no material change in our planned use of proceeds from the IPO from that described in the final prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) on March 20, 2013.

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	3/31/13	6/30/13	9/30/13	12/31/13
Tetraphase Pharmaceuticals	$100.00	$101.00	$100.43	$162.57	$193.14
NASDAQ Composite Index	$100.00	$100.41	$104.58	$115.90	$128.34
NASDAQ Biotechnology Index	$100.00	$102.51	$111.35	$134.43	$145.52

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 balance sheet data at December 31, 2013 and 2012 and the consolidated statement of operations data for each of the three years in the period ended December 31, 2013 and the period from July 7, 2006 (inception) to December 31, 2013 have been derived from our audited consolidated financial statements for such years, included elsewhere in this annual report on Form 10-K. The consolidated balance sheet data at December 31, 2011 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.

	Years Ended December 31,			The Period from July 7, 2006 (inception) to December 31,
	2013	2012	2011	2013
Statement of Operations Data:				
Contract and grant revenue	$ 10,486	$ 7,600	$ 185	$ 18,271
Operating expenses:				
Research and development	31,508	17,294	17,737	106,615
General and administrative	7,168	4,309	3,874	24,471
Total operating expenses	38,676	21,603	21,611	131,086
Loss from operations	(28,190)	(14,003)	(21,426)	(112,815)
Other income (expense):				
Interest income	10	—	1	618
Interest expense	(1,719)	(1,021)	(161)	(3,157)
Other income (expense)	263	(63)	22	(4,367)
Total other income (expense)	(1,446)	(1,084)	(138)	(6,906)
Net loss	$(29,636)	$(15,087)	$(21,564)	$ (119,721)
Net loss per share applicable to common stockholders-basic and diluted (1)	$ (1.78)	$ (47.54)	$ (73.34)	$ (49.36)
Weighted-average number of common shares used in net loss per share applicable to common stockholders-basic and diluted	16,665	317	294	2,425
Comprehensive loss	$(29,636)	$(15,087)	$(21,564)	

	As of December 31,		
	2013	2012	2011
		(in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 102,712	$ 9,079	$ 22,454
Working capital	92,229	3,720	16,400
Total assets	105,886	14,072	24,069
Current liabilities	13,191	8,661	6,974
Long-term obligations	4,887	8,619	5,857
Convertible preferred stock	—	79,841	79,841
Deficit accumulated during the development stage	(119,721)	(90,085)	(74,998)
Total stockholders' equity (deficit)	$ 87,808	$(83,049)	$(68,603)

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. Our lead product candidate, eravacycline, is a fully synthetic tetracycline derivative that we are developing as a broad-spectrum intravenous and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant Gram-negative infections. We are conducting a Phase 3 clinical trial of eravacycline with intravenous administration for the treatment of complicated intra-abdominal infections, or cIAI, and a second Phase 3 clinical trial of eravacycline for the treatment of complicated urinary tract infections, or cUTI, with intravenous-to-oral step-down therapy. We expect to have top-line data from the Phase 3 cIAI clinical trial in the first quarter of 2015, data from a lead-in portion of the Phase 3 cUTI clinical trial in mid-2014 and top-line data from the Phase 3 cUTI clinical trial in mid-2015. 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, we expect that positive results from these two Phase 3 clinical trials would be sufficient to support submission of a new drug application, or NDA, for eravacycline in the treatment of cIAI and cUTI. Subject to obtaining additional financing, we intend to pursue development of eravacycline for the treatment of additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections following our development of eravacycline for the treatment of cIAI and cUTI. We are also pursuing the discovery and development of TP-271, a preclinical compound that we are developing for respiratory diseases caused by bacterial biothreat pathogens, and additional antibiotics to target unmet medical needs, including multidrug-resistant Gram-negative bacteria.

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 the public offering and private placement of our equity securities, debt financings and revenue from U.S. government awards. As of December 31, 2013, we had received an aggregate of $217.4 million in net proceeds from the issuance of equity securities and borrowings under debt facilities and an aggregate of $16.7 million from government grants and contracts. As of December 31, 2013, our principal source of liquidity was cash and cash equivalents, which totaled $102.7 million.

As of December 31, 2013, we had a deficit accumulated during the development stage of $119.7 million. Our net losses were $29.6 million, $15.1 million and $21.6 million for the years ended December 31, 2013, 2012 and 2011, respectively. We expect that our expenses will increase substantially as we continue our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI and for the treatment of cUTI, seek marketing approval for eravacycline, pursue development of eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections, advance our other product candidates 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 administrative costs will increase as we grow and continue to operate as a public company. We will need to generate significant revenue to achieve profitability, and we may never do so.

We believe that our available funds will be sufficient to enable us to obtain top-line data from our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI and for the treatment of cUTI and to submit an NDA to the FDA for eravacycline. We expect that these funds will not, however, be sufficient to enable us to commercially launch eravacycline. 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.

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 $67.0 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. 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 $2.8 million over five years, 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 over five years, 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 five-year cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $39.8 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 five-year cost-plus-fixed-fee subcontract with CUBRC under which we may receive funding of up to approximately $13.3 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 55-month, no-fee subaward of approximately $980,000, 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 five-year terms, 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 $15.7 million from the initial contract date through April 30, 2015, of which $11.7 million had been received through December 31, 2013.

Similarly, although the NIAID Contract and our subcontract with CUBRC under the NIAID Contract have five-year terms, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond September 30, 2016. 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 $7.5 million, of which $4.4 million had been received through December 31, 2013. In addition, although the NIAID Grant has a term of five years and our subaward from CUBRC has a term of 55 months, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond May 31, 2016. 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 $0.7 million from the initial grant date through May 31, 2016, of which $0.5 million had been received through December 31, 2013.

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, which we do not expect will occur before 2016, 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:

- employee-related expenses, including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, or CROs, contract manufacturing organizations, or CMOs, and consultants that conduct our clinical trials and preclinical activities;
- 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 facility, insurance and other supplies; and
- costs associated with preclinical activities and regulatory operations.

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 lab 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, 2013 and 2012 and the period from July 7, 2006 (inception) to December 31, 2013:

	Years Ended December 31,		The Period from July 7, 2006 (inception) to December 31,
	2013	2012	2013
		(in thousands)	
Eravacycline	$17,671	$ 6,932	$ 48,396
BARDA Contract	7,341	4,279	11,620
NIAID Contract and NIAID Grant	2,625	2,537	5,335
Other development programs	1,041	1,071	21,489
Other research and development	2,830	2,475	19,775
Total research and development	$31,508	$17,294	$ 106,615

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, 2013, we had incurred an aggregate of $48.4 million in research and development expenses related to the development of eravacycline, excluding $11.6 million of expenses that were funded under the BARDA Contract. We expect that our research and development expenses will increase substantially as we continue our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI and the treatment of cUTI, pursue development of eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections, advance our other product candidates and satisfy our obligations under our license agreement with Harvard University. We expect that the total external costs of the Phase 3 clinical trials of eravacycline for the treatment of cIAI and the treatment of cUTI will be approximately $55.0-$60.0 million, of which $11.9 million had been incurred during the year ended December 31, 2013.

Because of the numerous risks and uncertainties associated with product development, however, we cannot determine with certainty the duration and completion costs of these or other 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 $3.8 million in upfront license fees and development milestone payments, including a $2.0 million milestone fee that we paid in October 2013 in connection with the dosing of the first patient in our Phase 3 clinical trial of eravacycline for the treatment of patients with cIAI. 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 by us, 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 that would come due under the license agreement with respect to eravacycline is a $3.0 million payment that would become due to Harvard upon acceptance of an NDA filing to the FDA for eravacycline.

General and Administrative Expenses

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

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;
- increases in payroll, expansion of infrastructure and higher consulting, legal, accounting and investor relations costs, and directors and officers insurance premiums, all associated with operating as a public company; and
- if and when we believe a regulatory approval of our first product candidate appears likely, anticipated increases in our payroll and expense 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 consists 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 expect that our interest expense will decrease in future periods as we pay down principal on our indebtedness to Silicon Valley Bank and Oxford Finance over the term of the loan.

Other Income (Expense)

Other income (expense) consists of fair value adjustments on warrants for the purchase of our preferred stock. We do not anticipate that we will recognize any further amounts with respect to these fair value adjustments as a result of the conversion of all outstanding warrants to purchase our preferred stock into warrants to purchase our common stock in connection with the completion of our initial public offering, or the IPO.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities 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 expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ 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.

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:

- CROs in connection with clinical trials;
- CMOs with respect to clinical materials and intermediaries;
- vendors in connection with preclinical development activities; and
- vendors related to manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs 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 differs 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

Since our inception in July 2006, we have applied the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation-Stock Compensation* , which we refer to as ASC 718, to account for all stock-based compensation. We recognize compensation costs related to stock options 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. Described below is the methodology we have utilized in measuring stock-based compensation expense.

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. We recognize stock-based compensation expense ratably over the requisite service period, which in most cases is the vesting period of the award. 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 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 grant for instruments with a similar expected life.

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. Stock-based compensation expense requires certain estimates by management. We cannot currently predict the total amount of stock-based compensation expense to be recognized in any future period because such amounts will depend on levels of stock-based payments granted in the future as well as the portion of the awards that actually vest. 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. During the years ended December 31, 2013, 2012 and 2011 our estimated annual forfeiture rate was 3%, 3% and 0%, respectively.

Stock-based compensation expense includes options granted to employees and non-employees and has been reported in our statements of operations and comprehensive loss as follows:

	Year Ended December 31,			The Period from July 7, 2006 (inception) to December 31,
	2013	2012	2011	2013
			(in thousands)	
Research and development	$ 690	$463	$175	$ 1,686
General and administrative	611	149	137	1,161
Total	$1,301	$612	$312	$ 2,847

We estimated the fair value of stock options at the grant date using the following assumptions:

	Years Ended December 31,		
	2013	2012	2011
Weighted average expected volatility	58%	67%	64%
Expected life (in years)	5.8-7.1	6.0-6.1	6.0-6.1
Risk free interest rate	0.91%-2.01%	0.85%-1.21%	1.21%-2.41%
Expected dividend yield	0%	0%	0%

The following table presents the grant dates and related exercise or purchase prices of stock options that we granted from January 1, 2012 through the date we became a public company, along with the corresponding exercise price for each option grant and the fair value per share utilized to calculate stock-based compensation expense:

Date of Grant	Number of shares underlying options granted	Exercise price per share	Common stock fair value per share on grant date
1/20/2012	24,786	$ 2.03	$ 2.03
1/26/2012	11,206	$ 2.03	$ 2.03
6/6/2012	170,676	$ 2.03	$ 3.77
11/19/2012	5,171	$ 5.22	$ 5.22

For grants made prior to the consummation of our IPO on March 25, 2013, the estimated fair value per share of common stock in the table above represents the determination by our board of directors of the fair value of our common stock as of the date of grant, taking into consideration various objective and subjective factors, including the conclusions of contemporaneous valuations of our common stock. For grants made following the consummation of our IPO, our board of directors determined that the fair value per share of our common stock on the date of grant is equal to the closing price of our common stock on The NASDAQ Global Market on the date of grant.

Prior to our IPO, due to the absence of an active market for our common stock, the fair value of our common stock was determined in good faith by our board of directors, with the assistance and upon the recommendations of management, based on objective and subjective factors consistent with the methodologies outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* , referred to as the AICPA Practice Aid, including:

- the shares of common stock were illiquid securities in a private company;
- the prices of shares of our preferred stock that we had sold to outside investors in arm's length transactions, and the rights, preferences and privileges of that preferred stock relative to our common stock;
- our results of operations, financial position and the status of our research and development efforts, including the status of clinical trials for our product candidates under development;
- the material risks related to our business;
- our business strategy;
- our achievement of key milestones, including the results of clinical trials;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors, and recently completed mergers and acquisitions of companies comparable to us;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as, sale of the company or an initial public offering given prevailing market conditions;
- external market conditions affecting the life sciences and biotechnology industry sectors; and
- contemporaneous and retrospective valuations of our common stock.

Since our IPO, the exercise price per share of all option grants has been set at the closing price of our common stock on The NASDAQ Global Market on the applicable date of grant, which our board of directors believes represents the fair value of our common stock.

Stock-based compensation expense related to awards granted to employees was $1.3 million and $0.3 million for the years ended December 31, 2013 and 2012, respectively. As of December 31, 2013, we had approximately $5.6 million of total unrecognized stock-based compensation expense related to unvested stock options, expected to be recognized over a weighted-average period of 3.3 years. We expect that our stock-based compensation expense for stock options granted to employees will grow in future periods due to the potential increases in the value of our common stock and headcount.

During 2009, we granted options to non-employees to purchase 232,758 shares of common stock. These options vested with respect to one-third of the underlying shares on the date of grant, with the remaining shares vesting quarterly over four years from date of grant and have a life of ten years. During 2010, we granted options to non-employees to purchase 12,972 shares of common stock. These non-employee options vest quarterly through the fourth anniversary of the vesting date and have a contractual term of ten years. Stock options issued to non-employees are accounted for at fair value. We periodically revalue the options as they vest and recognize expense over the related service period. The total expense related to all non-employee options was $39,000 and $307,000 for the years ended December 31, 2013 and 2012, respectively, and $621,000 for the period from July 7, 2006 (inception) through December 31, 2013.

Results of Operations

Comparison of Years Ended December 31, 2013 and 2012

The following tables summarize the results of our operations for each of the years ended December 31, 2013 and 2012, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2013	2012		
	(in thousands)			
Revenues	$ 10,486	$ 7,600	$ 2,886	38%
Operating expenses:				
Research and development	31,508	17,294	14,214	82%
General and administrative	7,168	4,309	2,859	66%
Total operating expenses	38,676	21,603	17,073	79%
Loss from operations	(28,190)	(14,003)	(14,187)	101%
Interest income	10	—	10	100%
Interest expense	(1,719)	(1,021)	(698)	68%
Other income (expense)	263	(63)	326	(517)%
Net loss	$(29,636)	$(15,087)	$(14,549)	96%

The following table sets forth our contract and grant revenue for the years ended December 31, 2013 and 2012:

Revenue	Years Ended December 31,		Increase/ (decrease)	%
	2013	2012		
	(in thousands)			
BARDA	$ 7,707	$4,876	$ 2,831	58%
NIAID Contract	2,512	2,451	61	2%
NIAID Grant	267	273	(6)	(2)%
	$10,486	$7,600	$ 2,886	38%

Contract and Grant Revenue

Contract and grant revenue was $10.5 million for the year ended December 31, 2013 compared to $7.6 million for the year ended December 31, 2012, an increase of $2.9 million, or 38%. This increase was primarily due to revenue associated with an increase in the activities under our subcontract with respect to the BARDA Contract.

Research and Development Expenses

Research and development expenses were $31.5 million for the year ended December 31, 2013 compared to $17.3 million for the year ended December 31, 2012, an increase of $14.2 million or 82%. This increase was primarily due to an increase of $8.5 million in clinical costs related to our Phase 3 clinical program for eravacycline for the treatment of cIAI and cUTI; an increase of $3.1 million in expenses related to activities under our subcontract with CUBRC with respect to the BARDA Contract; a $2.0 million milestone fee due under our license agreement with Harvard University that became payable during the year ended December 31, 2013 in connection with the dosing of the first patient in our Phase 3 cIAI clinical trial; an increase of $1.9 million in drug manufacturing costs associated with our Phase 3 clinical program for eravacycline for the treatment of cIAI and cUTI; an increase in personnel-related costs of $0.9 million to support our increased activities related to the

Phase 3 clinical program for eravacycline, the BARDA Contract, the NIAID Contract, and the NIAID Grant; and an increase of $0.6 million in development costs associated with the oral formulation of eravacycline. These increases were offset in part by a decrease in clinical and drug manufacturing costs of $3.3 million attributable to the completion of our Phase 2 clinical trial of eravacycline in the first half of 2012.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2013 were $7.2 million compared to $4.3 million for the year ended December 31, 2012, an increase of $2.9 million or 66%. This increase was primarily due to an increase of $1.3 million in audit, legal, insurance and consulting costs primarily due to operating as a public company; an increase in personnel-related costs of $0.8 million; and an increase in stock-based compensation expense of $0.5 million.

Interest Income

Interest income for the years ended December 31, 2013 and December 31, 2012 was immaterial.

Interest Expense

Interest expense for the year ended December 31, 2013 was $1.7 million compared to $1.0 million for the year ended December 31, 2012, an increase of approximately $0.7 million or 68%. The increase in interest expense was primarily attributable to an increase in debt under the term loan facility with Silicon Valley Bank and Oxford Finance associated with our borrowings in December 2012 and February 2013. We expect that our interest expense will decrease in future periods as we pay down principal on our indebtedness to Silicon Valley Bank and Oxford Finance over the term of the loan.

Other Income (Expense)

Other income (expense) for the year ended December 31, 2013 was $0.3 million compared to $(0.1) million for the year ended December 31, 2012. The increase in other income was primarily due to a decrease in the fair value of the underlying preferred stock, which impacted the fair value of our preferred stock warrants issued in connection with our December 2012 and February 2013 debt facility with Silicon Valley Bank and Oxford Finance. We do not anticipate that we will recognize any further amounts with respect to these fair value adjustments as a result of the conversion of all outstanding warrants to purchase our preferred stock into warrants to purchase our common stock in connection with the completion of our IPO.

Comparison of Years Ended December 31, 2012 and 2011

The following tables summarize the results of our operations for each of the years ended December 31, 2012 and 2011, together with the changes in those items in dollars and as a percentage:

	Years Ended December 31,		Increase/ (decrease)	%
	2012	2011		
	(in thousands)			
Revenues	$ 7,600	$ 185	$ 7,415	4,008%
Operating expenses:				
Research and development	17,294	17,737	(443)	(2)%
General and administrative	4,309	3,874	435	11%
Total operating expenses	21,603	21,611	(8)	—
Loss from operations	(14,003)	(21,426)	7,423	(35)%
Interest income	—	1	(1)	(100)%
Interest expense	(1,021)	(161)	(860)	(534)%
Other income (expense)	(63)	22	(85)	(386)%
Net loss	$(15,087)	$(21,564)	$ 6,477	(30)%

The following table sets forth our contract and grant revenue for the years ended December 31, 2012 and 2011:

Revenue	Years Ended December 31, 2012	2011	Increase/ (decrease)	%
			(in thousands)	
BARDA	$4,876	—	$ 4,876	100%
NIAID Contract	2,451	$183	2,268	1,239%
NIAID Grant	273	2	271	13,550%
	$7,600	$185	$ 7,415	4,008%

Contract and Grant Revenue

Contract and grant revenue was $7.6 million for year ended December 31, 2012 compared to $0.2 million for the year ended December 31, 2011, an increase of $7.4 million, or 4,008%. This increase was primarily due to the commencement of work under our subcontracts under the BARDA Contract and the NIAID Contract and our subaward under the NIAID Grant, which provided $4.9 million, $2.4 million and $0.3 million, respectively, of contract and grant revenue in the year ended December 31, 2012.

Research and Development Expenses

Research and development expenses were $17.3 million for the year ended December 31, 2012 compared to $17.7 million for the year ended December 31, 2011, a decrease of approximately $0.4 million or 2%. This decrease was primarily due to lower clinical costs of $1.2 million attributable to the completion of our Phase 2 clinical trial of eravacycline in the first half of 2012 and the completion of a Phase 1 clinical trial of another pipeline compound in the fourth quarter of 2011; a decrease in development milestone payments of $1.1 million under our license agreement with Harvard University reflecting various milestone payments made in 2011 primarily related to the initiation of the Phase 2 clinical trial for eravacycline and achievement of milestones for other preclinical compounds in development; and a decrease of $0.8 million in preclinical expenses for an oral formulation of eravacycline and for other pipeline compounds. These decreases were partially offset by increases in process chemistry costs of $1.9 million; clinical costs of $0.5 million; and preclinical costs of $0.2 million, in connection with our subcontracts under the NIAID Contract and the BARDA Contract and our subaward under the NIAID Grant.

General and Administrative Expenses

General and administrative expenses were $4.3 million for the year ended December 31, 2012 compared to $3.9 million for the year ended December 31, 2011, an increase of $0.4 million or 11%. This increase was primarily due to additional overhead and personnel costs to support our increased activities related to the NIAID Contract, the BARDA Contract and the NIAID Grant.

Interest Income

Interest income for the years ended December 31, 2012 and 2011 was immaterial.

Interest Expense

Interest expense was $1.0 million for the year ended December 31, 2012 compared to $0.2 million for the year ended December 31, 2011, an increase of approximately $0.9 million. The increase in interest expense was primarily attributable to an increase in debt under the term loan facility with Silicon Valley Bank and Oxford Finance that we entered into in May 2011, resulting primarily from borrowing $1.5 million under this term loan facility in May 2011 and an additional $6.5 million in December 2011.

Other Income (Expense)

Other income (expense) for the year ended December 31, 2012 was $(63,000) compared to $22,000 for the year ended December 31, 2011. Other income (expense) consisted of the fair value adjustment of our preferred stock warrants issued in connection with various debt financings in October 2007, May 2011 and December 2012, which are described in Note 7 to our consolidated financial statements appearing elsewhere in this annual report on Form 10-K. The decrease in other income (expense) from the year ended December 31, 2011 to the year ended December 31, 2012 of $85,000 was due primarily to an increase in the fair value of the underlying preferred stock.

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, 2013, we had cash and cash equivalents of approximately $102.7 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, 2013, our funds were held in cash and money market funds.

On November 13, 2013, we completed the sale of 4,500,000 shares of common stock in a follow-on public offering at a price to the public of $10.00 per share, resulting in net proceeds to us of $41.8 million after deducting underwriting discounts and commissions of $2.7 million and offering costs of $0.5 million. On November 19, 2013, we completed the sale of an additional 407,403 shares of common stock to underwriters under the underwriters' option to purchase additional shares of common stock at a price to the public of $10.00 per share, resulting in net proceeds to us of $3.8 million after deducting underwriting discounts and commissions.

On March 25, 2013, we completed the sale of 10,714,286 shares of common stock in our IPO at a price to the public of $7.00 per share, resulting in net proceeds to us of $68.0 million after deducting underwriting discounts and commissions of $4.4 million and offering costs of $2.5 million. On April 12, 2013, we completed the sale of an additional 797,792 shares of common stock to underwriters under the underwriters' option to purchase additional shares of common stock at a price to the public of $7.00 per share, resulting in net proceeds to us of $5.2 million after deducting underwriting discounts and commissions.

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

	Years Ended December 31,		
	2013	2012	2011
		(in thousands)	
Net cash used in operating activities	$ (24,506)	$(16,657)	$(19,876)
Net cash used in investing activities	(129)	(54)	(65)
Net cash provided by financing activities	118,268	3,336	7,810
Net increase (decrease) in cash and cash equivalents	$ 93,633	$(13,375)	$(12,131)

During the years ended December 31, 2013, 2012 and 2011, our operating activities used net cash of $24.5 million, $16.7 million and $19.9 million, respectively. The net cash used in operating activities in these periods primarily resulted from our net losses and changes in our working capital accounts. The increase in net cash used in operations for the year ended December 31, 2013 as compared to the year ended December 31, 2012 was due

primarily to higher operating expenses during the year ended December 31, 2013 of $38.7 million as compared to $21.6 million for the year ended December 31, 2012. The decrease in net cash used in operations for the year ended December 31, 2012 as compared to the year ended December 31, 2011 was due primarily to an increase in contract and grant revenue in 2012 in connection with our subcontracts under the BARDA Contract and the NIAID Contract and our subaward under the NIAID Grant.

During the years ended December 31, 2013, 2012 and 2011, our investing activities used net cash of $129,000, $54,000 and $65,000, respectively. The net cash used by investing activities during these periods resulted from purchases of property, plant and equipment to facilitate our increased research and development activities and increased headcount. The increase in net cash used in investing activities for the year ended December 31, 2013 as compared to the year ended December 31, 2012 was due to an increase in various property and equipment purchased during the year ended December 31, 2013. The decrease in net cash used in investing activities for the year ended December 31, 2012 as compared to the year ended December 31, 2011 primarily reflected a decrease in laboratory equipment purchases in 2012.

During the years ended December 31, 2013, 2012 and 2011 our net cash provided by financing activities was $118.3 million, $3.3 million and $7.8 million, respectively. The net cash provided by financing activities during the year ended December 31, 2013 was primarily related to proceeds from our IPO of $73.8 million, proceeds from our follow-on public offering of $45.6 million, and $3.0 million in borrowings that we made under our debt facility with Silicon Valley Bank and Oxford Finance, offset in part by repayments on our debt facility of $4.2 million. The net cash provided by financing activities during the year ended December 31, 2012 was primarily related to $6.2 million in borrowings that we made under our debt facility with Silicon Valley Bank and Oxford Finance, which amount was partially offset by $2.2 million in debt service costs. The net cash provided by financing activities during the year ended December 31, 2011 was due to $8.0 million in borrowings that we made in 2011 under our debt facility with Silicon Valley Bank and Oxford Finance.

Credit Facilities

In May 2011, we executed a Loan and Security Agreement with two financial institutions, Silicon Valley Bank and Oxford Finance, which provided for up to $8.0 million in funding, to be made available in two tranches. We borrowed the first $1.5 million in May 2011 and the second tranche for the remaining $6.5 million in December 2011. As of December 31, 2013, an aggregate of $2.9 million of principal and accrued interest remained outstanding under these two tranches. On December 20, 2012, we amended the Loan and Security Agreement to provide for up to an additional $9.2 million in funding, to be made available in two tranches, . We borrowed the first $6.2 million on December 20, 2012, of which $5.2 million remained outstanding at December 31, 2013. The second tranche of $3.0 million was borrowed by us on February 28, 2013 , of which $2.7 million of principal and accrued interest remained outstanding at December 31, 2013. As of December 31, 2013, the aggregate principal balance outstanding under loans was $10.8 million.

Of the $10.8 million of principal outstanding under the debt facility as of December 31, 2013, $2.9 million of the outstanding principal, which we originally borrowed in 2011, bears interest at 10% per annum with an additional payment of 2.75% of the original $8.0 million of principal due at the maturity date of November 1, 2014. We were required to pay interest only on the 2011 borrowing through February 28, 2012. We are now repaying indebtedness on the 2011 borrowing in equal monthly payments of $0.3 million through November 1, 2014. The additional payment of 2.75% of the original $8.0 million of principal will be due at the same time as the last loan payment. $5.2 million of outstanding principal, which we borrowed under the debt facility in December 2012, bears interest at 9% per annum with an additional payment of 2.9% of the original $6.2 million of principal due at the maturity date of March 1, 2016. We were required to pay interest only on the 2012 borrowing through June 1, 2013. We are now repaying this indebtedness in 33 equal monthly payments of $0.2 million through March 1, 2016. The additional payment of 2.9% of the original $6.2 million of principal will be due at the same time as the last loan payment. The remaining $2.7 million of outstanding principal, which we borrowed under the debt facility in February 2013, bears interest at 9% per annum with an additional payment of

2.9% of the original $3.0 million of principal due at the maturity date of May 1, 2016. We were required to pay interest only on the 2013 borrowing through August 1, 2013. We are now repaying this indebtedness in 33 equal monthly payments of $0.1 million through May 1, 2016. The additional payment of 2.9% will be due at the same time as the last loan payment.

The loans under the debt facility are collateralized by a blanket lien on all of our corporate assets, excluding intellectual property, and by a negative pledge on our intellectual property. The loan and security agreement contains customary default provisions that include material adverse events, as defined therein, that would entitle the lenders to declare all principal, interest and other amounts owed by us under the loan and security agreement immediately due and payable.

In connection with the December 2012 borrowing under the debt facility, we issued to the lenders 10-year warrants to purchase an aggregate of 964,605 shares of Series C preferred stock with an exercise price of $0.2571 per share. In connection with the February 2013 borrowing under the debt facility, the warrant we issued to Silicon Valley Bank automatically became exercisable for an additional 233,372 shares of Series C preferred stock. In addition, we issued to Oxford Finance a 10-year warrant to purchase an additional 233,372 shares of Series C preferred stock with an exercise price of $0.2571 per share. Upon completion of the IPO the warrants issued in connection with the December 2012 borrowing and the February 2013 borrowing became exercisable for an aggregate of 49,356 shares of our common stock at an exercise price of $7.46 per share and the related warrant liability was reclassified to additional paid-in capital.

Operating Capital Requirements

We expect to incur increasing operating losses for at least the next several years as we continue our ongoing Phase 3 clinical trials of eravacycline for the treatment of cIAI, and for the treatment of cUTI, seek marketing approval for eravacycline, pursue development of eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections, advance our other product candidates 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, the FDA or the European Medicines Agency 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 existing cash and cash equivalents will be sufficient to fund our current operating plan into the first quarter of 2016 and enable us to obtain top-line data from our ongoing Phase 3 clinical trials of eravacycline for the treatment of patients with cIAI and cUTI and to submit an NDA to the FDA for eravacycline. We expect that these funds will not, however, be sufficient to enable us to commercially launch eravacycline. 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, design and costs of our ongoing Phase 3 clinical trials of eravacycline for the treatment of patients with cIAI and cUTI;
- the timing and costs of developing eravacycline for additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections;
- 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 costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval revenue received from commercial sales of eravacycline;
- 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, 2013:

	Payment by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
			(in thousands)		
Term loan (1)	$ 12,279	$ 7,070	$5,209	$ —	$ —
Operating leases (2)	1,513	947	566	—	—
Harvard milestone payment (3)	3,325	—	3,325	—	—
	$ 17,117	$ 8,017	$9,100	$ —	$ —

(1) Consists of repayment obligations relating to principal and interest outstanding under our debt facility with Silicon Valley Bank and Oxford Finance as of December 31, 2013.

(2) On December 12, 2013, we amended our existing operating lease which extended our lease term through July 31, 2015, and entered into a new operating sublease for additional space with a lease term through July 31, 2015.
(3) Consists of milestone payments that would become due to Harvard of (i) $3.0 million upon acceptance from the FDA of an NDA filing for eravacycline, and (ii) an aggregate amount of $325,000 related to various development milestones for certain preclinical compounds.

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, 2013 and 2012. 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.

ITEM 8. Financial Statements and Supplementary Data

TETRAPHASE PHARMACEUTICALS, INC.
(A Development Stage Company)
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. (a development stage enterprise) (the Company) as of December 31, 2013 and 2012, and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2013 and the period from July 7, 2006 (inception) to December 31, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Tetraphase Pharmaceuticals, Inc. (a development stage enterprise) as of December 31, 2013 and 2012 and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2013 and the period from July 7, 2006 (inception) to December 31, 2013, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 6, 2014

Tetraphase Pharmaceuticals, Inc.
(A Development Stage Company)
Consolidated Balance Sheets

(In thousands except share and per share data)

	December 31, 2013	December 31, 2012
Assets		
Current assets:		
Cash and cash equivalents	$ 102,712	$ 9,079
Accounts receivable	1,706	2,452
Prepaid expenses and other current assets	1,002	850
Total current assets	105,420	12,381
Property and equipment, net	235	235
Restricted cash	199	161
Other assets	32	1,295
Total assets	$ 105,886	$ 14,072
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 1,881	$ 2,018
Accrued expenses	5,290	2,303
Deferred revenue	92	699
Current portion of term loan payable	5,928	3,641
Total current liabilities	13,191	8,661
Preferred stock warrant liability	—	610
Accrued final interest payment on term loan	327	128
Term loan	4,560	7,881
Commitments and contingencies		
Convertible preferred stock, par value $0.001 per share: no shares and 259,044,157 shares authorized at December 31, 2013 and 2012, respectively; no shares and 256,024,993 shares issued and outstanding at December 31, 2013 and 2012, respectively	—	79,841
Stockholders' equity (deficit):		
Preferred stock, par value $0.001 per share; 5,000,000 shares and no shares authorized at December 31, 2013 and 2012, respectively; no shares issued and outstanding December 31, 2013 and 2012	—	—
Common stock, par value $0.001 per share; 125,000,000 and 317,789,510 shares authorized at December 31, 2013 and 2012, respectively; 25,629,281 and 325,243 shares issued and outstanding at December 31, 2013 and 2012, respectively	26	—
Additional paid-in capital	207,503	7,036
Deficit accumulated during the development stage	(119,721)	(90,085)
Total stockholders' equity (deficit)	87,808	(83,049)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 105,886	$ 14,072

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
(A Development Stage Company)

Consolidated Statements of Operations and Comprehensive Loss

(In thousands except per share data)

	Year Ended December 31,			The Period from July 7, 2006 (inception) to December 31, 2013
	2013	2012	2011	
Revenues	$ 10,486	$ 7,600	$ 185	$ 18,271
Operating expenses:				
Research and development	31,508	17,294	17,737	106,615
General and administrative	7,168	4,309	3,874	24,471
Total operating expenses	38,676	21,603	21,611	131,086
Loss from operations	(28,190)	(14,003)	(21,426)	(112,815)
Other income (expense):				
Interest income	10	—	1	618
Interest expense	(1,719)	(1,021)	(161)	(3,157)
Other income (expense)	263	(63)	22	(4,367)
Other expense, net	(1,446)	(1,084)	(138)	(6,906)
Net loss	$(29,636)	$(15,087)	$(21,564)	$ (119,721)
Net loss per share applicable to common stockholders-basic and diluted	$ (1.78)	$ (47.54)	$ (73.34)	$ (49.36)
Weighted-average number of common shares used in net loss per share applicable to common stockholders-basic and diluted	16,665	317	294	2,425
Comprehensive loss	$(29,636)	$(15,087)	$(21,564)	$ (119,721)

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
(A Development Stage Company)
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)

(In thousands except share and per share data)

	Series A-1 Convertible Preferred Shares		Series A-2 Convertible Preferred Shares		Series B Convertible Preferred Shares		Series C Convertible Preferred Shares		Common Shares		Additional Paid-In Capital	Deficit Accumulated During the Development Stage	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at July 7, 2006 (inception)	—	$ —	—	$ —	—	$ —	—	$ —	—	$ —	$ —	$ —	$ —
Issuance of founders' common stock	—	—	—	—	—	—	—	—	141,028	—	4	—	4
Common stock issued for license	—	—	—	—	—	—	—	—	31,378	—	1	—	1
Issuance of Series A-1 convertible preferred stock, net of issuance costs of $115,049	10,040,000	6,712	—	—	—	—	—	—	—	—	—	—	—
Stock compensation expense	—	—	—	—	—	—	—	—	—	—	1	—	1
Net loss												(1,217)	(1,217)
Balance at December 31, 2006	10,040,000	6,712	—	—	—	—	—	—	172,406	—	6	(1,217)	(1,211)
Stock-based compensation	—	—	—	—	—	—	—	—	—	—	5	—	5
Net loss	—	—	—	—	—	—	—	—	—	—	—	(7,071)	(7,071)
Balance at December 31, 2007	10,040,000	6,712	—	—	—	—	—	—	172,406	—	11	(8,288)	(8,277)
Reclassification of Investor Rights/liability upon settlement	—	3,213	—	—	—	—	—	—	—	—	5,321	—	5,321
Vesting of restricted stock	—	—	—	—	—	—	—	—	10,660	—	9	—	9
Issuance of Series of A-2 convertible preferred stock, net of issuance costs of $5,428	—	—	13,095,646	15,055	—	—	—	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	—	—	1,552	—	1	—	1
Stock-based compensation expense			—	—	—	—	—	—	—	—	34		34
Net loss			—	—	—	—	—	—	—	—	—	(12,760)	(12,760)
Balance at December 31, 2008	10,040,000	9,925	13,095,646	15,055	—	—	—	—	184,618	—	5,376	(21,048)	(15,672)
Vesting of restricted stock	—	—	—	—	—	—	—	—	4,188	—	4	—	4
Issuance of Series B convertible preferred stock, net of issuance costs of $117,171	—	—	—	—	57,471,225	9,946	—	—	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	—	—	78,055	—	69	—	69
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	265	—	265
Net loss	—	—	—	—	—	—	—	—	—	—	—	(14,908)	(14,908)

Tetraphase Pharmaceuticals, Inc.
(A Development Stage Company)
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)—(Continued)

(In thousands except share and per share data)

	Series A-1 Convertible Preferred Shares		Series A-2 Convertible Preferred Shares		Series B Convertible Preferred Shares		Series C Convertible Preferred Shares		Common Shares		Additional	Deficit Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Paid-In Capital	During the Development Stage	Equity (Deficit)
Balance at December 31, 2009	10,040,000	9,925	13,095,646	15,055	57,471,225	9,946	—	—	266,861	—	5,714	(35,956)	(30,242)
Vesting of restricted stock	—	—	—	—	—	—	—	—	3,427	—	3	—	3
Issuance of Series C convertible preferred stock, net of issuance costs of $185,093	—	—	—	—	—	—	175,418,122	44,915	—	—	—	—	—
Exercise of stock options	—	—	—	—	—	—	—	—	16,183	—	16	—	16
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	317	—	317
Net loss	—	—	—	—	—	—	—	—	—	—	—	(17,478)	(17,478)
Balance at December 31, 2010	10,040,000	9,925	13,095,646	15,055	57,471,225	9,946	175,418,122	44,915	286,471	—	6,050	(53,434)	(47,384)
Exercise of stock options	—	—	—	—	—	—	—	—	19,809	—	33	—	33
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	312	—	312
Net loss	—	—	—	—	—	—	—	—	—	—	—	(21,564)	(21,564)
Balance at December 31, 2011	10,040,000	9,925	13,095,646	15,055	57,471,225	9,946	175,418,122	44,915	306,280	—	6,395	(74,998)	(68,603)
Exercise of stock options	—	—	—	—	—	—	—	—	18,963	—	29	—	29
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	612	—	612
Net loss	—	—	—	—	—	—	—	—	—	—	—	(15,087)	(15,087)
Balance at December 31, 2012	10,040,000	9,925	13,095,646	15,055	57,471,225	9,946	175,418,122	44,915	325,243	—	7,036	(90,085)	(83,049)
Exercise of stock options	—	—	—	—	—	—	—	—	56,119	—	96	—	96
Issuance of common stock from initial public offering (net of underwriters discounts and issuance costs of $7,391)	—	—	—	—	—	—	—	—	11,512,078	12	73,182	—	73,194
Conversion of convertible preferred stock into common stock	(10,040,000)	(9,925)	(13,095,646)	(15,055)	(57,471,225)	(9,946)	(175,418,122)	(44,915)	8,828,438	9	79,832	—	79,841
Reclassification of warrants for common stock	—	—	—	—	—	—	—	—	—	—	462	—	462
Issuance of common stock from follow-on public offering (net of underwriters													

discounts and issuance costs of $3,475)	—	—	—	—	—	—	—	—	4,907,403	5	45,594	—	45,599
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	1,301	—	1,301
Net loss	—	—	—	—	—	—	—	—	—	—	—	(29,636)	(29,636)
Balance at December 31, 2013	—	$ —	—	$ —	—	$ —	—	$ —	25,629,281	$ 26	$ 207,503	$ (119,721)	$ 87,808

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
(A Development Stage Company)

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,			The Period from July 7, 2006 (inception) to December 31,
	2013	2012	2011	2013
Operating activities				
Net loss	$ (29,636)	$(15,087)	$(21,564)	$ (119,721)
Adjustments to reconcile net loss to net cash used in operating activities				
Depreciation and amortization	129	353	521	2,508
Amortization of deferred financing costs and debt discount	342	175	78	641
Accretion of final interest payment on term loans	199	128	—	327
Fair value adjustment of warrants and investor right obligation	(263)	63	(22)	5,099
Stock-based compensation expense	1,301	612	312	2,847
Loss from disposal of property and equipment	—	—	1	5
Changes in operating assets and liabilities:				
Restricted cash	(63)	—	—	(224)
Accounts receivable	746	(2,267)	(185)	(1,706)
Prepaid expenses and other current assets	(154)	(227)	(167)	(973)
Accounts payable	310	772	(305)	1,882
Accrued expenses	3,190	(1,878)	1,455	5,290
Deferred Revenue	(607)	699	—	92
Net cash used in operating activities	(24,506)	(16,657)	(19,876)	(103,933)
Investing activities				
Purchases of property and equipment	(129)	(54)	(65)	(2,748)
Net cash used in investing activities	(129)	(54)	(65)	(2,748)
Financing activities				
Proceeds from sale of common stock, net of underwriter discounts and issuance costs	119,404	(611)	—	118,793
Proceeds from sale of convertible preferred stock, net of issuance costs	—	—	—	79,841
Deferred financing fees	—	(85)	(170)	(275)
Proceeds from issuance of term loan payable	3,000	6,200	8,000	18,750
Repayment of term loan payable	(4,232)	(2,197)	(52)	(7,979)
Proceeds from sale of restricted common stock and common stock to founders	—	—	—	20
Proceeds from exercise of stock options	96	29	32	243
Net cash provided by financing activities	118,268	3,336	7,810	209,393
Net increase (decrease) in cash and cash equivalents	$ 93,633	$(13,375)	$(12,131)	$ 102,712
Cash and cash equivalents at beginning of period	9,079	22,454	34,585	—
Cash and cash equivalents at end of period	$102,712	$ 9,079	$ 22,454	$ 102,712
Supplemental cash flow information				
Cash paid for interest	$ 1,142	$ 702	$ 78	$ 2,154
Fair value of warrants issued in connection with issuance of term loan	$ 115	$ 241	$ 302	$ 684
Reclassification of investors rights/liability to stockholders' equity	$ —	$ —	$ —	$ 5,321
Conversion of convertible preferred stock into common stock	$ 79,841	$ —	$ —	$ 79,832
Reclassification of warrant liability to additional paid-in-capital	$ 462	$ —	$ —	$ 462
Reclassification of deferred financing costs to additional paid-in-capital	$ 1,261	$ —	$ —	$ 1,261

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
(A Development Stage Company)

Notes to Consolidated Financial Statements

(1) Organization and Operations

The Company

Tetraphase Pharmaceuticals, Inc. (the "Company"), is a clinical-stage biopharmaceutical company that was incorporated in Delaware on July 7, 2006 and has a principal place of business in Watertown, Massachusetts. The Company is using its proprietary chemistry technology to create novel antibiotics for serious and life-threatening multidrug-resistant infections. The Company's lead product candidate, eravacycline, is a fully synthetic tetracycline derivative that the Company is developing as a broad-spectrum intravenous and oral antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including multidrug-resistant Gram-negative infections. The Company is conducting a Phase 3 clinical trial of eravacycline with intravenous administration for the treatment of complicated intra-abdominal infections ("cIAI") and a second Phase 3 clinical trial of eravacycline for the treatment of complicated urinary tract infections, ("cUTI"), with intravenous-to-oral step-down therapy. The Company expects to have top-line data from the Phase 3 cIAI clinical trial in the first quarter of 2015, data from the lead-in portion of the Phase 3 cUTI clinical trial in mid-2014 and top-line data from the Phase 3 cUTI clinical trial in mid-2015. Subject to obtaining additional financing, and following the Company's development of eravacycline for the treatment of cIAI and cUTI, the Company intends to pursue development of eravacycline for the treatment of additional indications, including hospital-acquired bacterial pneumonias and other serious and life-threatening infections. The Company is also pursuing the discovery and development of additional antibiotics to target unmet medical needs.

The Company is in the development stage, and is devoting substantially all of its efforts to product research and development, initial market development, and raising capital. The Company has not generated any product revenue related to its primary business purpose to date and is subject to a number of risks similar to those of other development stage life science companies, including dependence on key individuals, competition from other companies, the need for development of commercially viable products, and the need to obtain adequate additional financing to fund the development of its product candidates. The Company is also subject to a number of risks similar to other companies in the industry, including rapid technological change, regulatory approval of products, uncertainty of market acceptance of products, competition from substitute products and larger companies, the need to obtain additional financing, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability, and dependence on key individuals.

The Company has incurred annual net operating losses in every year since its inception. The Company has not generated any product revenues related to its primary business purpose and has financed its operations primarily through public offerings of its common stock, private placements of its preferred stock, debt financings and funding from the United States government. 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.

As of December 31, 2013, the Company had incurred losses since inception of $119.7 million. The Company expects to continue to incur losses and require additional financial resources to advance its product candidates to either commercial stage or liquidity events.

There can be no assurance that the Company will be able to obtain additional debt or equity financing or generate 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.

Liquidity

The Company's operations to date have been limited to organizing and staffing the Company, business planning, raising capital, acquiring and developing its proprietary chemistry technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of its product candidates. To date, the Company has not generated any product revenue and has primarily financed its operations through the public offering and private placement of equity securities, debt financings and funding from the United States government. As of December 31, 2013, the Company had received an aggregate of $217.4 million in net proceeds from the issuance of equity securities and borrowings under debt facilities and an aggregate of $16.7 million from government grants and contracts. As of December 31, 2013, the Company's principal source of liquidity was cash and cash equivalents, which totaled $102.7 million.

In May 2011, the Company executed a Loan and Security Agreement ("Term Loan") with two financial institutions, Silicon Valley Bank and Oxford Finance, that provided for up to $8.0 million in funding, to be made available in two tranches. The Company borrowed the first $1.5 million in May 2011 and the second tranche for the remaining $6.5 million in December 2011. On December 20, 2012, the Company amended the Term Loan to provide for up to an additional $9.2 million in funding, to be made available in two tranches ("2012 Term Loan"). The Company borrowed the first $6.2 million under the 2012 Term Loan on December 20, 2012. The Company borrowed the second tranche of $3.0 million on February 28, 2013.

In October 2011, the National Institutes of Health's ("NIH") National Institute of Allergy and Infectious Diseases ("NIAID") division awarded a contract of up to $35.8 million over a five-year term for the development of TP-271, a preclinical compound, for respiratory disease caused by bacterial biothreat pathogens ("NIAID Contract") (Note 3). The Company is collaborating with CUBRC Inc. ("CUBRC"), an independent, not for profit, research corporation that specializes in U.S. government-based contracts, on this NIAID Contract and has entered into a subcontract with CUBRC that could potentially provide funding to the Company of up to approximately $13.3 million over the five-year term, including committed funding of $7.5 million from the initial contract date through September 30, 2016, of which $4.4 million had been received by the Company through December 31, 2013. In addition during 2011, the Company was a subawardee under a separate grant from the NIAID ("NIAID Grant") (Note 3).

In February 2012 the Biomedical Advanced Research and Development Authority ("BARDA"), an agency of the U.S. Department of Health and Human Services, awarded a contract of up to $67.0 million for the development of eravacycline as a potential countermeasure for the treatment of disease caused by bacterial biothreat pathogens ("BARDA Contract"). The Company is also collaborating with CUBRC on the BARDA Contract and has entered into a subcontract with CUBRC that could potentially provide funding to the Company of up to approximately $39.8 million including committed funding of $15.7 million from the initial contract date through April 30, 2015, of which $11.7 million had been received by the Company through December 31, 2013 (Note 3).

On March 25, 2013, the Company completed the sale of 10,714,286 shares of common stock at a price to the public of $7.00 per share, resulting in net proceeds to the Company of $68.0 million after deducting underwriting discounts and commissions of $4.4 million and offering costs of $2.5 million (the "IPO"). The Company's common stock began trading on the NASDAQ Global Market under the symbol "TTPH" on March 20, 2013. On April 12, 2013, in connection with the underwriters' option to purchase additional shares of common stock at the initial public offering price to cover over allotments, the Company completed the additional sale of 797,792 shares of common stock under this option at a price to the public of $7.00 per share, resulting in net proceeds to the Company of $5.2 million after deducting underwriting discounts and commissions.

On November 13, 2013, the Company completed the sale of 4,500,000 shares of common stock in a follow-on public offering at a price to the public of $10.00 per share, resulting in net proceeds to the Company of $41.8 million after deducting underwriting discounts and commissions of $2.7 million and offering costs of $0.5 million. On November 19, 2013, in connection with the underwriters' option to purchase additional shares of

common stock at the follow-on offering price to cover over allotments, the Company completed the additional sale of 407,403 shares of common stock under this option at a price to the public of $10.00 per share, resulting in net proceeds to the Company of $3.8 million after deducting underwriting discounts and commissions.

The Company believes that its cash resources of approximately $102.7 million at December 31, 2013 will be sufficient to allow the Company to fund its current operating plan through at least the next twelve months. There can be no assurances, however, that the current operating plan will be achieved in the timeframe anticipated by the Company, or that its cash resources will fund the Company's operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to the Company, or at all.

On February 28, 2013, the Company's board of directors approved an amendment to the Company's certificate of incorporation to effect a 1-for-29 reverse split of its Common Stock (the "Reverse Split"). The Company effected this amendment to its certificate of incorporation on March 5, 2013. All references to shares of Common Stock outstanding, average number of shares outstanding and per share amounts in these consolidated financial statements and notes to consolidated financial statements have been restated to reflect the Reverse Split on a retroactive basis.

(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 multidrug-resistant infections.

Use of Estimates

The preparation of financial statements in conformity with 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 and reported amounts of contract and grant revenues and expenses during the reported period. 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 minimizes the exposure to concentration of credit risk. The Company has no financial instruments with off-balance-sheet risk of loss.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Tetraphase Securities Corporation, a Massachusetts Securities Corporation. 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, 2013 and 2012 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, accrued liabilities, term loan and liabilities related to warrants to purchase preferred stock. 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, 2013 and 2012 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, 2013				
Cash	$ 2,704	$ 2,704	$ —	$ —
Money market funds, included in cash equivalents	$100,008	$100,008	$ —	$ —
December 31, 2012				
Cash	$ 5,854	$ 5,854	$ —	$ —
Money market funds, included in cash equivalents	$ 3,225	$ 3,225	$ —	$ —
Preferred stock warrant liability (Note 7)	$ (610)	$ —	$ —	$ (610)

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. The fair value of the Company's term loan payable is determined using current applicable rates for similar instruments as of the balance sheet date. The carrying value of the Company's term loan payable approximates fair value because the Company's interest rate yield is near current market rates. The Company's term loan payable is a Level 3 liability within the fair value hierarchy.

The fair value of the Company's loans payable at December 31, 2013, computed pursuant to a discounted cash flow technique using the effective interest rate under the loan, is $11.3 million. The effective interest rate considers the fair value of the warrant issued in connection with the loan, loan issuance costs and the deferred charge. The fair value of the Company's term loan payable is determined using current applicable rates for similar instruments as of the balance sheet date.

The fair value of the preferred stock warrant liability as of December 31, 2012 and March 25, 2013 was determined based on "Level 3" inputs utilizing the Black-Scholes option pricing model (Note 7). On March 25, 2013, upon completion of the Company's initial public offering ("IPO"), the warrants to purchase preferred stock converted into warrants to purchase common stock and the Company reclassified the fair value of the warrants as of March 25, 2013 to additional paid-in capital. The following table presents activity in the preferred stock warrant liability during the year ended December 31, 2013 (in thousands):

	Balance
Fair value at December 31, 2011	$ 306
Value of warrants issued in 2012	241
Increase in fair value recognized in net loss	63
Fair value at December 31, 2012	$ 610
Value of warrants issued in 2013	115
Decrease in fair value recognized in net loss	(263)
Reclassification of fair value to additional paid-in capital	(462)
Fair value at December 31, 2013	$ —

Accounts Receivable

Accounts receivable at December 31, 2013 and 2012 represent amounts due from CUBRC under the Company's subcontracts under the NIAID Contract and the BARDA Contract and under the Company's subaward under the NIAID Grant. The Company's practice is to bill the prime contractor 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 was $0.8 million and $1.1 million at December 31, 2013 and 2012, respectively.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation and amortization are provided using the straight-line method over the estimated useful lives of the respective assets, 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, 2013 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 one of the Company's leased facilities. If the Company defaults on its rental obligations, $159,000 will be payable to the lessor of the leased facility. 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 subcontract with respect to the BARDA Contract is earned under a cost-reimbursable contract in which the Company is reimbursed for direct costs incurred plus allowable indirect costs. Billings under the Company's subcontract under the BARDA Contract are based on approved provisional indirect billing rates, which permit recovery of fringe benefits and allowable general and administrative expenses. During the years ended December 31, 2013 and 2012, and the period from July 7, 2006 (inception) to December 31, 2013, the Company recognized revenue of $7.7 million, $4.9 million and $12.6 million, respectively, from the Company's subcontract under the BARDA Contract.

Revenue under the Company's subcontract with respect to the NIAID Contract is earned under a cost-plus-fixed-fee contract in which the Company is reimbursed for direct costs incurred plus allowable indirect costs and a fixed-fee earned. Billings under the Company's subcontract under the NIAID Contract 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. During the years ended December 31, 2013, 2012, 2011 and the period from July 7, 2006 (inception) to December 31, 2013, the Company recognized revenue of $2.5 million, $2.5 million, $0.2 million and $5.1 million, respectively, from the Company's subcontract under the NIAID Contract.

Revenue under the Company's subaward with respect to the NIAID Grant is earned under a cost-reimbursable contract in 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, which permit recovery of fringe benefits and allowable general and administrative expenses. During the years ended December 31, 2013, 2012, 2011 and the period from July 7, 2006 (inception) to December 31, 2013, the Company recognized revenue of $267,000, $273,000, $2,000 and $542,000, respectively, from the Company's subaward under the NIAID Grant.

Organizational Costs

All organizational costs are expensed as incurred.

Research and Development Expenses

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

- employee-related expenses, including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with contract research organizations, contract manufacturing organizations and consultants that conduct clinical trials and preclinical studies;
- 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 and maintenance of facilities, insurance and other supplies; and
- costs associated with preclinical activities and regulatory operations.

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.

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 Expense

Stock-based compensation is recognized as expense for all stock-based awards based on estimated fair values. The Company determines equity-based compensation at the grant date using the Black-Scholes option pricing model. The value of the award that is ultimately expected to vest is recognized as 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.

Subsequent Events

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

Net Loss per Common Share

Basic net loss per share is calculated by dividing the net loss applicable to common stockholders 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 applicable to common stockholders by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, preferred stock, stock options and warrants 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.

Effective as of the completion of the IPO, all of the Company's preferred stock was converted to common stock at a 1-for-29 ratio as a result of the Reverse Split. For purposes of calculating net loss per common share for the year ended December 31, 2013 and the period from July 7, 2006 (inception) to December 31, 2013, the preferred stock that converted to common stock was included in the net loss per common share calculation on a post-conversion basis as of March 25, 2013, the effective date of conversion, and the corresponding converted shares were included on a pro-rata basis for each applicable reporting period. As a result, the weighted-average common shares outstanding during the years ended December 31, 2013, 2012 and 2011 and the period from July 7, 2006 (inception) to December 31, 2013, were 16.7 million, 0.3 million, 0.3 million and 2.4 million, respectively, as compared to 25.6 million shares outstanding as of December 31, 2013.

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:

	Years Ended December 31,			The Period from July 7, 2006 (inception) to December 31, 2013
	2013	2012	2011	
Preferred stock	—	8,828,438	8,828,438	—
Warrants	104,107	88,013	54,751	104,107
Outstanding stock options	2,844,343	1,442,810	1,253,167	2,844,343

(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, the Company has paid the University an aggregate of $3.8 million in upfront license fees and development milestone payments, and has issued 31,379 shares of common stock to the University.

The Company is obligated to make certain payments totaling up to approximately $15.1 million upon achievement of certain development and regulatory milestones and royalties on net sales of products covered by the agreement. 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. The Company paid a $2.0 million milestone fee in October 2013 in connection with the dosing of the first patient in the Company's Phase 3 clinical trial of eravacycline for the treatment of patients with cIAI. This amount was recorded as research and development expense during the year ended December 31, 2013.

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 $67.0 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens.

In connection with the BARDA Contract, in February 2012, the Company entered into a five-year cost-plus-fixed-fee subcontract with CUBRC under which it may receive funding of up to approximately $39.8 million, reflecting the portion of the BARDA 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 five-year terms, 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 $15.7 million through the current contract end date through April 30, 2015 as a result of the exercise of several options by BARDA under the BARDA Contract. Total funds of $11.7 million had been received by the Company through December 31, 2013 under this 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 $2.8 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 55-month, no-fee subaward of approximately $980,000, 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 five-year cost-plus-fixed-fee subcontract with CUBRC under which the Company may receive funding of up to approximately $13.3 million, reflecting the portion of the NIAID Contract funding that may be paid to the Company for its activities.

Although the NIAID Contract, the NIAID Grant and the Company's subcontract with CUBRC under the NIAID Contract have terms of five years, and the Company's subaward under the NIAID Grant has a term of 55 months, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond September 30, 2016. To the extent 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, 2013, committed funding from CUBRC under the Company's subcontract with respect to the NIAID Contract is $7.5 million through the current contract end date which has been extended to September 30, 2016. Total funds of $4.4 million had been received through December 31, 2013. Committed funding from CUBRC under the Company's subaward with respect to the NIAID Grant is $0.7 million through the current contract end date, which has been extended to May 31, 2016. Total funds of $0.5 million had been received through December 31, 2013.

(4) Property and Equipment

Property and equipment at December 31, 2013 and 2012 consisted of the following (in thousands):

	Estimated Useful Life	December 31,	
	In Years	2013	2012
Laboratory equipment	5	$ 1,806	$ 1,777
Furniture and fixtures	5	170	115
Office and computer equipment	3	176	143
Leasehold improvements		527	515
		2,679	2,550
Less accumulated depreciation and amortization		(2,444)	(2,315)
Property and equipment, net		$ 235	$ 235

Depreciation and amortization expense for the years ended December 31, 2013, 2012 and 2011 was $129,000, $353,000 and $521,000, respectively. Depreciation and amortization expense for the period from July 7, 2006 (inception) to December 31, 2013 was $2.5 million.

(5) Accrued Liabilities

Accrued liabilities at December 31, 2013 and 2012 consisted of the following (in thousands):

	December 31, 2013	December 31, 2012
Clinical trial related	1,849	470
Salaries and benefits	1,554	963
Drug supply and development	970	210
Professional fees	246	320
Other	671	340
Total	$ 5,290	$ 2,303

(6) Long-Term Debt

In October 2007, the Company entered into a Loan and Security Agreement with a bank, which provided for up to $1.6 million in debt financing to finance equipment purchases made by the Company (the “Equipment Term Loan”). The Equipment Term Loan had a 36 month term, an interest rate of prime + 1.00% and was collateralized by the underlying equipment. In connection with the Equipment Term Loan, the Company issued a 10-year warrant to purchase 32,000 shares of Series A-1 Preferred Stock at a purchase price of $1.00 per share. The Equipment Term Loan was paid in full in January 2011.

In May 2011, the Company executed a Loan and Security Agreement with Silicon Valley Bank and Oxford Finance (the “Term Loan”), which provided for up to $8.0 million funding, to be made available in two tranches. The Company borrowed the $8.0 million in two tranches during the year ended December 31, 2011. The Term Loan bears interest at 10% per annum and provides for a final payment of 2.75% of the original principal due at the maturity date of November 1, 2014. Under the terms of the Term Loan, the Company was only required to pay interest (and not principal) through February 28, 2012. Each tranche will be repaid in 33 monthly payments of equal principal, plus accrued interest, after the interest only period that ended February 28, 2012. The final payment of 2.75% will be due at the same time as the last loan payment. The Term Loan matures on November 1, 2014. In connection with the entry into the Loan and Security Agreement, the Company issued to the lenders 10-year warrants to purchase an aggregate of 1,555,815 shares of Series C Preferred Stock at a price of $0.2571 per share.

In December 2012, the Company entered into an amendment to 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. The Company borrowed the first tranche totaling $6.2 million under the 2012 Term Loan in December 2012 (“2012 Term A Loan”) and borrowed the remaining $3.0 million in February 2013 (“2012 Term B Loan”). Both the 2012 Term Loan A and the 2012 Term B Loan bear interest at 9% per annum.

The Company is only required to pay interest (and not principal) for the first six months of each tranche of the 2012 Term Loan. Each tranche of the 2012 Term Loan is to be repaid in 33 equal monthly payments of principal, plus accrued interest, after the interest only period. An additional payment of 2.90% of the original principal amount of each tranche will be due at the same time as the last loan payment for the tranche. The 2012 Term A Loan matures on March 1, 2016. In connection with the funding of the 2012 Term A Loan, the Company issued to the lenders 10-year warrants to purchase an aggregate of 964,605 shares of Series C Preferred Stock with an exercise price of $0.2571 per share. The 2012 Term B Loan matures on May 1, 2016. In connection with the funding of the 2012 Term B Loan, in February 2013, the warrant the Company issued to Silicon Valley Bank automatically became exercisable for an additional 233,372 shares of Series C Preferred Stock. In addition, the Company issued to Oxford Finance a 10-year warrant to purchase an additional 233,372 shares of Series C Preferred Stock with an exercise price of $0.2571 per share.

The Term Loan and the 2012 Term Loan are collateralized by a blanket lien on all corporate assets, excluding intellectual property, and by a negative pledge of the Company's intellectual property. The Term Loan and the 2012 Term Loan contain customary default provisions that include material adverse events, as defined therein. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and long-term liabilities based on scheduled principal payments.

Future principal payments on the Term Loan and the 2012 Term Loan are as follows (in thousands):

	December 31, 2013
2014	$ 6,126
2015	3,513
2016	1,132
Total term loan payments	10,771
Current term loan payable	6,126
Less debt discount and issuance costs	(198)
Current term loan payable (net)	5,928
Term loan payable, less current portion	4,645
Less debt discount and issuance costs	(85)
Term loan payable, net	$ 4,560

(7) Warrants

In October 2007, the Company issued a warrant to purchase 32,000 shares of Series A-1 Preferred Stock at an exercise price of $1.00 per share to a bank in connection with the Equipment Term Loan. The warrant was exercisable immediately and had a ten-year life. The Company initially valued the warrant at $26,000 using the Black-Scholes pricing model with the following assumptions; risk-free interest rate of 3.2%; dividend yield of zero; expected volatility rate of 75%; with an expected life of ten years. The Company was expensing the value of the warrant as additional interest over the term of the loan. The warrant was classified as a liability in accordance with Accounting Standards Codification ("ASC") 480 and was subject to remeasurement at each balance sheet date and changes to fair value were recognized as a component of other income (expense) in the statement of operations and comprehensive loss. The change in the fair value of the warrant was $6,000 during the year ended December 31, 2012. The fair value of the warrant at December 31, 2012 was $6,000.

In May 2011, the Company issued warrants to purchase an aggregate of 1,555,815 shares of Series C Preferred Stock at an exercise price of $0.2571 per share in connection with the Term Loan (Note 6). The warrants are exercisable immediately and have a ten year life. The warrants were initially valued at $302,000 using the Black-Scholes pricing model with the following assumptions; risk free interest rate of 3.2%; dividend yield of zero; expected volatility of 67%; with an expected life of ten years, and are being expensed as additional interest over the term of the loan. In accordance with ASC 480, the characteristics of these warrants and the rights and privileges of the underlying Series C Preferred Stock resulted in the classification of these warrants as a liability and changes to the fair value of the warrants were recognized as a component of other income (expense) in the statement of operations and comprehensive loss. The fair value of these warrants at December 31, 2012 was $364,000.

In December 2012, the Company issued warrants to purchase an aggregate of 964,605 shares of Series C Preferred Stock at an exercise price of $0.2571 per share in connection with the 2012 Term Loan (Note 6). The warrants are exercisable immediately and have a ten year life. The warrants were initially valued at $241,000 using the Black-Scholes pricing model with the following assumptions; risk free interest rate of 1.8%; dividend yield of zero; expected volatility of 61%; with an expected life of ten years, and are being expensed as additional

interest over the term of the loan. In accordance with ASC 480, the characteristics of these warrants and the rights and privileges of the underlying Series C Preferred Stock resulted in the classification of these warrants as a liability and changes to the fair value of the warrants were recognized as a component of other income (expense) in the statement of operations and comprehensive loss. The fair value of these warrants at December 31, 2012, was $240,000.

In connection with the February 2013 borrowing under the Term Loan, the warrant that the Company issued to Silicon Valley Bank in December 2012 automatically became exercisable for an additional 233,372 shares of Series C preferred stock. In addition, the Company issued to Oxford Finance a 10-year warrant to purchase an additional 233,372 shares of Series C preferred stock with an exercise price of $0.2571 per share. The warrants were initially valued at $115,000 using the Black-Scholes option pricing model with the following assumptions: risk-free interest rate of 1.89%, dividend yield of zero, expected volatility rate of 59% and an expected life of ten years, and are being expensed as additional interest over the term of the loan. The warrant was classified as a liability in accordance with ASC 480 and was subject to remeasurement at each balance sheet date and changes to the fair value were recognized as a component of other income (expense) in the statement of operations and comprehensive loss.

The Company estimated the fair value of the preferred stock warrants using the Black-Scholes option pricing model based on the following assumptions:

	December 31, 2012	December 31, 2011
Expected volatility	60%	67%
Expected term (in years)	5.0-10.0	6.0-10.0
Risk-free interest rate	0.72%-1.78%	1.09%-1.89%
Expected dividend yield	0%	0%
Estimated fair value of Series A-1 Preferred Stock	$0.45	$0.46
Estimated fair value of Series C Preferred Stock	$0.34	$0.32

Upon completion of the IPO, the warrants related to the Term Loan became exercisable for 53,648 shares of the Company's common stock at an exercise price of $7.46 per share, the warrants related to the 2012 Term A Loan became exercisable for 33,262 shares of the Company's common stock at an exercise price of $7.46 per share and the warrants related to the 2012 Term B Loan became exercisable for 16,094 shares of the Company's common stock at an exercise price of $7.46 per share. On the date of the conversion of the warrants, the Company revalued the outstanding warrants using the Black-Scholes option pricing model with the following assumptions: risk-free interest rate of 0.67% to 1.84%, dividend yield of zero, expected volatility rate of 59%, expected term of 5 to 10 years and stock price of $7.00. The fair value of the warrants at March 25, 2013 was $462,000. The Company recorded other income of $263,000 in the statement of operations and comprehensive loss during the year ended December 31, 2013 equal to the change in fair value of the warrants from December 31, 2012 to March 25, 2013. The Company reclassified the fair value of the warrants at March 25, 2013, of $462,000, to additional paid-in capital.

(8) Stockholders' Equity (Deficit)

Initial Public Offering

On March 25, 2013, the Company completed its IPO, issuing 10,714,286 shares of common stock at a price to the public of $7.00 per share, resulting in net proceeds to the Company of $68.0 million after deducting underwriting discounts of $4.4 million and offering costs of $2.5 million. Of the $2.5 million in offering costs, $1.3 million was included in other assets on the balance sheet at December 31, 2013.

In connection with the IPO, all of the Company's outstanding preferred stock automatically converted into a total of 8,828,438 shares of its common stock.

On April 12, 2013, the Company completed the sale of an additional 797,792 shares of Common Stock pursuant to the underwriters' option in the IPO at a price to the public of $7.00 per share, resulting in net proceeds to the Company of $5.2 million after deducting underwriting discounts and commissions.

Follow-on Public Offering

On November 13, 2013, the Company completed a follow-on public offering, issuing 4,500,000 shares of common stock at a price to the public of $10.00 per share, resulting in net proceeds to the Company of $41.8 million after deducting underwriting discounts of $2.7 million and offering costs of $0.5 million.

On November 19, 2013, the Company completed the sale of an additional 407,403 shares of Common Stock pursuant to the underwriters' option in the follow-on public offering at a price to the public of $10.00 per share, resulting in net proceeds to the Company of $3.8 million after deducting underwriting discounts and commissions.

(9) Stock-based Compensation

In August 2006, the Company adopted the Tetraphase Pharmaceuticals, Inc. Stock Incentive Plan (the "2006 Plan") under which it was able to grant incentive stock options, nonqualified stock options, restricted stock, and stock grants to purchase up to 1,128,183 shares of Common Stock. In May 2010, the Company amended the plan to increase the number of shares of Common Stock issuable under the 2006 Plan to 1,853,288. The options expire ten years after the grant date. As of December 31, 2013, no shares were available for future issuance under the 2006 Plan.

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 lowest of 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. As of December 31, 2013, 488,699 shares were available for future issuance under the 2013 Plan.

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 Market on the date of grant.

The following table summarizes stock option activity at December 31, 2013 and changes during the year then ended is 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, 2012	1,442,810	$ 1.67	7.43	$ 10,569
Granted	1,514,940	8.31		
Exercised	(56,119)	1.72		
Forfeited	—	—		
Canceled	(57,288)	6.89		
Options outstanding at December 31, 2013	2,844,343	$ 5.10	7.97	$ 23,960
Options vested or expected to vest at December 31, 2013 (1)	2,714,408	$ 5.00	7.93	$ 17,353
Options exercisable at December 31, 2013	1,169,518	$ 1.69	6.20	$ 13,841

(1) This represents the number of vested options as of December 31, 2013, plus the number of unvested options that the Company estimated as of December 31, 2013 would vest, based on the unvested options at December 31, 2013, as adjusted for the estimated forfeiture rate of 3%.

The total intrinsic value of options exercised in the years ended December 31, 2013, 2012, and 2011, and for the period July 7, 2006 (inception) to December 31, 2013 was $506,000, $25,000, $9,000 and $560,000, respectively. As of December 31, 2013, there was $5.6 million of total unrecognized stock-based compensation cost related to employee and non-employee nonvested stock options granted under the 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 3.3 years.

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

	Year Ended December 31,		
	2013	2012	2011
Weighted average expected volatility	58%	67%	64%
Expected life (in years)	5.8-7.1	6.0-6.1	6.0-6.1
Risk free interest rate	0.91%-2.01%	0.85% -1.21%	1.21% -2.41%
Expected dividend yield	0%	0%	0%

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 since March 2013, 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 companies based on their disease focus, stage of clinical trials, number of compounds in clinical trials and number of years since incorporation for which historical information was available. 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 nonemployee 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.

Compensation cost for stock options 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. 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, 2013, 2012 and 2011 and the period from July 7, 2006 (inception) to December 31, 2013 was $4.52, $2.32, $1.16 and $2.93 per share, respectively.

Restricted Stock

During 2006, the Company issued a total of 18,275 shares of Common Stock to employees pursuant to Stock Restriction and Repurchase Agreements. Under the terms of the agreements, the issued shares of Common Stock were subject to vesting and forfeiture. Under the agreements, vesting occurred periodically at specified time intervals and specified percentages. All shares of Common Stock become fully vested within four years of the date of issuance. As of December, 31, 2013, 18,275 shares of common stock were issued and outstanding under the Stock Restriction and Repurchase Agreements, and all of these shares were fully vested and not subject to repurchase.

In August 2006, the Company issued 87,586 shares of restricted Common Stock to certain founders and employees (the Recipients) for a price of $0.029 per share, for total proceeds of $3,000. The restricted stock vested over three years, during which time the Company had the right to repurchase the unvested shares at the amount paid if the relationship between the Recipients and the Company ceased. In 2006, the Company also issued an additional 53,448 shares of restricted Common Stock to a founder for $0.029 per share, for total proceeds of $2,000. These shares were not subject to vesting or any right to repurchase. At December 31, 2013 all 141,034 shares were vested and were held by the Recipients.

(10) Income Taxes

The Company accounts for income taxes under FASB Accounting Standards Codification 740 (ASC 740). 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.

For the years ended December 31, 2013, 2012 and 2011 and the period from July 7, 2006 (inception) to December 31, 2013, the Company did not have a current or deferred income tax expense or benefit.

As of December 31, 2013 the Company had federal net operating loss carryforwards of approximately $108.0 million and state net operating loss carryforwards of $92.1 million, which are available to reduce future taxable income. The federal net operating loss carryforwards exclude approximately $0.2 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 also had federal tax credits of $2.9 million and state tax credits of $1.1 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 2033. 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; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position.

The Company has recorded no reserves or unrecognized tax benefits for tax positions taken. Since a full valuation allowance has been provided against the Company's deferred tax assets, 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. As of December 31, 2013 and 2012, the Company had no accrued interest or penalties related to uncertain tax positions.

The principal components of the Company's deferred tax assets are as follows:

	Year ended December 31,	
	2013	2012
Deferred tax assets:		
Net operating loss carry forwards	$ 41,574	$ 31,958
Temporary differences	1,976	1,046
Research and development credit and carry forwards	3,609	2,326
Deferred tax assets	47,159	35,330
Less valuation allowance	(47,159)	(35,330)
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, 2013 and 2012, respectively, because the Company's management has determined that is it more likely than not that these assets will not be realized. The $11.8 million increase in the valuation allowance in 2013 primarily relates to the net loss incurred by the Company.

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 2009 through 2012. 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.

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

	Year ended December 31,		
	2013	2012	2011
Statutory tax rate	(34.00)%	(34.00)%	(34.00)%
State taxes, net of Federal benefits	(5.28)%	(5.28)%	(5.28)%
Permanent differences	0.93%	1.01%	0.39%
Credits	(4.33)%	(0.09)%	(4.85)%
Change in valuation allowance	39.92%	38.92%	42.37%
Other	2.76%	(0.56)%	1.37%
Effective tax rate	— %	— %	— %

(11) Commitments and Contingencies

Lease Commitments

The Company leases its facility under an operating lease that was to expire on November 30, 2012. On December 12, 2013 the Company amended its operating lease, which extended the lease term through July 31, 2015. The Company also entered into a sublease for an additional 7,828 square feet of office and laboratory space on December 12, 2013. This sublease is in a facility located next to the Company's current headquarters. The Company recognizes rent expense on a straight-line basis over the non-cancelable lease term.

As of December 31, 2013, the minimum future rent payments under the lease and sublease agreements are as follows:

	December 31, 2013
2014	$ 937
2015	566
Total minimum lease payments	$ 1,503

The Company recorded $612,000 and $550,000 in rent expense for the years ended December 31, 2013 and 2012, respectively. Total rent expense for the period from July 7, 2006 (inception) to December 31, 2013 was $3.6 million.

(12) Litigation

Litigation

The Company is not a party to any litigation and does not have contingency reserves established for any litigation liabilities.

(13) Quarterly Results (Unaudited)

	Three Months Ended			
	March 31, 2013	June 30, 2013	September 30, 2013	December 31, 2013
	(in thousands, except per share data) (unaudited)			
Revenue	$ 2,700	$ 3,722	$ 2,166	$ 1,898
Operating expenses	5,323	8,680	11,852	12,821
Loss from operations	(2,623)	(4,958)	(9,686)	(10,923)
Other expense, net	(168)	(468)	(430)	(380)
Net loss	$ (2,791)	$(5,426)	$ (10,116)	$ (11,303)
Net loss per share—basic and diluted	$ (1.51) [1]	$ (0.26)	$ (0.49)	$ (0.49)

	Three Months Ended			
	March 31, 2012	June 30, 2012	September 30, 2012	December 31, 2012
	(in thousands, except per share data) (unaudited)			
Revenue	$ 507	$ 1,316	$ 2,537	$ 3,240
Operating expenses	4,962	5,263	5,436	5,942
Loss from operations	(4,455)	(3,947)	(2,899)	(2,702)
Other expense, net	(234)	(321)	(179)	(350)
Net loss	$ (4,689)	$(4,268)	$ (3,078)	$ (3,052)
Net loss per share—basic and diluted	$ (15.20) [1]	$(13.42)	$ (9.63)	$ (9.43)

(1) The Company determined that in its previously issued unaudited financial statements for the three months ended March 31, 2013 and 2012, it incorrectly calculated the weighted average number of shares outstanding for the purpose of determining its net loss per share for each of these periods. The corrected amounts are included in the table above. The errors did not impact the Company's balance sheet at March 31, 2013 or the amount of net loss or statement of cash flows for the three months ended March 31, 2013 and 2012.

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

None.

ITEM 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2013. 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 Chief Financial Officer concluded that as of December 31, 2013, 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.

Internal Control Over Financial Reporting

Management's Report on Internal Control Over Financial Reporting

This annual report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of the company's independent registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2013 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 2013 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 2013 Annual Meeting of Stockholders and is incorporated by reference herein. The information required by this item relating to executive officers may be found in Part I, Item 1 of this annual report on Form 10-K under the heading “Business—Executive Officers” and is incorporated herein by reference.

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 2013 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 2013 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 2013 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 2013 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 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.

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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 6, 2014

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 6, 2014
/s/ David C. Lubner **David C. Lubner**	Senior Vice President and Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 6, 2014
/s/ L. Patrick Gage **L. Patrick Gage, Ph.D.**	Chairman	March 6, 2014
/s/ Garen Bohlin **Garen Bohlin**	Director	March 6, 2014
/s/ John G. Freund **John G. Freund**	Director	March 6, 2014
/s/ Steven R. Gullans **Steven R. Gullans**	Director	March 6, 2014

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EXHIBIT INDEX

Exhibit Number	Description	Incorporated by Reference from		
		Registrant's Form	Date Filed with the SEC	Exhibit Number
3.1	Restated Certificate of Incorporation of the Registrant	10-Q	5/13/13	3.1
3.2	Amended and Restated Bylaws of the Registrant	10-Q	5/13/13	3.2
4.1	Specimen certificate evidencing shares of common stock	S-1/A	3/5/13	4.1
10.1	Second Amended and Restated Registration Rights Agreement, dated as of May 14, 2010, as amended	S-1	2/11/13	10.1
10.2	Warrant to purchase shares of Series A-1 Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank expiring on September 27, 2017	S-1	2/11/13	10.2
10.3	Warrant to purchase shares of Series C Convertible Preferred Stock issued by the Registrant to Oxford Finance LLC expiring on May 16, 2021	S-1	2/11/13	10.3
10.4	Warrant to purchase shares of Series C Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank expiring on May 16, 2021	S-1	2/11/13	10.4
10.5#	2006 Stock Incentive Plan, as amended	S-1	2/11/13	10.5
10.6#	Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan	S-1	2/11/13	10.6
10.7#	Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan	S-1	2/11/13	10.7
10.8#	2013 Stock Incentive Plan	S-1/A	3/5/13	10.8
10.9#	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	3/5/13	10.9
10.10#	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	3/5/13	10.10
10.11#	Offer letter, dated as of December 4, 2007, by and between the Registrant and Guy Macdonald, as amended	S-1	2/11/13	10.11
10.12#	Offer letter, dated as of August 10, 2006, by and between the Registrant and David Lubner, as amended	S-1	2/11/13	10.12
10.13#	Offer letter, dated as of December 22, 2010, by and between the Registrant and Patrick T. Horn	S-1	2/11/13	10.13
10.14#	Offer letter, dated as of March 20, 2009, by and between the Registrant and Joyce Sutcliffe	S-1	2/11/13	10.14
10.15#	Offer letter, dated as of March 20, 2009, by and between the Registrant and Craig Thompson dated January 30, 2014	8-K	2/5/14	99.1
10.16	Loan and Security Agreement, dated as of May 16, 2011, among the Registrant, Tetraphase Securities Corporation, Silicon Valley Bank and Oxford Finance LLC	S-1	2/11/13	10.18
10.17*	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 and November 20, 2013			

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Exhibit Number	Description	Incorporated by Reference from Registrant's Form	Date Filed with the SEC	Exhibit Number
10.18†	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	2/11/13	10.20
10.19†	Subcontract Agreement, dated as of February 1, 2012, by and between the Registrant and CUBRC, Inc.	S-1	2/11/13	10.21
10.20†	Subcontract Agreement, dated as of September 30, 2011, by and between the Registrant and CUBRC, Inc.	S-1	2/11/13	10.22
10.21	Warrant to purchase shares of Series C Convertible Preferred Stock issued by the Registrant to Silicon Valley Bank expiring on December 20, 2022	S-1	2/11/13	10.24
10.22	Warrant to purchase shares of Series C Convertible Preferred Stock issued by the Registrant to Oxford Finance LLC expiring on December 20, 2022	S-1	2/11/13	10.25
10.23	Warrant to purchase shares of Series C Convertible Preferred Stock issued by the Registrant to Oxford Finance LLC expiring on February 27, 2023	S-1/A	3/5/13	10.26
10.24	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	2/11/13	10.23
10.25#	Form of Indemnification Agreement entered into between the Registrant and each of its directors and executive officers	S-1/A	3/5/13	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*	Chief 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*	Chief 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			

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Exhibit Number	Description	Incorporated by Reference from Registrant's Form	Date Filed with the SEC	Exhibit Number
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.
+ In accordance with Rule 406T of Regulation S-T, XBRL (Extensible Business Reporting Language) information is furnished and not filed or a part of this Form 10-K for purposes of Sections 11 or 12 of the Securities Act of 1933, as amended, is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not otherwise subject to liability under these sections.

LEASE AGREEMENT

THIS LEASE AGREEMENT is made as of this 16th day of November, 2006, between ARE-480 Arsenal Street, LLC, a Delaware limited liability company ("Landlord"), and Tetraphase Pharmaceuticals, Inc., a Delaware corporation ("Tenant").

BASIC LEASE PROVISIONS

Address: 480 Arsenal Street, Watertown, Massachusetts

Premises: That portion of the Project, containing approximately 15,149 rentable square feet, as determined by Landlord, consisting of Area 1-A East, as shown on **Exhibit A** .

Project: The real property on which the building (the " **Building** ") in which the Premises are located, together with all improvements thereon and appurtenances thereto as described on **Exhibit B** .

Base Rent: $40,271.09, per month **Rentable Area of Premises:** 15,149 sq. ft.

Rentable Area of Project: 140,744 sq. ft. **Tenant's Share of Operating Expenses:** 10.764%

Security Deposit: $120,813.27

Commencement Date: November 15, 2006

Rent Commencement Date: Commencement Date

Rent Adjustment Percentage: 3%

Base Term: A term beginning on the Commencement Date and ending on December 31, 2012

Permitted Use: research and development laboratory (including, without limitation, drug development research and process and medicinal chemistry), related office and other related uses consistent with the character of the Project and otherwise in compliance with the provisions of Section 8 hereof.

Address for Rent Payment:
385 E. Colorado Boulevard, Suite 299
Pasadena, CA 91101
Attention: Accounts Receivable

Landlord's Notice Address:
385 E. Colorado Boulevard, Suite 299
Pasadena, CA 91101
Attention: Accounts Receivable

Tenant's Notice Address:

_____

_____

_____

Attention:

The following Exhibits and Addenda are attached hereto and incorporated herein by this reference:

[X] **EXHIBIT A** – PREMISES DESCRIPTION
[X] **EXHIBIT B** – DESCRIPTION OF PROJECT
[X] **EXHIBIT C** – WORK LETTER
[X] **EXHIBIT D** – TENANT'S PERSONAL PROPERTY
[X] **EXHIBIT E** – RULES AND REGULATIONS
[X] **EXHIBIT F** – FORM OF LETTER OF CREDIT

1. **Lease of Premises.** Upon and subject to all of the terms and conditions hereof, Landlord hereby leases to Tenant and Tenant hereby leases from Landlord, the Premises. Tenant shall have, as appurtenant to the Premises, the right to use those portions of the Project which are for the non-exclusive use of tenants of the Project (collectively, the " **Common Areas** "), including, without limitation, those portions of the elevators and parking areas serving the Project which are included in the Common Areas. Notwithstanding the foregoing, Landlord reserves the right to modify Common Areas, provided that such modifications do not materially adversely affect Tenant's use of the Premises for the Permitted Use. Tenant shall have access to the Premises 24 hours per day, 365 days per year, subject to Landlord's reasonable requirements with regard to any work to be performed by Landlord on the Project or the Premises.

2. **Delivery; Acceptance of Premises; Commencement Date** . Tenant acknowledges and agrees that Landlord will be constructing Landlord's Work following the Commencement Date. Accordingly, the entire Premises will not be delivered to Tenant for Tenant's use on the Commencement Date. Landlord shall use reasonable efforts to deliver the entire Premises to Tenant, with Landlord's Work Substantially Completed, as soon as possible following the Commencement Date (" **Delivery** " or " **Deliver** "). Landlord shall not be liable to Tenant for any loss or damage resulting from delays in the Delivery of the Premises (subject to the provisions regarding Landlord's waiver of Base Rent and Operating Expenses during performance of Landlord's Work set forth in Section 4 hereof), and this Lease shall not be void or voidable except as provided herein. Notwithstanding the foregoing, in the event that Landlord has not Substantially Completed Landlord's Work on or before May 15, 2007 (" **Outside Date** "), then Tenant shall have the right to terminate this Lease by written notice to Landlord within 5 days after the Outside Date. As used herein, the terms " **Landlord's Work,** " " **Tenants' Work,** " , " **Force Majeure Delays,** " " **Tenant Delays** " and " **Substantially Completed** " shall have the meanings set forth for such terms in the work letter to be entered into by Landlord and Tenant, which work letter shall be in substantially the form attached hereto as **Exhibit C** (the " **Work Letter** ").

The " **Term** " of this Lease shall be the Base Term, as defined above in the Basic Lease Provisions and any Extension Terms which Tenant may elect pursuant to Section 40 hereof.

Except as set forth in the Work Letter, if applicable: (i) Tenant shall accept the Premises in their condition as of the Commencement Date, subject to all applicable Legal Requirements (as defined in Section 8 hereof); (ii) Landlord shall have no obligation for any defects in the Premises; and (iii) Tenant's taking possession of the Premises shall be conclusive evidence that Tenant accepts the Premises and that the Premises were in good condition at the time possession was taken. Any occupancy of the Premises by Tenant before the Commencement Date shall be subject to all of the terms and conditions of this Lease, including the obligation to pay Rent except as specifically set forth in Section 4 hereof.

Tenant agrees and acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the condition of all or any portion of the Premises or the Project, and/or the suitability of the Premises or the Project for the conduct of Tenant's business, and Tenant waives any implied warranty that the Premises or the Project are suitable for the Permitted Use. This Lease constitutes the complete agreement of Landlord and Tenant with respect to the subject matter hereof and supersedes any and all prior representations, inducements, promises, agreements, understandings and negotiations which are not contained herein. Landlord in executing this Lease does so in reliance upon Tenant's representations, warranties, acknowledgments and agreements contained herein.

3. **Right to Terminate** . Tenant may terminate the Term of this Lease for any reason effective as of the last calendar day of the 42 nd full calendar month of the Term hereof (the " **Early Termination Date** "), upon 9 months' prior written notice to Landlord. Such notice to Landlord (a " **Termination Notice** ") shall be accompanied by Tenant's payment to Landlord of a termination payment in an amount equal to 9 months' Base Rent at the rate which will be in effect as of the Early Termination Date. Any Termination Notice so delivered shall apply to the entire Premises and shall be final and irrevocable. If Tenant delivers a Termination Notice in accordance with the foregoing requirements, then

(i) the Early Termination Date shall be deemed to be the date on which the Term expires for all purposes under the Lease, (ii) Tenant shall comply with all of the obligations of Tenant under this Lease that arise during or are attributable to the period ending on such Early Termination Date, (iii) Tenant shall have no further right to exercise the Extension Option set forth in Section 40 hereof, and (iv) Tenant shall vacate and surrender the Premises on the Early Termination Date in accordance with Section 29 hereof. Such termination right shall not apply to any assignee of Tenant's interest in the Lease that requires Landlord's consent under Section 23 hereof or, at Landlord's election, if an Event of Default (as hereinafter defined) has occurred and is continuing at the time of Tenant's exercise of such option.

4. **Rent** .

(a) **Base Rent** . The first month's Base Rent and the Security Deposit shall be due and payable on delivery of an executed copy of this Lease to Landlord. Tenant shall pay to Landlord in advance, without demand, abatement, deduction or set-off except as expressly set forth herein, monthly installments of Base Rent on or before the first day of each calendar month during the Term hereof, in lawful money of the United States of America, at the office of Landlord for payment of Rent set forth above, or to such other person or at such other place as Landlord may from time to time designate in writing. Payments of Base Rent for any fractional calendar month shall be prorated. The obligation of Tenant to pay Base Rent and other sums to Landlord and the obligations of Landlord under this Lease are independent obligations. Tenant shall have no right at any time to abate, reduce, or set-off any Rent (as defined in Section 6) due hereunder except for any abatement as may be expressly provided in this Lease. Notwithstanding the foregoing, Base Rent due and payable during the first 12 calendar months of the Term (including any partial month following the Commencement Date), i.e., from the Commencement Date until November 14, 2007, shall be reduced to an amount equal to 50% of the Base Rent set forth above, or $20,135.55 per month. Thereafter, Base Rent due and payable during the immediately succeeding 6 calendar months of the Term (increased by the Rent Adjustment Percentage as provided in Section 5 hereof), i.e., November 15, 2007 until May 14, 2008, shall be increased to an amount equal to 72.5% of such increased Base Rent, or $30,072.44. Commencing on May 15, 2008, and continuing thereafter for the remainder of the Term, Base Rent shall be due and payable in the amount set forth above, subject to adjustment as provided in Section 5 hereof.

(b) **Rent During Construction of Landlord's Work** . Notwithstanding anything herein to the contrary, Landlord agrees that, during Landlord's construction of Landlord's Work following the Commencement Date, in addition to the reduction in Base Rent set forth in Section 4(a) , Landlord shall waive Tenant's obligation to pay Base Rent and Operating Expenses hereunder on a day-for-day basis with respect to the portion of the Premises which is rendered unusable to Tenant due to such construction activity. Such waiver with respect to Base Rent shall only take effect if and to the extent that more than 50% of the Premises is rendered unusable as aforesaid. By way of example, and without intending to limit the generality of the foregoing, if 60% of the Premises is rendered unusable due to such construction activity, 60% of Operating Expenses shall be waived and 10% of Base Rent shall be waived, in each case for the number of days that such portion of the Premises is rendered unusable. Following Substantial Completion of Landlord's Work, Landlord shall prepare and deliver to Tenant an accounting of the reduction in Base Rent and Operating Expenses to which Tenant is entitled pursuant to this section, and such amounts shall be deducted from Tenant's next payment of Base Rent and Operating Expenses hereunder. Calculation of any credit against Base Rent hereunder shall be based on the full amount of Base Rent set forth in the Basic Lease Provisions above, not the reduced amount to be paid by Tenant pursuant to Section 4(a) .

(c) **Additional Rent.** In addition to Base Rent, Tenant agrees to pay to Landlord as additional rent (" **Additional Rent** "): (i) Tenant's Share of "Operating Expenses" (as defined in Section 6), and (ii) any and all other amounts Tenant assumes or agrees to pay under the provisions of this Lease, including, without limitation, any and all other sums that may become due by reason of any default of Tenant or failure to comply with the agreements, terms, covenants and conditions of this Lease to be performed by Tenant, after any applicable notice and cure period.

5. **Base Rent Adjustments** . Base Rent shall be increased on each annual anniversary of the first day of the first full month during the Term of this Lease, i.e., each December 1 (each an " **Adjustment Date** ") by multiplying the Base Rent payable immediately before such Adjustment Date by the Rent Adjustment Percentage and adding the resulting amount to the Base Rent payable immediately before such Adjustment Date. Base Rent, as so adjusted, shall thereafter be due as provided herein. Base Rent adjustments for any fractional calendar month shall be prorated.

6. **Operating Expense Payments** . Landlord shall deliver to Tenant a written estimate of Operating Expenses for each calendar year during the Term (the " **Annual Estimate** "), which may be revised by Landlord from time to time during such calendar year. During each month of the Term, on the same date that Base Rent is due, Tenant shall pay Landlord an amount equal to 1/12 th of Tenant's Share of the Annual Estimate. Payments for any fractional calendar month shall be prorated.

The term " **Operating Expenses** " means all Building and Project related operating costs in connection with the shell and core of the Building, site improvements, maintenance, taxes, utilities, transportation services, insurance, the costs of capital repairs and improvements amortized over the lesser of 7 years and the useful life of such capital items, in the case of repairs or improvements to the HVAC system and equipment serving the Premises, or, in the case of any other work, over the useful life of such capital items, and the costs of Landlord's third party property manager, not to exceed 3.0% of Base Rent, or, if there is no third party property manager, administration rent in the amount of 3.0% of Base Rent), excluding only:

(a) the original construction costs of the Project and renovation prior to the date of the Lease and costs of correcting defects in such original construction or renovation;

(b) capital expenditures for expansion of the Project;

(c) interest, principal payments of Mortgage (as defined in Section 28) debts of Landlord, financing costs and amortization of funds borrowed by Landlord, whether secured or unsecured and all payments of base rent (but not taxes or operating expenses) under any ground lease or other underlying lease of all or any portion of the Project;

(d) depreciation of the Project (except for capital improvements, the cost of which are includable in Operating Expenses);

(e) advertising, legal and space planning expenses and leasing commissions and other costs and expenses incurred in procuring and leasing space to tenants for the Project, including any leasing office maintained in the Project, free rent and construction allowances for tenants;

(f) legal and other expenses incurred in the negotiation or enforcement of leases;

(g) completing, fixturing, improving, renovating, painting, redecorating or other work, which Landlord pays for or performs for other tenants within their premises, and costs of correcting defects in such work;

(h) costs of utilities outside normal business hours sold to tenants of the Project;

(i) costs to be reimbursed by other tenants of the Project or Taxes to be paid directly by Tenant or other tenants of the Project, whether or not actually paid;

(j) salaries, wages, benefits and other compensation paid to officers and employees of Landlord who are not assigned in whole or in part to the operation, management, maintenance or repair of the Project;

(k) general organizational, administrative and overhead costs relating to maintaining Landlord's existence, either as a corporation, partnership, or other entity, including general corporate, legal and accounting expenses;

(l) costs (including attorneys' fees and costs of settlement, judgments and payments in lieu thereof) incurred in connection with disputes with tenants, other occupants, or prospective tenants, and costs and expenses, including legal fees, incurred in connection with negotiations or disputes with employees, consultants, management agents, leasing agents, purchasers or mortgagees of the Building;

(m) costs incurred by Landlord due to the violation by Landlord, its employees, agents or contractors or any tenant of the terms and conditions of any lease of space in the Project or any Legal Requirement (as defined in Section 8);

(n) penalties, fines or interest incurred as a result of Landlord's inability or failure to make payment of Taxes and/or to file any tax or informational returns when due, or from Landlord«'s failure to make any payment of Taxes required to be made by Landlord hereunder before delinquency;

(o) overhead and profit increment paid to Landlord or to subsidiaries or affiliates of Landlord for goods and/or services in or to the Project to the extent the same exceeds the costs of such goods and/or services rendered by unaffiliated third parties on a competitive basis;

(p) costs of Landlord's charitable or political contributions, or of fine art maintained at the Project;

(q) costs in connection with services (including electricity), items or other benefits of a type which are not standard for the Project and which are not available to Tenant without specific charges therefor, but which are provided to another tenant or occupant of the Project, whether or not such other tenant or occupant is specifically charged therefor by Landlord;

(r) costs incurred in the sale or refinancing of the Project;

(s) net income taxes of Landlord or the owner of any interest in the Project, franchise, capital stock, gift, estate or inheritance taxes or any federal, state or local documentary taxes imposed against the Project or any portion thereof or interest therein, or any income taxes arising out of or related to ownership and operation of income producing real estate, or any excise taxes imposed upon Landlord based upon gross or net rentals or other income received by it;

(t) costs incurred in connection with upgrading the Building to comply with laws, rules, codes and other Legal Requirements in effect prior to the Commencement Date; and

(u) any expenses otherwise includable within Operating Expenses to the extent actually reimbursed by persons other than tenants of the Project under leases for space in the Project.

Within 90 days after the end of each calendar year (or such longer period as may be reasonably required), Landlord shall furnish to Tenant a statement (an " **Annual Statement** ") showing in reasonable detail: (a) the total and Tenant's Share of actual Operating Expenses for the previous calendar year, and (b) the total of Tenant's payments in respect of Operating Expenses for such year. If Tenant's Share of actual Operating Expenses for such year exceeds Tenant's payments of Operating Expenses for such year, the excess shall be due and payable by Tenant as Rent within 30 days after delivery of such Annual Statement to Tenant. If Tenant's payments of Operating Expenses for such year exceed Tenant's Share of actual Operating Expenses for such year Landlord shall pay the excess to Tenant within 30 days after delivery of such Annual Statement, except that after the expiration, or earlier termination of the Term or if Tenant is delinquent in its obligation to pay Rent, Landlord shall pay the excess to Tenant after deducting all other amounts due Landlord.

The Annual Statement shall be final and binding upon Tenant unless Tenant, within 90 days after Tenant's receipt thereof, shall contest any item therein by giving written notice to Landlord, specifying each item contested and the reason therefor. If, during such 90 day period, Tenant reasonably and in good faith questions or contests the accuracy of Landlord's statement of Tenant's Share of Operating Expenses, Landlord will provide Tenant with access to Landlord's books and records relating to the operation of the Project and such information as Landlord reasonably determines to be responsive to Tenant's questions (the " **Expense Information** "). If, after Tenant's review of such Expense Information, Landlord and Tenant cannot agree upon the amount of Tenant's Share of Operating Expenses, then Tenant shall have the right to have an independent public accounting firm selected by Tenant working pursuant to a fee arrangement other than a contingent fee (at Tenant's sole cost and expense) and approved by Landlord (which approval shall not be unreasonably withheld or delayed), audit and/or review the Expense Information for the year in question (the " **Independent Review** "). The results of any such Independent Review shall be binding on Landlord and Tenant. If the Independent Review shows that the payments actually made by Tenant with respect to Operating Expenses for the calendar year in question exceeded Tenant's Share of Operating Expenses for such calendar year, Landlord shall at Landlord's option either (i) credit the excess amount to the next succeeding installments of estimated Operating Expenses or (ii) pay the excess to Tenant within 30 days after delivery of such statement, except that after the expiration or earlier termination of this Lease or if Tenant is delinquent in its obligation to pay Rent, Landlord shall pay the excess to Tenant after deducting all other amounts due Landlord. If the Independent Review shows that Tenant's payments with respect to Operating Expenses for such calendar year were less than Tenant's Share of Operating Expenses for the calendar year, Tenant shall pay the deficiency to Landlord within 30 days after delivery of such statement. If the Independent Review shows that Tenant has overpaid with respect to Operating Expenses by more than 5% then Landlord shall reimburse Tenant for all costs incurred by Tenant for the Independent Review. Operating Expenses for the calendar years in which Tenant's obligation to share therein begins and ends shall be prorated. Notwithstanding anything set forth herein to the contrary, if the Project is not at least 95% occupied on average during any year of the Term, Tenant's Share of Operating Expenses for such year shall be computed as though the Building had been 95% occupied on average during such year.

" **Tenant's Share** " shall be the percentage set forth in the Basic Lease Provisions as Tenant's Share as reasonably adjusted by Landlord for changes in the physical size of the Premises or the Project occurring thereafter. Landlord may equitably increase Tenant's Share for any item of expense or cost reimbursable by Tenant that relates to a repair, replacement, or service that benefits only the Premises or only a portion of the Project that includes the Premises or that varies with occupancy or use. Base Rent, Tenant's Share of Operating Expenses and all other amounts payable by Tenant to Landlord hereunder are collectively referred to herein as " **Rent** ."

7. **Security Deposit** . Tenant shall deposit with Landlord, upon delivery of an executed copy of this Lease to Landlord, a security deposit (the " **Security Deposit** ") for the performance of all of Tenant's obligations hereunder in the amount set forth in the Basic Lease Provisions, which Security Deposit shall be in the form of an unconditional and irrevocable letter of credit (the " **Letter of Credit** "): (i) substantially in the form attached hereto as **Exhibit F** or such other form satisfactory to Landlord, (ii) naming Landlord as beneficiary, (iii) expressly allowing Landlord to draw upon it at any time from time to time by delivering to the issuer notice that Landlord is entitled to draw thereunder, (iv) issued by an FDIC-insured financial institution satisfactory to Landlord; Landlord approves Silicon Valley Bank as an approved issuer, and (v) redeemable by presentation of a sight draft in the State of California. If Tenant does not provide Landlord with a substitute Letter of Credit complying with all of the requirements hereof at least 10 days before the stated expiration date of any then current Letter of Credit, Landlord shall have the right to draw the full amount of the current Letter of Credit and hold the funds drawn in cash without obligation for interest thereon as the Security Deposit. The Security Deposit shall be held by Landlord as security for the performance of Tenant's obligations under this Lease. The Security Deposit is not an advance rental deposit or a measure of Landlord's damages in case of Tenant's default. Upon each occurrence of a Default (as defined in Section 21), Landlord may use all or any part of the Security Deposit to pay delinquent payments due under this Lease, and the cost of any damage, injury, expense or liability caused by such Default, without prejudice to any other remedy provided herein or provided by law. Upon any such use of all or any portion of the Security Deposit,

Tenant shall pay Landlord on demand the amount that will restore the Security Deposit to the amount set forth in the Basic Lease Provisions. Tenant hereby waives the provisions of any law, now or hereafter in force, which provide that Landlord may claim from a security deposit only those sums reasonably necessary to remedy defaults in the payment of Rent, to repair damage caused by Tenant or to clean the Premises, it being agreed that Landlord may, in addition, claim those sums reasonably necessary to compensate Landlord for any other loss or damage, foreseeable or unforeseeable, caused by the act or omission of Tenant or any officer, employee, agent or invitee of Tenant. Upon bankruptcy or other debtor-creditor proceedings against Tenant, the Security Deposit shall be deemed to be applied first to the payment of Rent and other charges due Landlord for periods prior to the filing of such proceedings. Upon any such use of all or any portion of the Security Deposit, Tenant shall, within 5 days after demand from Landlord, restore the Security Deposit to its original amount. If Tenant shall fully perform every provision of this Lease to be performed by Tenant, the Security Deposit, or any balance thereof (i.e., after deducting therefrom all amounts to which Landlord is entitled under the provisions of this Lease), shall be returned to Tenant (or, at Landlord's option, to the last assignee of Tenant's interest hereunder) within 30 days after the expiration or earlier termination of this Lease.

If Landlord transfers its interest in the Project or this Lease, Landlord shall either (a) transfer any Security Deposit then held by Landlord to a person or entity assuming Landlord's obligations under this Section 7 , or (b) return to Tenant any Security Deposit then held by Landlord and remaining after the deductions permitted herein. Upon such transfer to such transferee or the return of the Security Deposit to Tenant, Landlord shall have no further obligation with respect to the Security Deposit, and Tenant's right to the return of the Security Deposit shall apply solely against Landlord's transferee. The Security Deposit is not an advance rental deposit or a measure of Landlord's damages in case of Tenant's default. Landlord's obligation respecting the Security Deposit is that of a debtor, not a trustee, and no interest shall accrue thereon.

8. **Use** . The Premises shall be used solely for the Permitted Use set forth in the Basic Lease Provisions, and in compliance with all laws, orders, judgments, ordinances, regulations, codes, directives, permits, licenses, covenants and restrictions now or hereafter applicable to the Premises, and to the use and occupancy thereof, including, without limitation, the Americans With Disabilities Act, 42 U.S.C. § 12101, et seq. (together with the regulations promulgated pursuant thereto, " **ADA** ") (collectively, " **Legal Requirements** " and each, a " **Legal Requirement** "). Tenant shall, upon 5 days' written notice from Landlord (a " **Discontinuance Notice** "), discontinue any use of the Premises which is declared by any Governmental Authority (as defined in Section 10) having jurisdiction to be a violation of a Legal Requirement. Upon receipt of any Discontinuance Notice, Tenant shall have the right to terminate this Lease by written notice to Landlord given not more than 90 days thereafter. Tenant will not use or permit the Premises to be used for any purpose or in any manner that would void Tenant's or Landlord's insurance, increase the insurance risk, or cause the disallowance of any sprinkler or other credits. Tenant shall not permit any part of the Premises to be used as a "place of public accommodation", as defined in the ADA or any similar legal requirement. Tenant shall reimburse Landlord promptly upon demand for any additional premium charged for any such insurance policy by reason of Tenant's failure to comply with the provisions of this Section or otherwise caused by Tenant's use and/or occupancy of the Premises. Tenant will use the Premises in a careful, safe and proper manner and will not commit or permit waste, overload the floor or structure of the Premises, subject the Premises to use that would damage the Premises or obstruct or interfere with the rights of Landlord or other tenants or occupants of the Project, including conducting or giving notice of any auction, liquidation, or going out of business sale on the Premises, or using or allowing the Premises to be used for any unlawful purpose. Tenant shall cause any equipment or machinery to be installed in the Premises so as to reasonably prevent sounds or vibrations from the Premises from extending into Common Areas, or other space in the Project. Tenant shall not place any machinery or equipment weighing 500 pounds or more in or upon the Premises or transport or move such items through the Common Areas of the Project or in the Project elevators without the prior written consent of Landlord. Landlord consents to the installation of NMR machinery in the Premises. Except as may be provided under the Work Letter, Tenant shall not, without the prior written consent of Landlord, use the Premises in any manner which will require ventilation, air exchange, heating, gas, steam, electricity or water beyond the existing capacity of the Project as proportionately allocated to the Premises based upon Tenant's Share as usually furnished for the Permitted Use.

Landlord shall, as an Operating Expense (to the extent such Legal Requirement is generally applicable to similar buildings in the area in which the Project is located) or at Tenant's expense (to the extent such Legal Requirement is applicable solely by reason of Tenant's, as compared to other tenants of the Project, particular use of the Premises) make any alterations or modifications to the Common Areas or the exterior of the Building that are required by Legal Requirements, including the Americans With Disabilities Act, 42 U.S.C. § 12101, et seq. (together with regulations promulgated pursuant thereto, " **ADA** "). Tenant, at its sole expense, shall make any alterations or modifications to the interior of the Premises that are required by Legal Requirements (including, without limitation, compliance of the Premises with the ADA. Notwithstanding any other provision herein to the contrary, Tenant shall be responsible for any and all demands, claims, liabilities, losses, costs, expenses, actions, causes of action, damages or judgments, and all reasonable expenses incurred in investigating or resisting the same (including, without limitation, reasonable attorneys' fees, charges and disbursements and costs of suit) (collectively, " **Claims** ") arising out of or in connection with any Legal Requirements which apply to Tenant's particular use of the Premises, as opposed to general use categories such as research and development or office use, and Tenant shall indemnify, defend, hold and save Landlord harmless from and against any and all Claims arising out of or in connection with any failure of the Premises to comply with any Legal Requirement. Notwithstanding the foregoing or any other provision of this Lease, however, Tenant shall not be responsible for compliance with any such Legal Requirements requiring (a) any structural repairs or modifications; (b) any repairs or modification of any condition existing in the Premises or the Building prior to the Lease Commencement Date; (c) repairs or modifications to any utility or any building service equipment; or (c) installation of new building service equipment, such as fire detection or suppression equipment, unless such repairs, modifications, or installations shall (i) be due to Tenant's particular manner of use of the Premises (as opposed to research and development or office use generally), or (ii) be due to the negligence or willful misconduct of Tenant or any agent, employee, or contractor of Tenant.

9. **Holding Over** . If, with Landlord's express written consent, Tenant retains possession of the Premises after the termination of the Term, (i) unless otherwise agreed in such written consent, such possession shall be subject to immediate termination by Landlord at any time, (ii) all of the other terms and provisions of this Lease (including, without limitation, the adjustment of Base Rent pursuant to Section 5 hereof) shall remain in full force and effect (excluding any expansion or renewal option or other similar right or option) during such holdover period, (iii) Tenant shall continue to pay Base Rent in the amount payable upon the date of the expiration or earlier termination of this Lease or such other amount as Landlord may indicate, in Landlord's sole and absolute discretion, in such written consent, and (iv) all other payments shall continue under the terms of this Lease. If Tenant remains in possession of the Premises after the expiration or earlier termination of the Term without the express written consent of Landlord, (A) Tenant shall become a tenant at sufferance upon the terms of this Lease except that the monthly rental shall be equal to 150% of Rent in effect during the last 30 days of the Term, and (B) if Tenant holds over for more than 30 days and Landlord gives Tenant written notice that Landlord requires possession of the Premises for delivery to a subsequent tenant, Tenant shall be responsible for all damages suffered by Landlord resulting from or occasioned by Tenant's holding over, including consequential damages of which Tenant has received prior notice. No holding over by Tenant, whether with or without consent of Landlord, shall operate to extend this Lease except as otherwise expressly provided, and this Section 9 shall not be construed as consent for Tenant to retain possession of the Premises. Acceptance by Landlord of Rent after the expiration of the Term or earlier termination of this Lease shall not result in a renewal or reinstatement of this Lease.

10. **Taxes** . Landlord shall pay, as part of Operating Expenses, all taxes, levies, assessments and governmental charges of any kind (collectively referred to as " **Taxes** ") imposed by any federal, state, regional, municipal, local or other governmental authority or agency, including, without limitation, quasi-public agencies (collectively, " **Governmental Authority** ") during the Term, including, without limitation, all Taxes: (i) imposed on or measured by or based, in whole or in part, on rent payable to Landlord under this Lease and/or from the rental by Landlord of the Project or any portion thereof, or (ii) based on the square footage, assessed value or other measure or evaluation of any kind of the Premises or the Project, or (iii) assessed or imposed by or on the operation or maintenance of any portion of the Premises or the Project, including parking, or (iv) assessed or imposed by, or at the direction of, or resulting from

statutes or regulations, or interpretations thereof, promulgated by, any Governmental Authority, or (v) imposed as a license or other fee on Landlord's business of leasing space in the Project. Landlord may contest by appropriate legal proceedings the amount, validity, or application of any Taxes or liens securing Taxes. Taxes shall not include any net income taxes imposed on Landlord. If any such Tax is levied or assessed directly against Tenant, then Tenant shall be responsible for and shall pay the same at such times and in such manner as the taxing authority shall require. Tenant shall pay, prior to delinquency, any and all Taxes levied or assessed against any personal property or trade fixtures placed by Tenant in the Premises, whether levied or assessed against Landlord or Tenant. If any Taxes on Tenant's personal property or trade fixtures are levied against Landlord or Landlord's property, or if the assessed valuation of the Project is increased by a value attributable to improvements in or alterations to the Premises, whether owned by Landlord or Tenant and whether or not affixed to the real property so as to become a part thereof, higher than the base valuation on which Landlord from time-to-time allocates Taxes to all tenants in the Project, Landlord shall have the right, but not the obligation, to pay such Taxes. Landlord's determination of any excess assessed valuation shall be binding and conclusive, absent manifest error. The amount of any such payment by Landlord shall constitute Additional Rent due from Tenant to Landlord immediately upon demand. The Landlord's taxes shall mean such amounts as shall be finally determined after deducting abatements, rebates or refunds, if any, less the costs and expenses of obtaining the same. For the purposes of determining payments due from Tenant to Landlord, the Landlord's taxes shall be deemed to be the taxes assessed for each calendar year until such time as an abatement, rebate or refund shall be made for such tax year, and if any such abatement, rebate or refund shall be made for any tax year, an appropriate adjustment or refund shall be made within thirty (30) days of receipt of the same by Landlord in the amount due from or paid by Tenant to Landlord on account of such Taxes dependent upon the amount of such abatement, rebate or refund less the cost and expense of obtaining the same. Landlord's obligations pursuant to this Section 10 to rebate, refund or otherwise adjust any payment by Tenant of Additional Rent shall survive the expiration or earlier termination of this Lease.

11. **Parking** . Subject to all matters of record, Force Majeure, a Taking (as defined in Section 19 below) and the exercise by Landlord of its rights hereunder, Tenant shall have the right, at no additional cost to Tenant, in common with other tenants of the Project pro rata in accordance with the rentable area of the Premises and the rentable areas of the Project occupied by such other tenants, to park in those areas designated for non-reserved parking, subject in each case to Landlord's rules and regulations. Landlord may allocate parking spaces among Tenant and other tenants in the Project pro rata as described above if Landlord determines that such parking facilities are becoming crowded, provided that, subject to all matters of record, Force Majeure, a Taking and the exercise by Landlord of its rights hereunder as aforesaid, Tenant shall at all times be entitled to use 22 parking spaces. Landlord shall not be responsible for enforcing Tenant's parking rights against any third parties, including other tenants of the Project. Notwithstanding anything herein to the contrary, Tenant shall at all times be entitled to 22 parking spaces.

12. **Utilities, Services.**

Landlord shall provide, subject to the terms of this Section 12 , water, electricity, heat, light, power, telephone, sewer, and other utilities (including gas and fire sprinklers to the extent the Project is plumbed for such services), refuse and trash collection and janitorial services (collectively, " **Utilities** "). Landlord shall pay, as Operating Expenses or subject to Tenant's reimbursement obligation, for all Utilities used on the Premises, all maintenance charges for Utilities, and any storm sewer charges or other similar charges for Utilities imposed by any Governmental Authority or Utility provider, and any taxes, penalties, surcharges or similar charges thereon. Landlord may cause, at Tenant's expense, any Utilities to be separated metered or charged directly to Tenant by the provider. Landlord represents that the Premises are currently submetered with respect to electrical service and that Landlord shall pass through to Tenant the actual amount charged by the electrical provider, as measured by such submeter, without any mark-up by Landlord. Tenant shall pay directly to the Utility provider, prior to delinquency, any separately metered Utilities and services which may be furnished to Tenant or the Premises during the Term. Tenant shall pay, as part of Operating Expenses, its share of all charges for jointly metered Utilities based upon consumption, as reasonably determined by Landlord. No

interruption or failure of Utilities, from any cause whatsoever other than Landlord's willful misconduct, shall result in eviction or constructive eviction of Tenant, termination of this Lease or the abatement of Rent. Tenant agrees to limit use of water and sewer with respect to Common Areas to normal restroom use.

13. **Alterations and Tenant's Property** . Any alterations, additions, or improvements made to the Premises by or on behalf of Tenant, including additional locks or bolts of any kind or nature upon any doors or windows in the Premises, but excluding installation, removal or realignment of furniture systems (other than removal of furniture systems owned or paid for by Landlord) not involving any modifications to the structure or connections (other then by ordinary plugs or jacks) to Building Systems (as defined in Section 14) (" **Alterations** ") shall be subject to Landlord's prior written consent, which may be given or withheld in Landlord's sole discretion if any such Alteration affects the structure or Building Systems, but which shall otherwise not be unreasonably withheld or delayed. Notwithstanding the foregoing, Tenant may make alterations to the Premises which do not affect the Building structure without Landlord's consent and without the need for construction documents, provided that such alterations involve only non-structural work to the Premises (such as replacement of floor coverings, window coverings, fixtures, equipment and signage), and do not exceed $50,000 in cost for any one project. If Landlord approves any Alterations, Landlord may impose such conditions on Tenant in connection with the commencement, performance and completion of such Alterations as Landlord may deem appropriate in Landlord's reasonable discretion. Any request for approval shall be in writing, delivered not less than 15 business days in advance of any proposed construction, and accompanied by plans, specifications, bid proposals, work contracts and such other information concerning the nature and cost of the alterations as may be reasonably requested by Landlord, including the identities and mailing addresses of all persons performing work or supplying materials. Landlord's right to review plans and specifications and to monitor construction shall be solely for its own benefit, and Landlord shall have no duty to ensure that such plans and specifications or construction comply with applicable Legal Requirements. Tenant shall cause, at its sole cost and expense, all Alterations to comply with insurance requirements and with Legal Requirements and shall implement at its sole cost and expense any alteration or modification required by Legal Requirements as a result of any Alterations. Tenant shall reimburse Landlord, as Additional Rent, for the actual out-of pocket expense incurred by Landlord (in an amount not to exceed $2,000 for any one project) for review and approval of Tenant's plans and specifications and monitoring of construction (i.e., engineering plan review, on-site inspections of work and similar work by or on behalf of Landlord). Before Tenant begins any Alteration, Landlord may post on and about the Premises notices of non-responsibility pursuant to applicable law. Tenant shall reimburse Landlord for, and indemnify and hold Landlord harmless from, any expense incurred by Landlord by reason of faulty work done by Tenant or its contractors, delays caused by such work, or inadequate cleanup.

Tenant shall furnish security or make other arrangements satisfactory to Landlord to assure payment for the completion of all Alterations work free and clear of liens, and shall provide (and cause each contractor or subcontractor to provide) certificates of insurance for workers' compensation and other coverage in amounts and from an insurance company satisfactory to Landlord protecting Landlord against liability for personal injury or property damage during construction. Upon completion of any Alterations, Tenant shall deliver to Landlord: (i) sworn statements setting forth the names of all contractors and subcontractors who did the work and final lien waivers from all such contractors and subcontractors; and (ii) "as built" plans for any such Alteration.

Other than (i) the items, if any, listed on **Exhibit E** attached hereto, (ii) any items agreed by Landlord in writing to be included on **Exhibit E** in the future, and (iii) any trade fixtures, machinery, equipment and other personal property not paid for out of the TI Fund (as defined in the Work Letter) which may be removed without material damage to the Premises, which damage shall be repaired (including capping or terminating utility hook-ups behind walls) by Tenant during the Term (collectively, " **Tenant's Property** "), all property of any kind paid for with the TI Fund, all Alterations, real property fixtures, built-in machinery and equipment, built-in casework and cabinets and other similar additions and improvements built into the Premises so as to become an integral part of the Premises such as fume hoods which penetrate the roof or plenum area, built-in cold rooms, built-in warm rooms, walk-in cold rooms, walk-in warm rooms, deionized water systems, glass

washing equipment, autoclaves, chillers, built-in plumbing, electrical and mechanical equipment and systems, and any power generator and transfer switch (collectively, " **Installations** ") shall be and shall remain the property of Landlord during the Term and following the expiration or earlier termination of the Term, shall not be removed by Tenant at any time during the Term and shall remain upon and be surrendered with the Premises as a part thereof in accordance with Section 29 following the expiration or earlier termination of this Lease; provided , however , that Landlord shall, at the time its approval of such Installation is requested, notify Tenant if it has elected to cause Tenant to remove such Installation upon the expiration or earlier termination of this Lease. Landlord agrees that Tenant shall have no obligation to remove any Installation included within the initial Landlord's Work. If Landlord so elects, Tenant shall remove such Installation upon the expiration or earlier termination of this Lease and restore any damage caused by or occasioned as a result of such removal, including, when removing any of Tenant's Property which was plumbed, wired or otherwise connected to any of the Building Systems, capping off all such connections behind the walls of the Premises and repairing any holes. During any such restoration period, Tenant shall pay Rent to Landlord as provided herein as if said space were otherwise occupied by Tenant.

14. **Landlord's Repairs** . Landlord, as an Operating Expense, shall maintain all of the structural, exterior, parking and other Common Areas of the Project, including foundation, roof, exterior walls, structural floors, HVAC, plumbing, fire sprinklers, elevators and all other building systems serving the Premises and other portions of the Project (" **Building Systems** "), in good repair, reasonable wear and tear and uninsured losses and damages caused by Tenant, or by any of Tenant's agents, servants, employees, invitees and contractors (collectively, " **Tenant Parties** ") excluded. Losses and damages caused by Tenant or any Tenant Party shall be repaired by Landlord, to the extent not covered by insurance, at Tenant's sole cost and expense. Landlord reserves the right to stop Building Systems services when necessary (i) by reason of accident or emergency, or (ii) for planned repairs, alterations or improvements, which are, in the judgment of Landlord, desirable or necessary to be made, until said repairs, alterations or improvements shall have been completed. Landlord shall have no responsibility or liability for failure to supply Building Systems services during any such period of interruption; provided , however , that Landlord shall, except in case of emergency, make a commercially reasonable effort to give Tenant 24 hours advance notice of any planned stoppage of Building Systems services for routine maintenance, repairs, alterations or improvements. Tenant shall promptly give Landlord written notice of any repair required by Landlord pursuant to this Section, after which Landlord shall have a reasonable opportunity to effect such repair. Landlord shall not be liable for any failure to make any repairs or to perform any maintenance unless such failure shall persist for an unreasonable time after Tenant's written notice of the need for such repairs or maintenance. Tenant waives its rights under any state or local law to terminate this Lease or to make such repairs at Landlord's expense and agrees that the parties' respective rights with respect to such matters shall be solely as set forth herein. Repairs required as the result of fire, earthquake, flood, vandalism, war, or similar cause of damage or destruction shall be controlled by Section 19 .

15. **Tenant's Repairs** . Subject to Section 14 hereof, Tenant, at its expense, shall repair, replace and maintain in good condition all portions of the Premises, including, without limitation, entries, doors, ceilings, interior windows, interior walls, and the interior side of demising walls. Should Tenant fail to make any such repair or replacement or fail to maintain the Premises, Landlord shall give Tenant notice of such failure. If Tenant fails to commence cure of such failure within 10 days of Landlord's notice, and thereafter diligently prosecute such cure to completion, Landlord may perform such work and shall be reimbursed by Tenant within 10 days after demand therefor; provided, however, that if such failure by Tenant creates or could create an emergency, Landlord may immediately commence cure of such failure and shall thereafter be entitled to recover the costs of such cure from Tenant. Subject to Sections 18 and 19, Tenant shall bear the full uninsured cost of any repair or replacement to any part of the Project that results from damage caused by Tenant or any Tenant Party and any repair that benefits only the Premises.

16. **Mechanic's Liens** . Tenant shall discharge, by bond or otherwise, any mechanic's lien filed against the Premises or against the Project for work claimed to have been done for, or materials

claimed to have been furnished to, Tenant within 10 days after the filing thereof, at Tenant's sole cost and shall otherwise keep the Premises and the Project free from any liens arising out of work performed, materials furnished or obligations incurred by Tenant. Should Tenant fail to discharge any lien described herein, Landlord shall have the right, but not the obligation, to pay such claim or post a bond or otherwise provide security to eliminate the lien as a claim against title to the Project and the cost thereof shall be immediately due from Tenant as Additional Rent. If Tenant shall lease or finance the acquisition of office equipment, furnishings, or other personal property of a removable nature utilized by Tenant in the operation of Tenant's business, Tenant warrants that any Uniform Commercial Code Financing Statement filed as a matter of public record by any lessor or creditor of Tenant will upon its face or by exhibit thereto indicate that such Financing Statement is applicable only to removable personal property of Tenant located within the Premises. In no event shall the address of the Project be furnished on the statement without qualifying language as to applicability of the lien only to removable personal property, located in an identified suite held by Tenant.

17. **Indemnification** . Tenant hereby indemnifies and agrees to defend, save and hold Landlord harmless from and against any and all Claims for injury or death to persons or damage to property occurring within or about the Premises, arising directly or indirectly out use or occupancy of the Premises or a breach or default by Tenant in the performance of any of its obligations hereunder, unless caused solely by the willful misconduct or negligence of Landlord or any of Landlord's agents, employees or contractors. Landlord shall not be liable to Tenant for, and Tenant assumes all risk of damage to, personal property (including, without limitation, loss of records kept within the Premises). Tenant further hereby irrevocably waives any and all Claims for injury to Tenant's business or loss of income relating to any such damage or destruction of personal property (including, without limitation, any loss of records), unless caused by the willful misconduct or negligence of Landlord. Landlord shall not be liable for any damages arising from any act, omission or neglect of any tenant in the Project or of any other third party.

Landlord shall indemnify and save harmless Tenant, and the directors, officers, agents, and employees of Tenant, against and from all claims, expenses, or liabilities of whatever nature (a) arising directly or indirectly from any default or breach by Landlord or Landlord's contractors, licensees, agents, servants, or employees under any of the terms or covenants of this Lease or failure of Landlord or such persons to comply with any rule, order, regulation, or lawful direction now or hereafter in force of any public authority, in each case to the extent the same related, directly or indirectly to the management operation or repair of the Building and/or the use of the common areas; or (b) arising directly or indirectly from any accident, injury, or damage, however caused, to any person or property, on the common area; or (c) arising directly or indirectly from any accident, injury, or damage to any person or property occurring outside the Premises but within the Building or on the land, to the extent such accident, injury, or damage results, or is claimed to have resulted, from any negligent act or omission, or negligence on the part of Landlord, or Landlord's contractors, licensees, agents, servants, employees, or customers, or anyone claiming by or through Landlord; provided, however, that in no event shall Landlord be obligated under this Section 17 to indemnify or save harmless Tenant, or the directors, officers, agents, employees of Tenant, to the extent such claim, expense, or liability results from any omission, fault, negligence, or other misconduct of Tenant or the officers, agents, or employees of Tenant.

This indemnity and hold harmless agreement shall include, without limitation, indemnity against all expenses, attorneys' fees and liabilities incurred in connection with any such claim or proceeding brought thereon and the defense thereof with counsel reasonably acceptable to Tenant. At the request of Tenant, Landlord shall defend any such claim or proceeding directly on behalf and for the benefit of Tenant. The provisions of this Section shall survive the Term of this Lease.

18. **Insurance** . Landlord shall maintain all risk property and, if applicable, sprinkler damage insurance covering the full replacement cost of the Project. Landlord shall further procure and maintain commercial general liability insurance with a single loss limit of not less than $2,000,000 for bodily injury and property damage with respect to the Project. Landlord may, but is not obligated to, maintain such other insurance and additional coverages as it may deem necessary, including, but not limited to, flood, environmental hazard and earthquake, loss or failure of building equipment, errors and omissions, rental loss during the period of repair or rebuilding, workers' compensation insurance and fidelity bonds for

employees employed to perform services and insurance for any improvements installed by Tenant or which are in addition to the standard improvements customarily furnished by Landlord without regard to whether or not such are made a part of the Project. All such insurance shall be included as part of the Operating Expenses. The Project may be included in a blanket policy (in which case the cost of such insurance allocable to the Project will be determined by Landlord based upon the insurer's cost calculations).

Tenant, at its sole cost and expense, shall maintain during the Term: all risk property insurance with business interruption and extra expense coverage, covering the full replacement cost of all property and improvements installed or placed in the Premises by Tenant at Tenant's expense; workers' compensation insurance with no less than the minimum limits required by law; employer's liability insurance with such limits as required by law; and commercial general liability insurance, with a minimum limit of not less than $2,000,000 per occurrence for bodily injury and property damage with respect to the Premises. The commercial general liability insurance policy shall name Landlord and Alexandria Real Estate Equities, Inc. and their respective officers, directors, employees, managers, agents, invitees and contractors (collectively, " **Landlord Parties** "), as additional insureds. In addition, the commercial general liability insurance policy shall insure on an occurrence and not a claims-made basis; shall be issued by insurance companies which have a rating of not less than policyholder rating of A and financial category rating of at least Class X in "Best's Insurance Guide"; shall not be cancelable for nonpayment of premium unless 30 days prior written notice shall have been given to Landlord from the insurer; shall contain a hostile fire endorsement and a contractual liability endorsement; and shall provide primary coverage to Landlord (any policy issued to Landlord providing duplicate or similar coverage shall be deemed excess over Tenant's policies). Copies of such policies (if requested by Landlord), or certificates of insurance showing the limits of coverage required hereunder and showing Landlord and Alexandria Real Estate Equities, Inc. as additional insureds, along with reasonable evidence of the payment of premiums for the applicable period, shall be delivered to Landlord by Tenant upon commencement of the Term and upon each renewal of said insurance. Tenant's policy may be a "blanket policy" with an aggregate per location endorsement which specifically provides that the amount of insurance shall not be prejudiced by other losses covered by the policy. Tenant shall, at least 5 days prior to the expiration of such policies, furnish Landlord with renewal certificates.

In each instance where insurance is to name Landlord as an additional insured, Tenant shall upon written request of Landlord also designate and furnish certificates so evidencing Landlord as additional insured to: (i) any lender of Landlord holding a security interest in the Project or any portion thereof, (ii) the landlord under any lease wherein Landlord is tenant of the real property on which the Project is located, if the interest of Landlord is or shall become that of a tenant under a ground or other underlying lease rather than that of a fee owner, and/or (iii) any management company retained by Landlord to manage the Project.

The property insurance obtained by Landlord and Tenant shall include a waiver of subrogation by the insurers and all rights based upon an assignment from its insured, against Landlord or Tenant, and their respective officers, directors, employees, managers, agents, invitees and contractors (" **Related Parties** "), in connection with any loss or damage thereby insured against. Neither party nor its respective Related Parties shall be liable to the other for loss or damage caused by any risk insured against under property insurance required to be maintained hereunder, and each party waives any claims against the other party, and its respective Related Parties, for such loss or damage. The failure of a party to insure its property shall not void this waiver. Landlord and its respective Related Parties shall not be liable for, and Tenant hereby waives all claims against such parties for, business interruption and losses occasioned thereby sustained by Tenant or any person claiming through Tenant resulting from any accident or occurrence in or upon the Premises or the Project from any cause whatsoever. If the foregoing waivers shall contravene any law with respect to exculpatory agreements, the liability of Landlord or Tenant shall be deemed not released but shall be secondary to the other's insurer.

Landlord may require insurance policy limits to be raised to conform with requirements of Landlord's lender and/or to bring coverage limits to levels then being generally required of new tenants within the Project.

19. **Restoration** . If, at any time during the Term, the Project or the Premises are damaged or destroyed by a fire or other insured casualty, Landlord shall notify Tenant within 60 days after discovery of such damage as to the amount of time Landlord reasonably estimates it will take to restore the Project or the Premises, as applicable (the " **Restoration Period** "). If the Restoration Period is estimated to exceed 12 months (the " **Maximum Restoration Period** "), either Landlord or Tenant may, by written notice to the other within 30 days after Tenant's receipt of such estimate, elect to terminate this Lease as of the date that is 75 days after the date of discovery of such damage or destruction. Unless either party so elects to terminate this Lease, Landlord shall, subject to receipt of sufficient insurance proceeds (with any deductible to be treated as a current Operating Expense), promptly restore the Premises, including the initial Landlord's Work (excluding any improvements installed thereafter by Tenant or by Landlord and paid for by Tenant), subject to delays arising from the collection of insurance proceeds, from Force Majeure events or as needed to obtain any license, clearance or other authorization of any kind required to enter into and restore the Premises issued by any Governmental Authority having jurisdiction over the use, storage, handling, treatment, generation, release, disposal, removal or remediation of Hazardous Materials (as defined in Section 31) in, on or about the Premises (collectively referred to herein as " **Hazardous Materials Clearances** "); provided , however , that if repair or restoration of the Premises is not substantially complete as of the end of the Maximum Restoration Period or, if longer, the Restoration Period, (a) Landlord may, in its sole and absolute discretion, elect not to proceed with such repair and restoration, in which event Landlord shall be relieved of its obligation to make such repairs or restoration, or (b) Tenant may elect to terminate this Lease by notice thereof to Landlord, and, in either case, this Lease shall terminate as of the date that is 75 days after the later of: (i) discovery of such damage or destruction, or (ii) the date all required Hazardous Materials Clearances are obtained, but Landlord shall retain any Rent paid and the right to any Rent payable by Tenant prior to such election by Landlord or Tenant.

Tenant, at its expense, shall promptly perform, subject to delays arising from the collection of insurance proceeds, from Force Majeure (as defined in Section 35) events or to obtain Hazardous Material Clearances, all repairs or restoration not required to be done by Landlord and shall promptly re-enter the Premises and commence doing business in accordance with this Lease. Notwithstanding the foregoing, either Landlord or Tenant may terminate this Lease if the Premises are damaged during the last 1 year of the Term and Landlord reasonably estimates that it will take more than 2 months to repair such damage, or if insurance proceeds are not available for such restoration. Rent shall be abated from the date all required Hazardous Material Clearances are obtained until the Premises are repaired and restored, in the proportion which the area of the Premises, if any, which is not usable by Tenant bears to the total area of the Premises. Such abatement shall be the sole remedy of Tenant, and except as provided in this Section 19 , Tenant waives any right to terminate the Lease by reason of damage or casualty loss.

The provisions of this Lease, including this Section 19 , constitute an express agreement between Landlord and Tenant with respect to any and all damage to, or destruction of, all or any part of the Premises, or any other portion of the Project, and any statute or regulation which is now or may hereafter be in effect shall have no application to this Lease or any damage or destruction to all or any part of the Premises or any other portion of the Project, the parties hereto expressly agreeing that this Section 19 sets forth their entire understanding and agreement with respect to such matters.

20. **Condemnation** . If the whole or any material part of the Premises or the Project is taken for any public or quasi-public use under governmental law, ordinance, or regulation, or by right of eminent domain, or by private purchase in lieu thereof (a " **Taking** " or " **Taken** "), and the Taking would in Landlord's reasonable judgment either prevent or materially interfere with Tenant's use of the Premises for the conduct of Tenant's business, including parking and access, or materially interfere with or impair Landlord's ownership or operation of the Project, then upon written notice by Landlord or Tenant this Lease shall terminate and Rent shall be apportioned as of said date. If part of the Premises shall be Taken, and this Lease is not terminated as provided above, Landlord shall promptly restore the Premises and the Project as nearly as is commercially reasonable under the circumstances to their condition prior to such partial Taking and the rentable square footage of the Building, the rentable square footage of the Premises, Tenant's Share of Operating Expenses and the Rent payable hereunder during the unexpired

Term shall be reduced to such extent as may be fair and reasonable under the circumstances. During the performance of such restoration by Landlord, Rent shall be abated in the proportion which the area of the Premises, if any, which is not usable by Tenant bears to the total area of the Premises. Upon any such Taking, Landlord shall be entitled to receive the entire price or award from any such Taking without any payment to Tenant, and Tenant hereby assigns to Landlord Tenant's interest, if any, in such award. Tenant shall have the right, to the extent that same shall not diminish Landlord's award, to make a separate claim against the condemning authority (but not Landlord) for such compensation as may be separately awarded or recoverable by Tenant for moving expenses and damage to Tenant's Property, if a separate award for such items is made to Tenant. Tenant hereby waives any and all rights it might otherwise have pursuant to any provision of state law to terminate this Lease upon a partial Taking of the Premises or the Project.

21. **Events of Default** . Each of the following events shall be a default (" **Default** ") by Tenant under this Lease:

(a) **Payment Defaults** . Tenant shall fail to pay any installment of Rent or any other payment hereunder within 5 days after written notice from Landlord that the same is due, provided that Landlord shall not be obligated to give such a notice more than one time in any 12 month period.

(b) **Insurance** . Any insurance required to be maintained by Tenant pursuant to this Lease shall be canceled or terminated or shall expire or shall be reduced or materially changed, and Tenant shall fail to obtain replacement insurance within 30 days after receipt of notice thereof from Landlord or Tenant's insurer, as applicable, or Landlord shall receive a notice of nonrenewal of any such insurance and Tenant shall fail to obtain replacement insurance at least 20 days before the expiration of the current coverage.

(c) **Abandonment** . Tenant shall abandon the Premises. Landlord agrees that Tenant shall not be deemed to have abandoned the Premises if (i) Tenant provides Landlord with reasonable advance notice prior to vacating and, at the time of vacating the Premises, (ii) Tenant completes Tenant's obligations with respect to the Surrender Plan in compliance with Section 29 , (iii) Tenant has made reasonable arrangements with Landlord for the security of the Premises for the balance of the Term, and (iv) Tenant continues during the balance of the Term to satisfy all of its obligations under the Lease as they come due.

(d) **Improper Transfer** . Tenant shall assign, sublease or otherwise transfer or attempt to transfer all or any portion of Tenant's interest in this Lease or the Premises except as expressly permitted herein, or Tenant's interest in this Lease shall be attached, executed upon, or otherwise judicially seized and such action is not released within 90 days of the action.

(e) **Liens** . Tenant shall fail to discharge, bond over or otherwise obtain the release of any lien placed upon the Premises in violation of this Lease within 10 days after any notice to Tenant that such lien is filed against the Premises.

(f) **Insolvency Events** . Tenant or any guarantor or surety of Tenant's obligations hereunder shall: (A) make a general assignment for the benefit of creditors; (B) commence any case, proceeding or other action seeking to have an order for relief entered on its behalf as a debtor or to adjudicate it a bankrupt or insolvent, or seeking reorganization, arrangement, adjustment, liquidation, dissolution or composition of it or its debts or seeking appointment of a receiver, trustee, custodian or other similar official for it or for all or of any substantial part of its property (collectively a " **Proceeding for Relief** "); (C) become the subject of any Proceeding for Relief which is not dismissed within 90 days of its filing or entry; or (D) die or suffer a legal disability (if Tenant, guarantor, or surety is an individual) or be dissolved or otherwise fail to maintain its legal existence (if Tenant, guarantor or surety is a corporation, partnership or other entity).

(g) **Estoppel Certificate or Subordination Agreement.** Tenant fails to execute any document required from Tenant under Sections 24 or 28 within 5 business days after a second notice requesting such document.

(h) **Other Defaults** . Tenant shall fail to comply with any provision of this Lease other than those specifically referred to in this Section 21 , and, except as otherwise expressly provided herein, such failure shall continue for a period of 21 days after written notice thereof from Landlord to Tenant.

Any notice given under Section 21(h) hereof shall: (i) specify the alleged default, (ii) demand that Tenant cure such default, (iii) be in lieu of, and not in addition to, or shall be deemed to be, any notice required under any provision of applicable law, and (iv) not be deemed a forfeiture or a termination of this Lease unless Landlord elects otherwise in such notice; provided that if the nature of Tenant's default pursuant to Section 21(h) is such that it cannot be cured by the payment of money and reasonably requires more than 21 days to cure, then Tenant shall not be deemed to be in default if Tenant commences such cure within said 21 day period and thereafter diligently prosecutes the same to completion; provided , however , that such cure shall be completed no later than 45 days from the date of Landlord's notice.

22. **Landlord's Remedies** .

(a) **Payment By Landlord; Interest** . Upon a Default by Tenant hereunder, Landlord may, without waiving or releasing any obligation of Tenant hereunder, make such payment or perform such act. All sums so paid or incurred by Landlord, together with interest thereon, from the date such sums were paid or incurred, at the annual rate equal to 12% per annum or the highest rate permitted by law (the " **Default Rate** "), whichever is less, shall be payable to Landlord on demand as Additional Rent. Nothing herein shall be construed to create or impose a duty on Landlord to mitigate any damages resulting from Tenant's Default hereunder.

(b) **Late Payment Rent** . Late payment by Tenant to Landlord of Rent and other sums due will cause Landlord to incur costs not contemplated by this Lease, the exact amount of which will be extremely difficult and impracticable to ascertain. Such costs include, but are not limited to, processing and accounting charges and late charges which may be imposed on Landlord under any Mortgage covering the Premises. Therefore, if any installment of Rent due from Tenant is not received by Landlord within 5 days after the date such payment is due, Tenant shall pay to Landlord an additional sum equal to 3% of the overdue Rent as a late charge. The parties agree that this late charge represents a fair and reasonable estimate of the costs Landlord will incur by reason of late payment by Tenant. In addition to the late charge, Rent not paid when due shall bear interest at the Default Rate from the 5th day after the date due until paid.

(c) **Remedies** . Upon the occurrence of a Default, Landlord, at its option, without further notice or demand to Tenant, shall have in addition to all other rights and remedies provided in this Lease, at law or in equity, the option to pursue any one or more of the following remedies, each and all of which shall be cumulative and nonexclusive, without any notice or demand whatsoever.

(i) Terminate this Lease, or at Landlord's option, Tenant's right to possession only, in which event Tenant shall immediately surrender the Premises to Landlord, and if Tenant fails to do so, Landlord may, without prejudice to any other remedy which it may have for possession or arrearages in rent, enter upon and take possession of the Premises and expel or remove Tenant and any other person who may be occupying the Premises or any part thereof, without being liable for prosecution or any claim or damages therefor;

(ii) Upon any termination of this Lease, whether pursuant to the foregoing Section 22(c)(i) or otherwise, Landlord may recover from Tenant the following:

(1) The worth at the time of award of any unpaid rent which has been earned at the time of such termination; plus

(2) The worth at the time of award of the amount by which the unpaid rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(3) The worth at the time of award of the amount by which the unpaid rent for the balance of the Term after the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided; plus

(4) Any other amount necessary to compensate Landlord for costs incurred by Landlord as a result of Tenant's default hereunder, specifically including, but not limited to, brokerage commissions and advertising expenses incurred, expenses of remodeling the Premises or any portion thereof for a new tenant, whether for the same or a different use, and any special concessions made to obtain a new tenant; and

(5) At Landlord's election, such other amounts in addition to or in lieu of the foregoing as may be permitted from time to time by applicable law.

The term " **rent** " as used in this Section 22 shall be deemed to be and to mean all sums of every nature required to be paid by Tenant pursuant to the terms of this Lease, whether to Landlord or to others. As used in Sections 22(c)(ii) (A) and (B) , above, the " **worth at the time of award** " shall be computed by allowing interest at the Default Rate. As used in Section 22(c)(ii)(C) above, the " **worth at the time of award** " shall be computed by discounting such amount at the discount rate of the Federal Reserve Bank of San Francisco at the time of award plus 1%.

(iii) Landlord may continue this Lease in effect after Tenant's Default and recover rent as it becomes due (Landlord and Tenant hereby agreeing that Tenant has the right to sublet or assign hereunder, subject only to reasonable limitations). Accordingly, if Landlord does not elect to terminate this Lease following a Default by Tenant, Landlord may, from time to time, without terminating this Lease, enforce all of its rights and remedies hereunder, including the right to recover all Rent as it becomes due.

(iv) Whether or not Landlord elects to terminate this Lease following a Default by Tenant, Landlord shall have the right to terminate any and all subleases, licenses, concessions or other consensual arrangements for possession entered into by Tenant and affecting the Premises or may, in Landlord's sole discretion, succeed to Tenant's interest in such subleases, licenses, concessions or arrangements. Upon Landlord's election to succeed to Tenant's interest in any such subleases, licenses, concessions or arrangements, Tenant shall, as of the date of notice by Landlord of such election, have no further right to or interest in the rent or other consideration receivable thereunder.

(v) Independent of the exercise of any other remedy of Landlord hereunder or under applicable law, Landlord may conduct an environmental test of the Premises as generally described in Section 31(d) hereof, at Tenant's expense.

(d) **Effect of Exercise** . Exercise by Landlord of any remedies hereunder or otherwise available shall not be deemed to be an acceptance of surrender of the Premises and/or a termination of this Lease by Landlord, it being understood that such surrender and/or termination can be effected only by the express written agreement of Landlord and Tenant. Any law, usage, or custom to the contrary notwithstanding, Landlord shall have the right at all times to enforce the provisions of this Lease in strict accordance with the terms hereof; and the failure of Landlord at any time to enforce its rights under this Lease strictly in accordance with same shall not be construed as having created a custom in any way or manner contrary to the specific terms, provisions, and covenants of this Lease or as having modified the same and shall not be deemed a waiver of Landlord's right to enforce one or more of its

rights in connection with any subsequent default. A receipt by Landlord of Rent or other payment with knowledge of the breach of any covenant hereof shall not be deemed a waiver of such breach, and no waiver by Landlord of any provision of this Lease shall be deemed to have been made unless expressed in writing and signed by Landlord. To the greatest extent permitted by law, Tenant waives the service of notice of Landlord's intention to re-enter, re-take or otherwise obtain possession of the Premises as provided in any statute, or to institute legal proceedings to that end, and also waives all right of redemption in case Tenant shall be dispossessed by a judgment or by warrant of any court or judge. Any reletting of the Premises or any portion thereof shall be on such terms and conditions as Landlord in its sole discretion may determine. Upon termination of this Lease by Landlord, Landlord shall use commercially reasonable efforts to relet the Premises. Landlord shall not be liable for, nor shall Tenant's obligations hereunder be diminished because of, Landlord's failure to relet the Premises or collect rent due in respect of such reletting or otherwise to mitigate any damages arising by reason of Tenant's Default.

23. **Assignment and Subletting** .

(a) **General Prohibition** . Without Landlord's prior written consent, subject to and on the conditions described in this Section 23 , except for any Permitted Assignment, Tenant shall not, directly or indirectly, voluntarily or by operation of law, assign this Lease or sublease the Premises or any part thereof or mortgage, pledge, or hypothecate its leasehold interest or grant any concession or license within the Premises, and any attempt to do any of the foregoing shall be void and of no effect. Except for any Permitted Assignment, if Tenant is a corporation, partnership or limited liability company, the shares or other ownership interests thereof which are not actively traded upon a stock exchange or in the over-the-counter market, a transfer or series of transfers whereby 50% or more of the issued and outstanding shares or other ownership interests of such corporation are, or voting control is, transferred (but excepting transfers upon deaths of individual owners) from a person or persons or entity or entities which were owners thereof at time of execution of this Lease to persons or entities who were not owners of shares or other ownership interests of the corporation, partnership or limited liability company at time of execution of this Lease, shall be deemed an assignment of this Lease requiring the consent of Landlord as provided in this Section 23 . Notwithstanding the foregoing, neither an initial public offering of shares by Tenant, nor any private financing by institutional investors who regularly invest in private life science companies shall be deemed an assignment of this Lease requiring the consent of Landlord as provided in this Section 23 .

(b) **Permitted Transfers** . If Tenant desires to assign, sublease, hypothecate or otherwise transfer this Lease or sublet the Premises other than pursuant to a Permitted Assignment (as defined below), then at least 10 business days, but not more than 45 days, before the date Tenant desires the assignment or sublease to be effective (the " **Assignment Date** "), Tenant shall give Landlord a notice (the " **Assignment Notice** ") containing such information about the proposed assignee or sublessee, including the proposed use of the Premises and any Hazardous Materials proposed to be used, stored handled, treated, generated in or released or disposed of from the Premises, the Assignment Date, any relationship between Tenant and the proposed assignee or sublessee, and all material terms and conditions of the proposed assignment or sublease, including a copy of any proposed assignment or sublease in its final form, and such other information as Landlord may deem reasonably necessary or appropriate to its consideration whether to grant its consent. Landlord may, by giving written notice to Tenant within 10 business days after receipt of the Assignment Notice: (i) grant such consent, (ii) refuse such consent, in its sole and absolute discretion, if the proposed assignment, hypothecation or other transfer or subletting concerns more than (together with all other then effective subleases) 50% of the Premises, (iii) refuse such consent, in its reasonable discretion, if the proposed subletting concerns (together with all other then effective subleases) 50% or less of the Premises (provided that Landlord shall further have the right to review and approve or disapprove the proposed form of sublease prior to the effective date of any such subletting), or (iv) if the proposed assignment or sublease is for greater than 50% of the Premises or for the remainder of the Base Term or the Extension Term (as hereinafter defined), as applicable, terminate this Lease with respect to the space described in the Assignment Notice as of the Assignment Date (an " **Assignment Termination** "). If Landlord delivers notice of its election to exercise an Assignment Termination, Tenant shall have the right to withdraw such

Assignment Notice by written notice to Landlord of such election within 5 business days after Landlord's notice electing to exercise the Assignment Termination. If Tenant withdraws such Assignment Notice, this Lease shall continue in full force and effect. If Tenant does not withdraw such Assignment Notice, this Lease, and the term and estate herein granted, shall terminate as of the Assignment Date with respect to the space described in such Assignment Notice. No failure of Landlord to exercise any such option to terminate this Lease, or to deliver a timely notice in response to the Assignment Notice, shall be deemed to be Landlord's consent to the proposed assignment, sublease or other transfer. Tenant shall reimburse Landlord for all of Landlord's reasonable out-of-pocket expenses in connection with its consideration of any Assignment Notice.

Notwithstanding the foregoing, Landlord's consent to an assignment of this Lease or a subletting of any portion of the Premises to any entity controlling, controlled by or under common control with Tenant shall not be required. In addition, Tenant shall have the right to assign this Lease, upon 30 days prior written notice to Landlord but without obtaining Landlord's prior written consent, to a corporation or other entity which is a successor-in-interest to Tenant, by way of merger, consolidation or corporate reorganization, or by the purchase of all or substantially all of the assets or the ownership interests of Tenant provided that (i) such merger or consolidation, or such acquisition or assumption, as the case may be, is for a good business purpose and not principally for the purpose of transferring the Lease, and (ii) the net worth (as determined in accordance with generally accepted accounting principles (" **GAAP** ")) of the assignee is not less than the net worth (as determined in accordance with GAAP) of Tenant as of the date of Tenant's most current quarterly or annual financial statements, and (iii) such assignee shall agree in writing to assume all of the terms, covenants and conditions of this Lease arising after the effective date of the assignment (all of the transfers described in this paragraph are sometimes hereinafter referred to as a " **Permitted Assignment** ").

(c) **Additional Conditions** . As a condition to any such assignment or subletting, whether or not Landlord's consent is required, Landlord may require:

(i) that any assignee or subtenant agree, in writing at the time of such assignment or subletting, that if Landlord gives such party notice that Tenant is in default under this Lease, such party shall thereafter make all payments otherwise due Tenant directly to Landlord, which payments will be received by Landlord without any liability except to credit such payment against those due under the Lease, and any such third party shall agree to attorn to Landlord or its successors and assigns should this Lease be terminated for any reason; provided , however , in no event shall Landlord or its successors or assigns be obligated to accept such attornment; and

(ii) A list of Hazardous Materials, certified by the proposed assignee or sublessee to be true and correct, which the proposed assignee or sublessee intends to use, store, handle, treat, generate in or release or dispose of from the Premises, together with copies of all documents relating to such use, storage, handling, treatment, generation, release or disposal of Hazardous Materials by the proposed assignee or subtenant in the Premises or on the Project, prior to the proposed assignment or subletting, including, without limitation: permits; approvals; reports and correspondence; storage and management plans; plans relating to the installation of any storage tanks to be installed in or under the Project (provided, said installation of tanks shall only be permitted after Landlord has given its written consent to do so, which consent may be withheld in Landlord's sole and absolute discretion); and all closure plans or any other documents required by any and all federal, state and local Governmental Authorities for any storage tanks installed in, on or under the Project for the closure of any such tanks. Neither Tenant nor any such proposed assignee or subtenant is required, however, to provide Landlord with any portion(s) of the such documents containing information of a proprietary nature which, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities.

(d) **No Release of Tenant, Sharing of Excess Rents** . Notwithstanding any assignment or subletting, Tenant and any guarantor or surety of Tenant's obligations under this Lease shall at all times remain fully and primarily responsible and liable for the payment of Rent and for

compliance with all of Tenant's other obligations under this Lease. If the Rent due and payable by a sublessee or assignee (or a combination of the rental payable under such sublease or assignment plus any bonus or other consideration therefor or incident thereto in any form) exceeds the sum of the rental payable under this Lease (excluding however, any Rent payable under this Section) and actual and reasonable brokerage fees, legal costs and any design fees or construction costs directly related to and required pursuant to the terms of any such sublease and any tenant concessions granted to obtain such sublease or assignment (" **Excess Rent** "), then Tenant shall be bound and obligated to pay Landlord as Additional Rent hereunder 50% of such Excess Rent within 10 days following receipt thereof by Tenant. If Tenant shall sublet the Premises or any part thereof, Tenant hereby immediately and irrevocably assigns to Landlord, as security for Tenant's obligations under this Lease, all rent from any such subletting, and Landlord as assignee and as for Tenant, or a receiver for Tenant appointed on Landlord's application, may collect such rent and apply it toward Tenant's obligations under this Lease; except that, until the occurrence of a Default, Tenant shall have the right to collect such rent.

(e) **No Waiver** . The consent by Landlord to an assignment or subletting shall not relieve Tenant or any assignees of this Lease or any sublessees of the Premises from obtaining the consent of Landlord to any further assignment or subletting nor shall it release Tenant or any assignee or sublessee of Tenant from full and primary liability under the Lease. The acceptance of Rent hereunder, or the acceptance of performance of any other term, covenant, or condition thereof, from any other person or entity shall not be deemed to be a waiver of any of the provisions of this Lease or a consent to any subletting, assignment or other transfer of the Premises.

(f) **Prior Conduct and Nature of Proposed Transferee.** Notwithstanding any other provision of this Section 23 , except for any Permitted Assignment (as to which the terms of this Section 23(f) shall not apply, if (i) the proposed assignee or sublessee of Tenant has been required by any prior landlord, lender or Governmental Authority to take remedial action in connection with Hazardous Materials contaminating a property, where the contamination resulted from such party's action or use of the property in question, (ii) the proposed assignee or sublessee is subject to an enforcement order issued by any Governmental Authority in connection with the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials (including, without limitation, any order related to the failure to make a required reporting to any Governmental Authority), or (iii) because of the existence of a pre-existing environmental condition in the vicinity of or underlying the Project, the risk that Landlord would be targeted as a responsible party in connection with the remediation of such pre-existing environmental condition would be materially increased or exacerbated by the proposed use of Hazardous Materials by such proposed assignee or sublessee, Landlord shall have the absolute right to refuse to consent to any assignment or subletting to any such party. In addition, it shall be reasonable for Landlord to withhold its consent to any assignment or sublease to a proposed assignee or sublessee who, in Landlord's reasonable judgment, has an objectionable business reputation or intends to use the Premises or the Project for any purpose which may be controversial. Finally, it shall be reasonable for Landlord to withhold its consent to any assignment or sublease to a proposed assignee or sublessee who has been offered and is considering a lease of comparable space in any of Landlord's properties located in Watertown or Waltham, Massachusetts.

24. **Estoppel Certificate.** Tenant shall, within 10 business days of written notice from Landlord, execute, acknowledge and deliver a statement in writing in any form reasonably requested by a proposed lender or purchaser, (i) certifying that this Lease is unmodified and in full force and effect (or, if modified, stating the nature of such modification and certifying that this Lease as so modified is in full force and effect) and the dates to which the rental and other charges are paid in advance, if any, (ii) acknowledging that there are not any uncured defaults on the part of Landlord hereunder, or specifying such defaults if any are claimed, and (iii) setting forth such further information with respect to the status of this Lease or the Premises as may be requested thereon. Any such statement may be relied upon by any prospective purchaser or encumbrancer of all or any portion of the real property of which the Premises are a part. Tenant's failure to deliver such statement within such time shall, at the option of Landlord, be conclusive upon Tenant that the Lease is in full force and effect and without modification except as may be represented by Landlord in any certificate prepared by Landlord and delivered to Tenant for execution.

25. **Quiet Enjoyment** . So long as Tenant shall perform all of the covenants and agreements herein required to be performed by Tenant, Tenant shall, subject to the terms of this Lease, at all times during the Term, have peaceful and quiet enjoyment of the Premises against any person claiming by, through or under Landlord.

26. **Prorations.** All prorations required or permitted to be made hereunder shall be made on the basis of a 360 day year and 30 day months.

27. **Rules and Regulations** . Tenant shall, at all times during the Term and any extension thereof, comply with all reasonable rules and regulations at any time or from time to time established by Landlord covering use of the Premises and the Project. The current rules and regulations are attached hereto as **Exhibit D** . If there is any conflict between said rules and regulations and other provisions of this Lease, the terms and provisions of this Lease shall control. Landlord shall not have any liability or obligation for the breach of any rules or regulations by other tenants in the Project and shall not enforce such rules and regulations in a discriminatory manner.

28. **Subordination** . This Lease and Tenant's interest and rights hereunder are hereby made and shall be subject and subordinate at all times to the lien of any Mortgage now existing or hereafter created on or against the Project or the Premises, and all amendments, restatements, renewals, modifications, consolidations, refinancing, assignments and extensions thereof, without the necessity of any further instrument or act on the part of Tenant; provided , however that so long as there is no Default hereunder, Tenant's right to possession of the Premises shall not be disturbed by the Holder of any such Mortgage. Tenant agrees, at the election of the Holder of any such Mortgage, to attorn to any such Holder. Tenant agrees upon demand to execute, acknowledge and deliver such instruments, confirming such subordination, and such instruments of attornment as shall be requested by any such Holder, provided any such instruments contain appropriate non-disturbance provisions assuring Tenant's quiet enjoyment of the Premises as set forth in Section 25 hereof. Notwithstanding the foregoing, any such Holder may at any time subordinate its Mortgage to this Lease, without Tenant's consent, by notice in writing to Tenant, and thereupon this Lease shall be deemed prior to such Mortgage without regard to their respective dates of execution, delivery or recording and in that event such Holder shall have the same rights with respect to this Lease as though this Lease had been executed prior to the execution, delivery and recording of such Mortgage and had been assigned to such Holder. The term " **Mortgage** " whenever used in this Lease shall be deemed to include deeds of trust, security assignments and any other encumbrances, and any reference to the " **Holder** " of a Mortgage shall be deemed to include the beneficiary under a deed of trust.

29. **Surrender** . Prior to the Commencement Date, Landlord shall use reasonable efforts to deliver a copy of the Surrender Plan of the prior tenant in the Premises with evidence that such Surrender Plan is complete. Notwithstanding the foregoing, Landlord's inability to deliver such Surrender Plan, despite reasonable efforts to do so, shall not be deemed a default hereunder or otherwise excuse Tenant from any of Tenant's obligations under this Section 29 or any other provision of this Lease. Upon the expiration of the Term or earlier termination of Tenant's right of possession, Tenant shall surrender the Premises to Landlord in the same condition as received, subject to any Alterations or Installations permitted by Landlord to remain in the Premises, free of Hazardous Materials brought upon, kept, used, stored, handled, treated, generated in, or released or disposed of from, the Premises by Tenant or any Tenant Party (collectively, " **Tenant HazMat Operations** ") and released of all Hazardous Materials Clearances, broom clean, ordinary wear and tear and casualty loss and condemnation covered by Sections 19 and 20 excepted. At least 3 months prior to the surrender of the Premises, Tenant shall deliver to Landlord a narrative description of the actions proposed (or required by any Governmental Authority) to be taken by Tenant in order to surrender the Premises (including any Installations permitted by Landlord to remain in the Premises) at the expiration or earlier termination of the Term, free from any residual impact from the Tenant HazMat Operations and otherwise released for unrestricted use and occupancy (the " **Surrender Plan** "). Such Surrender Plan shall be accompanied by a current listing of (i) all Hazardous Materials licenses and permits held by or on behalf of any Tenant Party with respect to the Premises, and (ii) all Hazardous Materials used, stored, handled, treated, generated, released or disposed of from the Premises by Tenant or any Tenant Party, and shall be subject to the review and

approval of Landlord's environmental consultant. In connection with the review and approval of the Surrender Plan, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such additional non-proprietary information concerning Tenant HazMat Operations as Landlord shall request. On or before such surrender, Tenant shall deliver to Landlord evidence that the approved Surrender Plan shall have been satisfactorily completed and Landlord shall have the right, subject to reimbursement at Tenant's expense as set forth below, to cause Landlord's environmental consultant to inspect the Premises and perform such additional procedures as may be deemed reasonably necessary to confirm that the Premises are, as of the effective date of such surrender or early termination of the Lease, free from any residual impact from Tenant HazMat Operations. Tenant shall reimburse Landlord, as Additional Rent, for the actual out-of pocket expense incurred by Landlord for Landlord's environmental consultant to review and approve the Surrender Plan and to visit the Premises and verify satisfactory completion of the same, which cost shall not exceed $5,000. Landlord shall have the unrestricted right to deliver such Surrender Plan and any report by Landlord's environmental consultant with respect to the surrender of the Premises to third parties.

If Tenant shall fail to prepare or submit a Surrender Plan approved by Landlord, or if Tenant shall fail to complete the approved Surrender Plan, or if such Surrender Plan, whether or not approved by Landlord, shall fail to adequately address any residual effect of Tenant HazMat Operations in, on or about the Premises, Landlord shall have the right to take such actions as Landlord may deem reasonable or appropriate to assure that the Premises and the Project are surrendered free from any residual impact from Tenant HazMat Operations, the cost of which actions shall be reimbursed by Tenant as Additional Rent, without regard to the limitation set forth in the first paragraph of this Section 29 .

Tenant shall immediately return to Landlord all keys and/or access cards to parking, the Project, restrooms or all or any portion of the Premises furnished to or otherwise procured by Tenant. If any such access card or key is lost, Tenant shall pay to Landlord, at Landlord's election, either the cost of replacing such lost access card or key or the cost of reprogramming the access security system in which such access card was used or changing the lock or locks opened by such lost key. Any Tenant's Property, Alterations and property not so removed by Tenant as permitted or required herein shall be deemed abandoned and may be stored, removed, and disposed of by Landlord at Tenant's expense, and Tenant waives all claims against Landlord for any damages resulting from Landlord's retention and/or disposition of such property. All obligations of Tenant hereunder not fully performed as of the termination of the Term, including the obligations of Tenant under Section 31 hereof, shall survive the expiration or earlier termination of the Term, including, without limitation, indemnity obligations, payment obligations with respect to Rent and obligations concerning the condition and repair of the Premises.

30. **Waiver of Jury Trial** . TENANT AND LANDLORD WAIVE ANY RIGHT TO TRIAL BY JURY OR TO HAVE A JURY PARTICIPATE IN RESOLVING ANY DISPUTE, WHETHER SOUNDING IN CONTRACT, TORT, OR OTHERWISE, BETWEEN LANDLORD AND TENANT ARISING OUT OF THIS LEASE OR ANY OTHER INSTRUMENT, DOCUMENT, OR AGREEMENT EXECUTED OR DELIVERED IN CONNECTION HEREWITH OR THE TRANSACTIONS RELATED HERETO.

31. **Environmental Requirements** .

(a) **Prohibition/Compliance/Indemnity** . Tenant shall not cause or permit any Hazardous Materials (as hereinafter defined) to be brought upon, kept, used, stored, handled, treated, generated in or about, or released or disposed of from, the Premises or the Project in violation of applicable Environmental Requirements (as hereinafter defined) by Tenant or any Tenant Party. If Tenant breaches the obligation stated in the preceding sentence, or if the presence of Hazardous Materials used by Tenant or any Tenant Party in the Premises during the Term or any holding over results in contamination of the Premises, the Project or any adjacent property or if contamination of the Premises, the Project or any adjacent property by Hazardous Materials brought into, kept, used, stored, handled, treated, generated in or about, or released or disposed of from, the Premises by Tenant or any Tenant Party otherwise occurs during the Term or any holding over, Tenant hereby indemnifies and shall defend and hold Landlord, its officers, directors, employees, agents and contractors harmless from any

and all actions (including, without limitation, remedial or enforcement actions of any kind, administrative or judicial proceedings, and orders or judgments arising out of or resulting therefrom), costs, claims, damages (including, without limitation, punitive damages and damages based upon diminution in value of the Premises or the Project, or the loss of, or restriction on, use of the Premises or any portion of the Project), expenses (including, without limitation, attorneys', consultants' and experts' fees, court costs and amounts paid in settlement of any claims or actions), fines, forfeitures or other civil, administrative or criminal penalties, injunctive or other relief (whether or not based upon personal injury, property damage, or contamination of, or adverse effects upon, the environment, water tables or natural resources), liabilities or losses (collectively, " **Environmental Claims** ") which arise during or after the Term as a result of such contamination. Notwithstanding the foregoing, Tenant shall in no event be liable to Landlord or any Landlord Party hereunder as a result of, and this indemnification of Landlord and the Landlord Parties by Tenant shall not include Environmental Claims arising from known conditions existing in, on, under or about the Premises on or before the date hereof, as disclosed by those certain environmental reports more particularly described on Exhibit G hereto (each, a "Pre-existing Condition"), to the extent that the Tenant can reasonably prove that any such Environmental Claim does not arise or result, in whole or part, from any exacerbation of or contribution to, such a Pre-existing Condition, by (x) the actions of Tenant or any Tenant Party, or (y) any contamination emanating from in, on or under the Premises during the Term. This indemnification of Landlord by Tenant includes, without limitation, costs incurred in connection with any investigation of site conditions or any cleanup, treatment, remedial, removal, or restoration work required by any federal, state or local Governmental Authority because of Hazardous Materials present in the air, soil or ground water above, on, or under the Premises. Without limiting the foregoing, if the presence of any Hazardous Materials on the Premises, the Project or any adjacent property caused or permitted by Tenant or any Tenant Party results in any contamination of the Premises, the Project or any adjacent property, Tenant shall promptly take all actions at its sole expense and in accordance with applicable Environmental Requirements as are necessary to return the Premises, the Project or any adjacent property to the condition existing prior to the time of such contamination, provided that Landlord's approval of such action shall first be obtained, which approval shall not unreasonably be withheld so long as such actions would not potentially have any material adverse long-term or short-term effect on the Premises or the Project.

(b) **Business.** Landlord acknowledges that it is not the intent of this Section 31 to prohibit Tenant from using the Premises for the Permitted Use. Tenant may operate its business according to prudent industry practices so long as the use or presence of Hazardous Materials is strictly and properly monitored according to all then applicable Environmental Requirements. As a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with its business, Tenant agrees to deliver to Landlord prior to the Commencement Date a list identifying each type of Hazardous Materials to be brought upon, kept, used, stored, handled, treated, generated on, or released or disposed of from, the Premises and setting forth any and all governmental approvals or permits required in connection with the presence, use, storage, handling, treatment, generation, release or disposal of such Hazardous Materials on or from the Premises (" **Hazardous Materials List** "). Tenant shall deliver to Landlord an updated Hazardous Materials List at least once a year and shall also deliver an updated list before any new Hazardous Material is brought onto, kept, used, stored, handled, treated, generated on, or released or disposed of from, the Premises. Tenant shall deliver to Landlord true and correct copies of the following documents (the " **Haz Mat Documents** ") relating to the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials prior to the Commencement Date, or if unavailable at that time, concurrent with the receipt from or submission to a Governmental Authority: permits; approvals; reports and correspondence; storage and management plans, notice of violations of any Legal Requirements; plans relating to the installation of any storage tanks to be installed in or under the Project (provided, said installation of tanks shall only be permitted after Landlord has given Tenant its written consent to do so, which consent may be withheld in Landlord's sole and absolute discretion); all closure plans or any other documents required by any and all federal, state and local Governmental Authorities for any storage tanks installed in, on or under the Project for the closure of any such tanks; and a Surrender Plan (to the extent surrender in accordance with Section 29 cannot be accomplished in 3 months). Tenant is not required, however, to provide Landlord with any portion(s) of the Haz Mat Documents containing information of a proprietary nature which, in and of themselves, do not contain a reference to any Hazardous Materials or hazardous activities. It is not the intent of this Section to provide Landlord with information which could be detrimental to Tenant's business should such information become possessed by Tenant's competitors.

(c) **Tenant Representation and Warranty** . Tenant hereby represents and warrants to Landlord that (i) neither Tenant nor any of its legal predecessors has been required by any prior landlord, lender or Governmental Authority at any time to take remedial action in connection with

Hazardous Materials contaminating a property which contamination was permitted by Tenant of such predecessor or resulted from Tenant's or such predecessor's action or use of the property in question, and (ii) Tenant is not subject to any enforcement order issued by any Governmental Authority in connection with the use, storage, handling, treatment, generation, release or disposal of Hazardous Materials (including, without limitation, any order related to the failure to make a required reporting to any Governmental Authority). If Landlord determines that this representation and warranty was not true as of the date of this lease, Landlord shall have the right to terminate this Lease in Landlord's sole and absolute discretion.

(d) **Testing** . Landlord shall have the right to conduct annual tests of the Premises to determine whether any contamination of the Premises or the Project has occurred as a result of Tenant's use. Tenant shall be required to pay the cost of such annual test of the Premises; provided, however, that if Tenant conducts its own tests of the Premises using third party contractors and test procedures acceptable to Landlord which tests are certified to Landlord, Landlord shall accept such tests in lieu of the annual tests to be paid for by Tenant. In addition, at any time, and from time to time, but not more frequently than once per year unless (i) Landlord has reasonable grounds to believe or release of Hazardous Materials has occurred, or (ii) more frequent testing is required by the Holder of any Mortgage affecting the Project, prior to the expiration or earlier termination of the Term, Landlord shall have the right to conduct appropriate tests of the Premises and the Project to determine if contamination has occurred as a result of Tenant's use of the Premises. In connection with such testing, upon the request of Landlord, Tenant shall deliver to Landlord or its consultant such non-proprietary information concerning the use of Hazardous Materials in or about the Premises by Tenant or any Tenant Party. If contamination has occurred for which Tenant is liable under this Section 31 , Tenant shall pay all costs to conduct such tests. If no such contamination is found, Landlord shall pay the costs of such tests (which shall not constitute an Operating Expense). Landlord shall provide Tenant with a copy of all third party, non-confidential reports and tests of the Premises made by or on behalf of Landlord during the Term without representation or warranty and subject to a confidentiality agreement. Tenant shall, at its sole cost and expense, promptly and satisfactorily remediate any environmental conditions identified by such testing in accordance with all Environmental Requirements. Landlord's receipt of or satisfaction with any environmental assessment in no way waives any rights which Landlord may have against Tenant.

(e) **Underground Tanks** . If underground or other storage tanks storing Hazardous Materials located on the Premises or the Project are used by Tenant or are hereafter placed on the Premises or the Project by Tenant, Tenant shall install, use, monitor, operate, maintain, upgrade and manage such storage tanks, maintain appropriate records, obtain and maintain appropriate insurance, implement reporting procedures, properly close any underground storage tanks, and take or cause to be taken all other actions necessary or required under applicable state and federal Legal Requirements, as such now exists or may hereafter be adopted or amended in connection with the installation, use, maintenance, management, operation, upgrading and closure of such storage tanks.

(f) **Tenant's Obligations** . Tenant's obligations under this Section 31 shall survive the expiration or earlier termination of the Lease. During any period of time after the expiration or earlier termination of this Lease required by Tenant or Landlord to complete the removal from the Premises of any Hazardous Materials (including, without limitation, the release and termination of any licenses or permits restricting the use of the Premises and the completion of the approved Surrender Plan), Tenant shall continue to pay the full Rent in accordance with this Lease for any portion of the Premises not relet by Landlord in Landlord's sole discretion, which Rent shall be prorated daily.

(g) **Definitions.** As used herein, the term " **Environmental Requirements** " means all applicable present and future statutes, regulations, ordinances, rules, codes, judgments, orders or other similar enactments of any Governmental Authority regulating or relating to health, safety, or environmental conditions on, under, or about the Premises or the Project, or the environment, including without limitation, the following: the Comprehensive Environmental Response, Compensation and Liability Act; the Resource Conservation and Recovery Act; and all state and local counterparts thereto, and any regulations or policies promulgated or issued thereunder. As used herein, the term " **Hazardous Materials** " means and includes any substance, material, waste, pollutant, or contaminant listed or defined

as hazardous or toxic, or regulated by reason of its impact or potential impact on humans, animals and/or the environment under any Environmental Requirements, asbestos and petroleum, including crude oil or any fraction thereof, natural gas liquids, liquefied natural gas, or synthetic gas usable for fuel (or mixtures of natural gas and such synthetic gas). As defined in Environmental Requirements, Tenant is and shall be deemed to be the " **operator** " of Tenant's " **facility** " and the " **owner** " of all Hazardous Materials brought on the Premises by Tenant or any Tenant Party, and the wastes, by-products, or residues generated, resulting, or produced therefrom.

32. **Tenant's Remedies/Limitation of Liability** . Landlord shall not be in default hereunder unless Landlord fails to perform any of its obligations hereunder within 30 days after written notice from Tenant specifying such failure (unless such performance will, due to the nature of the obligation, require a period of time in excess of 30 days, then after such period of time as is reasonably necessary). Upon any default by Landlord, Tenant shall give notice by registered or certified mail to any Holder of a Mortgage covering the Premises and to any landlord of any lease of property in or on which the Premises are located and Tenant shall offer such Holder and/or landlord a reasonable opportunity to cure the default, including time to obtain possession of the Project by power of sale or a judicial action if such should prove necessary to effect a cure; provided Landlord shall have furnished to Tenant in writing the names and addresses of all such persons who are to receive such notices. All obligations of Landlord hereunder shall be construed as covenants, not conditions; and, except as may be otherwise expressly provided in this Lease, Tenant may not terminate this Lease for breach of Landlord's obligations hereunder.

All obligations of Landlord under this Lease will be binding upon Landlord only during the period of its ownership of the Premises and not thereafter. The term " **Landlord** " in this Lease shall mean only the owner for the time being of the Premises. Upon the transfer by such owner of its interest in the Premises, such owner shall thereupon be released and discharged from all obligations of Landlord thereafter accruing, but such obligations shall be binding during the Term upon each new owner for the duration of such owner's ownership.

33. **Inspection and Access** . Landlord and its agents, representatives, and contractors may enter the Premises at any reasonable time to inspect the Premises and to make such repairs as may be required or permitted pursuant to this Lease and for any other business purpose. Landlord and Landlord's representatives may enter the Premises during business hours on not less than 48 hours advance written notice (except in the case of emergencies in which case no such notice shall be required and such entry may be at any time) for the purpose of effecting any such repairs, inspecting the Premises, showing the Premises to prospective purchasers and, during the last year of the Term, to prospective tenants or for any other business purpose. Landlord may erect a suitable sign on the Premises stating the Premises are available to let or that the Project is available for sale. Landlord may grant easements, make public dedications, designate Common Areas and create restrictions on or about the Premises, provided that no such easement, dedication, designation or restriction materially, adversely affects Tenant's use or occupancy of the Premises for the Permitted Use. At Landlord's request, Tenant shall execute such instruments as may be necessary for such easements, dedications or restrictions. Tenant shall at all times, except in the case of emergencies, have the right to escort Landlord or its agents, representatives, contractors or guests while the same are in the Premises, provided such escort does not materially and adversely affect Landlord's access rights hereunder.

34. **Security** . Tenant acknowledges and agrees that security devices and services, if any, while intended to deter crime may not in given instances prevent theft or other criminal acts and that Landlord is not providing any security services with respect to the Premises. Tenant agrees that Landlord shall not be liable to Tenant for, and Tenant waives any claim against Landlord with respect to, any loss by theft or any other damage suffered or incurred by Tenant in connection with any unauthorized entry into the Premises or any other breach of security with respect to the Premises. Tenant shall be solely responsible for the personal safety of Tenant's officers, employees, agents, contractors, guests and invitees while any such person is in, on or about the Premises and/or the Project. Tenant shall at Tenant's cost obtain insurance coverage to the extent Tenant desires protection against such criminal acts.

35. **Force Majeure** . Other than for the obligations of either party under this Lease that can be performed by the payment of money, neither Landlord nor Tenant shall be responsible or liable for delays in the performance of its obligations hereunder when caused by, related to, or arising out of acts of God, strikes, lockouts, or other labor disputes, embargoes, quarantines, weather, national, regional, or local disasters, calamities, or catastrophes, inability to obtain labor or materials (or reasonable substitutes therefor) at reasonable costs or failure of, or inability to obtain, utilities necessary for performance, governmental restrictions, orders, limitations, regulations, or controls, national emergencies, delay in issuance or revocation of permits, enemy or hostile governmental action, terrorism, insurrection, riots, civil disturbance or commotion, fire or other casualty, and other causes or events beyond the reasonable control of Landlord or Tenant, as applicable (" **Force Majeure** ").

36. **Brokers, Entire Agreement, Amendment** . Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, " **Broker)** in connection with this transaction and that no Broker brought about this transaction other than Meredith & Grew, Inc. and CB Richard Ellis/Whittier Partners (whose commission shall in each case be payable by Landlord under a separate agreement). Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than the broker, if any named in this Section 36 , claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.

37. **Limitation on Landlord's Liability.** NOTWITHSTANDING ANYTHING SET FORTH HEREIN OR IN ANY OTHER AGREEMENT BETWEEN LANDLORD AND TENANT TO THE CONTRARY: (A) LANDLORD SHALL NOT BE LIABLE TO TENANT OR ANY OTHER PERSON FOR (AND TENANT AND EACH SUCH OTHER PERSON ASSUME ALL RISK OF) LOSS, DAMAGE OR INJURY, WHETHER ACTUAL OR CONSEQUENTIAL TO: TENANT'S PERSONAL PROPERTY OF EVERY KIND AND DESCRIPTION, INCLUDING, WITHOUT LIMITATION TRADE FIXTURES, EQUIPMENT, INVENTORY, SCIENTIFIC RESEARCH, SCIENTIFIC EXPERIMENTS, LABORATORY ANIMALS, PRODUCT, SPECIMENS, SAMPLES, AND/OR SCIENTIFIC, BUSINESS, ACCOUNTING AND OTHER RECORDS OF EVERY KIND AND DESCRIPTION KEPT AT THE PREMISES AND ANY AND ALL INCOME DERIVED OR DERIVABLE THEREFROM; (B) THERE SHALL BE NO PERSONAL RECOURSE TO LANDLORD FOR ANY ACT OR OCCURRENCE IN, ON OR ABOUT THE PREMISES OR ARISING IN ANY WAY UNDER THIS LEASE OR ANY OTHER AGREEMENT BETWEEN LANDLORD AND TENANT WITH RESPECT TO THE SUBJECT MATTER HEREOF AND ANY LIABILITY OF LANDLORD HEREUNDER SHALL BE STRICTLY LIMITED SOLELY TO LANDLORD'S INTEREST IN THE PROJECT OR ANY PROCEEDS FROM SALE OR CONDEMNATION THEREOF AND ANY INSURANCE PROCEEDS PAYABLE IN RESPECT OF LANDLORD'S INTEREST IN THE PROJECT OR IN CONNECTION WITH ANY SUCH LOSS; AND (C) IN NO EVENT SHALL ANY PERSONAL LIABILITY BE ASSERTED AGAINST ANY OF LANDLORD'S OFFICERS, DIRECTORS, EMPLOYEES, AGENTS OR CONTRACTORS. UNDER NO CIRCUMSTANCES SHALL LANDLORD OR ANY OF LANDLORD'S OFFICERS, DIRECTORS, EMPLOYEES, AGENTS OR CONTRACTORS BE LIABLE FOR INJURY TO TENANT'S BUSINESS OR FOR ANY LOSS OF INCOME OR PROFIT THEREFROM.

38. **Severability** . If any clause or provision of this Lease is illegal, invalid or unenforceable under present or future laws, then and in that event, it is the intention of the parties hereto that the remainder of this Lease shall not be affected thereby. It is also the intention of the parties to this Lease that in lieu of each clause or provision of this Lease that is illegal, invalid or unenforceable, there be added, as a part of this Lease, a clause or provision as similar in effect to such illegal, invalid or unenforceable clause or provision as shall be legal, valid and enforceable.

39. **Signs; Exterior Appearance** . Tenant shall not, without the prior written consent of Landlord, which may be granted or withheld in Landlord's sole discretion: (i) attach any awnings, exterior lights, decorations, balloons, flags, pennants, banners, painting or other projection to any outside wall of the Project, (ii) use any curtains, blinds, shades or screens other than Landlord's standard window coverings, (iii) coat or otherwise sunscreen the interior or exterior of any windows, (iv) place any bottles, parcels, or other articles on the window sills, (v) place any equipment, furniture or other items of personal

property on any exterior balcony, or (vi) paint, affix or exhibit on any part of the Premises or the Project any signs, notices, window or door lettering, placards, decorations, or advertising media of any type which can be viewed from the exterior of the Premises other than signage in Tenant reception area. Interior signs on doors shall be inscribed, painted or affixed for Tenant by Landlord at the sole cost and expense of Tenant, and shall be of a size, color and type acceptable to Landlord. Interior signs on the directory tablet within the Building shall be affixed for Tenant by Landlord at Landlord's expense, and shall be of a size, color and type acceptable to Landlord. Nothing may be placed on the exterior of corridor walls or corridor doors other than Landlord's standard lettering. The directory tablet shall be provided exclusively for the display of the name and location of tenants.

40. **Right to Extend Term.** Tenant shall have the right to extend the Term of the Lease upon the following terms and conditions:

(a) **Extension Rights** . Tenant shall have one right (the " **Extension Right** ") to extend the term of this Lease for 5 years (the " **Extension Term** ") on the same terms and conditions as this Lease (other than Base Rent) by giving Landlord written notice of its election to exercise each Extension Right at least 12 months prior, and no earlier than 9 months prior, to the expiration of the Base Term of the Lease or the expiration of any prior Extension Term.

Upon the commencement of any Extension Term, Base Rent shall be payable at the Market Rate (as defined below). Base Rent shall thereafter be adjusted on each annual anniversary of the commencement of such Extension Term by multiplying the Base Rent payable immediately before such adjustment by the Rent Adjustment Percentage and adding the resulting amount to the Base Rent payable immediately before such adjustment. The term "Market Rate" for purposes of this Lease shall mean the annual amount per rentable square foot that a willing, comparable, new non-renewal tenant of credit quality similar to Tenant would pay, and a willing, comparable landlord of the Building or a comparable office building in the immediate vicinity of the Building would accept, at arms length, giving appropriate consideration to annual rental rates per rentable square foot, and abatement provisions reflecting free rent, length of lease term, size and location of premises being leased, improvement allowances (if any), brokerage commissions (if any) and any other concessions which would be granted by Landlord or a comparable landlord and other generally applicable terms and conditions. As used herein, "Market Rate" shall be determined by Landlord in accordance with the provisions hereof and agreed to by Tenant, but shall in no event be less than the Base Rent payable as of the date immediately preceding the commencement of such Extension Term increased by the Rent Adjustment Percentage multiplied by such Base Rent. In addition, Landlord may impose a market rent for the parking rights provided hereunder.

If, on or before the date which is 120 days prior to the expiration of the Base Term of this Lease, or the expiration of any prior Extension Term, Tenant has not agreed with Landlord's determination of the Market Rate and the rent escalations during such subsequent Extension Term after negotiating in good faith, Tenant may by written notice to Landlord not later than 120 days prior to the expiration of the Base Term of this Lease, or the expiration of any then effective Extension Term, elect arbitration as described in Section 40(b) below. If Tenant does not elect such arbitration, Tenant shall be deemed to have waived any right to extend, or further extend, the Term of the Lease and all of the remaining Extension Rights shall terminate.

(b) **Arbitration** .

(i) Within 10 days of Tenant's notice to Landlord of its election to arbitrate Market Rate and escalations, each party shall deliver to the other a proposal containing the Market Rate and escalations that the submitting party believes to be correct (" **Extension Proposal** "). If either party fails to timely submit an Extension Proposal, the other party's submitted proposal shall determine the Base Rent and escalations for the Extension Term. If both parties submit Extension Proposals, then Landlord and Tenant shall meet within 7 days after delivery of the last Extension Proposal and make a good faith attempt to mutually appoint a single Arbitrator (and defined below) to determine the Market

Rate and escalations. If Landlord and Tenant are unable to agree upon a single Arbitrator, then each shall, by written notice delivered to the other within 10 days after the meeting, select an Arbitrator. If either party fails to timely give notice of its selection for an Arbitrator, the other party's submitted proposal shall determine the Base Rent for the Extension Term. The 2 Arbitrators so appointed shall, within 5 business days after their appointment, appoint a third Arbitrator. If the 2 Arbitrators so selected cannot agree on the selection of the third Arbitrator within the time above specified, then either party, on behalf of both parties, may request such appointment of such third Arbitrator by application to any state court of general jurisdiction in the jurisdiction in which the Premises are located, upon 10 days prior written notice to the other party of such intent.

(ii) The decision of the Arbitrator(s) shall be made within 30 days after the appointment of a single Arbitrator or the third Arbitrator, as applicable. The decision of the single Arbitrator shall be final and binding upon the parties. The average of the two closest Arbitrators in a three Arbitrator panel shall be final and binding upon the parties. Each party shall pay the fees and expenses of the Arbitrator appointed by or on behalf of such party and the fees and expenses of the third Arbitrator shall be borne equally by both parties. If the Market Rate and escalations are not determined by the first day of the Extension Term, then Tenant shall pay Landlord Base Rent in an amount equal to the Base Rent in effect immediately prior to the Extension Term and increased by the Rent Adjustment Percentage until such determination is made. After the determination of the Market Rate and escalations, the parties shall make any necessary adjustments to such payments made by Tenant. Landlord and Tenant shall then execute an amendment recognizing the Market Rate and escalations for the Extension Term.

(iii) An " **Arbitrator** " shall be any person appointed by or on behalf of either party or appointed pursuant to the provisions hereof and: (i) shall be (A) a member of the American Institute of Real Estate Appraisers with not less than 10 years of experience in the appraisal of improved office and high tech industrial real estate in the Watertown, Massachusetts metropolitan area, or (B) a licensed commercial real estate broker with not less than 15 years experience representing landlords and/or tenants in the leasing of high tech or life sciences space in the Watertown, Massachusetts metropolitan area, (ii) devoting substantially all of their time to professional appraisal or brokerage work, as applicable, at the time of appointment and (iii) be in all respects impartial and disinterested.

(c) **Rights Personal.** Extension Rights are personal to Tenant and any Permitted Assignees and are not otherwise assignable without Landlord's consent, which may be granted or withheld in Landlord's sole discretion separate and apart from any consent by Landlord to an assignment of Tenant's interest in the Lease .

(d) **Exceptions** . Notwithstanding anything set forth above to the contrary, Extension Rights shall not be in effect and Tenant may not exercise any of the Extension Rights during any period of time that Tenant is in Default under any provision of this Lease.

(e) **No Extensions** . The period of time within which any Extension Rights may be exercised shall not be extended or enlarged by reason of Tenant's inability to exercise the Extension Rights.

(f) **Termination** . The Extension Rights shall terminate and be of no further force or effect even after Tenant's due and timely exercise of an Extension Right, if, after such exercise, but prior to the commencement date of an Extension Term, (i) Tenant fails to timely cure any default by Tenant under this Lease; or (ii) Tenant has Defaulted 3 or more times during the period from the date of the exercise of an Extension Right to the date of the commencement of the Extension Term, whether or not such Defaults are cured.

41. **Representations** . Landlord represents and warrants to Tenant that, as of the date of this Lease, Landlord has full power and authority to enter into this Lease and has obtained all consents and taken all actions necessary in connection therewith. Tenant represents and warrants to Landlord that, as of the date of this Lease, Tenant has full power and authority to enter into this Lease and has obtained all consents and take all actions necessary in connection therewith.

42. **Miscellaneous** .

(a) **Notices** . All notices or other communications between the parties shall be in writing and shall be deemed duly given upon delivery or refusal to accept delivery by the addressee thereof if delivered in person, or upon actual receipt if delivered by reputable overnight guaranty courier, addressed and sent to the parties at their addresses set forth above. Landlord and Tenant may from time to time by written notice to the other designate another address for receipt of future notices.

(b) **Joint and Several Liability** . If and when included within the term " **Tenant** ," as used in this instrument, there is more than one person or entity, each shall be jointly and severally liable for the obligations of Tenant.

(c) **Financial Information** . Tenant shall furnish Landlord with true and complete copies of (i) Tenant's most recent audited annual financial statements within 45 days of the end of each of Tenant's fiscal years during the Term, (ii) Tenant's most recent unaudited quarterly financial statements within 45 days of the end of each of Tenant's first three fiscal quarters of each of Tenant's fiscal years during the Term, (iii) at Landlord's request from time to time, updated business plans, including cash flow projections and/or pro forma balance sheets and income statements, all of which shall be treated by Landlord as confidential information belonging to Tenant, (iv) corporate brochures and/or profiles prepared by Tenant for prospective investors, and (v) any other financial information or summaries that Tenant typically provides to its lenders or shareholders.

(d) **Recordation** . This Lease shall not be filed by or on behalf of Tenant in any public record. At the request of either party hereto, the other party shall execute and deliver a memorandum of lease in statutory form which may be recorded at the expense of the requesting party. Tenant shall execute and deliver a termination of such memorandum of lease, in recordable form, to Landlord upon the expiration or earlier termination of this Lease.

(e) **Interpretation** . The normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Lease or any exhibits or amendments hereto. Words of any gender used in this Lease shall be held and construed to include any other gender, and words in the singular number shall be held to include the plural, unless the context otherwise requires. The captions inserted in this Lease are for convenience only and in no way define, limit or otherwise describe the scope or intent of this Lease, or any provision hereof, or in any way affect the interpretation of this Lease.

(f) **Not Binding Until Executed** . The submission by Landlord to Tenant of this Lease shall have no binding force or effect, shall not constitute an option for the leasing of the Premises, nor confer any right or impose any obligations upon either party until execution of this Lease by both parties.

(g) **Limitations on Interest** . It is expressly the intent of Landlord and Tenant at all times to comply with applicable law governing the maximum rate or amount of any interest payable on or in connection with this Lease. If applicable law is ever judicially interpreted so as to render usurious any interest called for under this Lease, or contracted for, charged, taken, reserved, or received with respect to this Lease, then it is Landlord's and Tenant's express intent that all excess amounts theretofore collected by Landlord be credited on the applicable obligation (or, if the obligation has been or would thereby be paid in full, refunded to Tenant), and the provisions of this Lease immediately shall be deemed reformed and the amounts thereafter collectible hereunder reduced, without the necessity of the execution of any new document, so as to comply with the applicable law, but so as to permit the recovery of the fullest amount otherwise called for hereunder.

(h) **Choice of Law** . Construction and interpretation of this Lease shall be governed by the internal laws of the state in which the Premises are located, excluding any principles of conflicts of laws.

(i) **Time** . Time is of the essence as to the performance of Tenant's obligations under this Lease.

(j) **Incorporation by Reference** . All exhibits and addenda attached hereto are hereby incorporated into this Lease and made a part hereof. If there is any conflict between such exhibits or addenda and the terms of this Lease, such exhibits or addenda shall control.

(k) **Hazardous Activities** . Notwithstanding any other provision of this Lease, Landlord, for itself and its employees, agents and contractors, reserves the right to refuse to perform any repairs or services in any portion of the Premises which, pursuant to Tenant's routine safety guidelines, practices or custom or prudent industry practices, require any form of protective clothing or equipment other than safety glasses. In any such case, Tenant shall contract with parties who are acceptable to Landlord, in Landlord's reasonable discretion, for all such repairs and services, and Landlord shall, to the extent required, equitably adjust Tenant's Share of Operating Expenses in respect of such repairs or services to reflect that Landlord is not providing such repairs or services to Tenant.

[Signatures appear on following page]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Lease as of the day and year first above written.

TENANT:

Tetraphase Pharmaceuticals, Inc., a Delaware corporation

By: /s/ David Lubner
Its: Sr. VP, COO

LANDLORD:

ARE-480 Arsenal Street, LLC, a Delaware limited liability company

By: Alexandria Real Estate Equities, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS Corp., a Maryland
corporation, general partner

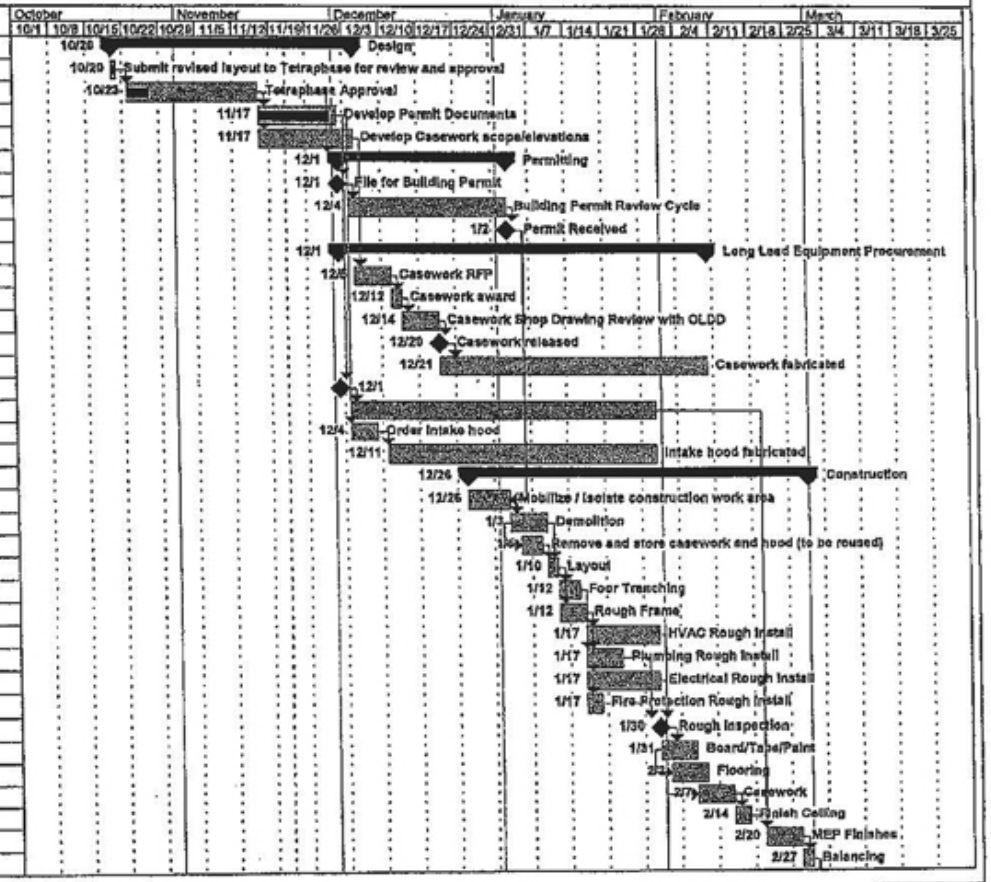
By: (illegible)
Its: VP

EXHIBIT A TO LEASE

DESCRIPTION OF PREMISES

TetraPhase Pharmaceuticals
480 Arsenal Street
Watertown, MA
Research and Administrative Renovations

ID		Task Name	Duration	Start	Finish	Predecessors
1		Design	30 days	Fri 10/20/06	Mon 12/4/06	
2	✓	Submit revised layout to Tetraphase for review and approval	1 day	Fri 10/20/06	Fri 10/20/06	
3		Tetraphase Approval	19 days	Mon 10/23/06	Thu 11/16/06	2
4		Develop Permit Documents	9 days	Fri 11/17/06	Fri 12/1/06	3
5		Develop Casework scope/elevations	10 days	Fri 11/17/06	Mon 12/4/06	3
6		Permitting	29 days	Fri 12/1/06	Tue 1/2/07	3
7		File for Building Permit	0 days	Fri 12/1/06	Fri 12/1/06	4
8		Building Permit Review Cycle	20 days	Mon 12/4/06	Tue 1/2/07	7
9		Permit Received	0 days	Tue 1/2/07	Tue 1/2/07	8
10		Long Lead Equipment Procurement	48 days	Fri 12/1/06	Fri 2/9/07	
11		Casework RFP	5 days	Tue 12/5/06	Mon 12/11/06	5
12		Casework award	2 days	Tue 12/12/06	Wed 12/13/06	11
13		Casework Shop Drawing Review with OLDD	5 days	Thu 12/14/06	Wed 12/20/06	12
14		Casework released	0 days	Wed 12/20/06	Wed 12/20/06	13
15		Casework fabricated	35 days	Thu 12/21/06	Fri 2/9/07	14
16		Release hood management controls	0 days	Fri 12/1/06	Fri 12/1/06	4
17		Fabricate and deliver hood management system	40 days	Mon 12/4/06	Tue 1/30/07	16
18		Order intake hood	5 days	Mon 12/4/06	Fri 12/8/06	4
19		Intake hood fabricated	35 days	Mon 12/11/06	Tue 1/30/07	18
20		Construction	45 days	Tue 12/26/06	Wed 2/28/07	
21		Mobilize / Isolate construction work area	5 days	Tue 12/26/06	Tue 1/2/07	9FF
22		Demolition	5 days	Wed 1/3/07	Tue 1/9/07	21
23		Remove and store casework and hood (to be reused)	2 days	Fri 1/5/07	Mon 1/8/07	22SS+2 days
24		Layout	2 days	Wed 1/10/07	Thu 1/11/07	22,23
25		Foor Trenching	2 days	Fri 1/12/07	Mon 1/15/07	24
26		Rough Frame	3 days	Fri 1/12/07	Tue 1/16/07	24
27		HVAC Rough Install	10 days	Wed 1/17/07	Tue 1/30/07	26
28		Plumbing Rough Install	5 days	Wed 1/17/07	Tue 1/23/07	26,25
29		Electrical Rough Install	10 days	Wed 1/17/07	Tue 1/30/07	25
30		Fire Protection Rough Install	3 days	Wed 1/17/07	Fri 1/19/07	28
31		Rough Inspection	0 days	Tue 1/30/07	Tue 1/30/07	27,28,29,30
32		Board/Tape/Paint	5 days	Wed 1/31/07	Tue 2/6/07	31
33		Flooring	5 days	Fri 2/2/07	Thu 2/8/07	32SS+2 days
34		Casework	5 days	Wed 2/7/07	Tue 2/13/07	33SS+3 days
35		Finish Ceiling	3 days	Wed 2/14/07	Fri 2/16/07	34
36		MEP Finishes	5 days	Tue 2/20/07	Mon 2/26/07	35,34,17
37		Balancing	2 days	Tue 2/27/07	Wed 2/28/07	36



Project: tetraphase schedule 3.mpp
Date: Wed 11/22/06

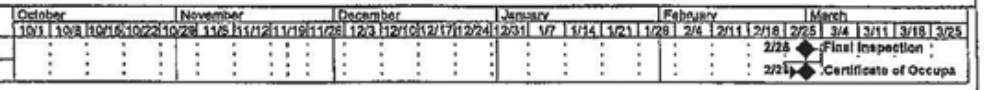
Task · Split · Progress · Milestone · Summary · Project Summary · External Tasks · External Milestone · Deadline

Page 1

RICHMOND

TetraPhase Pharmaceuticals
480 Arsenal Street
Watertown, MA
Research and Administrative Renovations

ID	Task Name	Duration	Start	Finish	Predecessors
38	Final Inspection	0 days	Wed 2/28/07	Wed 2/28/07	37
39	Certificate of Occupancy	0 days	Wed 2/28/07	Wed 2/28/07	38



Project: tetraphase schedule 3.mpp
Date: Wed 11/22/06

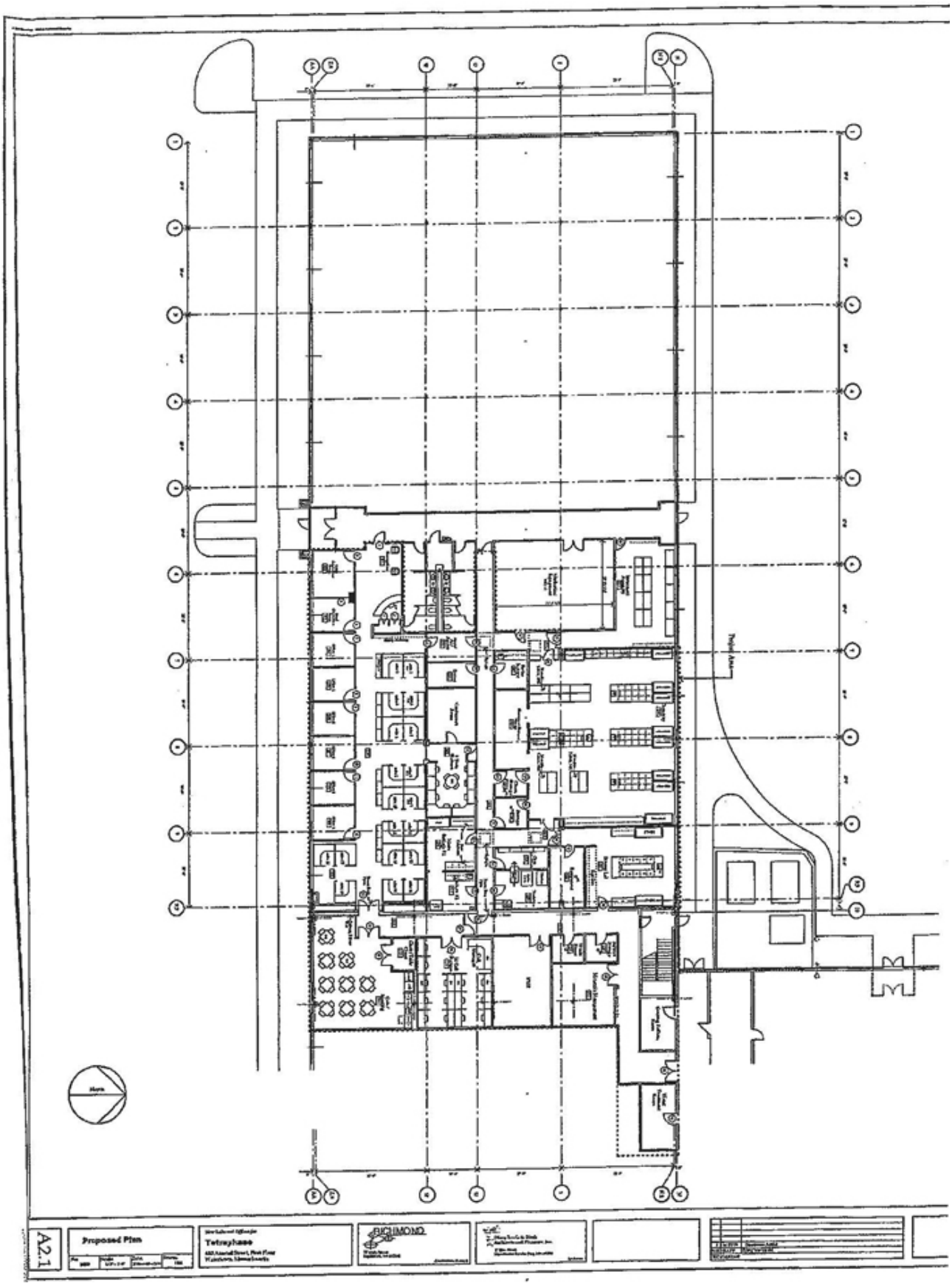
Task | Progress | Summary | External Tasks | Deadline
Split | Milestone | Project Summary | External Milestone

RICHMOND

EXHIBIT B TO LEASE

DESCRIPTION OF PROJECT

(see attached)



TetraPhase
480 Arsenal Street
MEP Scope of Work
November 22, 2006

Based on Architectural Drawing A-2.1 dated 16 November 2006

1. FIRE PROTECTION

    1.1. Modify *existing* fire protection system to accommodate new architectural layout.

2. PLUMBING

    2.1. Connect and trim four {4) new lab sinks.

    2.2. Vacuum service to one {1) BSC. No C02 (assumed local)

    2.3. Nitrogen, compressed air, vacuum and NPCW to two walk-in hoods.

    2.4. Chilled water piping to one (1) Huber Chiller (approximately 25 feet)

    2.5. Connect to existing nitrogen and compressed air piping and extend nitrogen and compressed air to benchtop hoods and NMR drops (wall turrets).

    2.6. New compressed air, and NPCW to hoods.

    2.7. Four (4) RODIpoints of use piped from existing RODIsystem.

    2.8. Four (4) new deck mounted emergency eyewash units.

    2.9. Helium and C02 to be local, by tenant.

3. HVAC

    3.1. Hoods to be exhausted based on ASHRAE/ANSIstandards.

    3.2. One (1) new lab exhaust fan (15 hp)

    3.3. One (1) new air handling unit (5 hp)

    3.4. Hot water reheat piping

    3.5. Ductwork demolition, modifications, and installation.

    3.6. Control modifications to accommodate modified layout.

    3.7. Tek-air hood management system

4. ELECTRICAL

4.1. Remove wiremold, circuits to wiremold, cord drops, and outlets in affected area.

4.2. Remove lighting.

4.3. Provide new wiremold on benches with circuits, and new hood wiring.

4.4. Reinstall existing fixtures and provide new fixtures for coordinated layout.

4.5. New localcontrolswitching.

4.6. Rework exit/emergency lighting.

4.7. Relocate fire alarm devices.

4.8. Remove and reinstall tel/data for new floor plan.

4.9. Furnish and install transformation and panels as required.

4.10. Power to new HVAC equipment.

TETRAPHASE Date 11/29/2006

480 ARSENAL STREET
WATERTOWN, MASSACHUSETTS
PRELIMINARY BUDGET ESTIMATE

DIVISION/DESCRIPTION	QTY	UNIT$	LINE SUM	DIV.SUM
DEMOLITION				
MAKESAFE ELECTRIC	1 LS	800	800	
REMOVE WALLS	730 SF	2.50	1,825	
REMOVE FLOORING	3098 SF	0.85	2,633	
REMOVE CEILINGS	3098 SF	0.80	2,478	
DEMOUTIONDUMPSTERS (SUB)	2 EA	675	1,350	
DISMANTLE CASEWORK AND BENCHES	6 MD	540	3,240	
REMOVE EXISTING HOOD	1 EA	400	400	
HOOD DECONTAMINATION BY OTHERS			NIC	
REMOVE GLAZE WALL AT LAB ENTRANCE	1 lS	600	600	
REMOVE EXISTING SUPPLY DUCTWORK & REGISTEF	1 lS	900	900	
GENERAL lABOR (2 DAYS PER WEEK)	9 WKS	600	5,400	
			$ 19,627	
CARPENTRY I MILLWORK				
INSTALL DOUBLE DOORS	1 PR	300	300	
INSTALL SINGLE DOOR	3 EA	225	675	
EXHAUST FAN PLATFORM	1 EA	600	600	
CARPENTRY & MATERIALS	10 DVS	600	6,000	
				$ 7,575
ROOF WORK AND CAULKING				
FLASHING FOR NEW EXHAUST FAN	EA	950	950	
FlASHING INTAKE AIR HOOD	EA	950	950	
INTERIOR CAULKING	LS	600	600	
				$ 2,500
DOORS				
DOUBLE SOLID CORE WOOD DRS & HDWRE	1 PR	1,775	1,775	
SINGLE SOLID CORE WOOD DR & HDWRE	1 EA	930	930	
SINGLE RATED H.M.OR & HDWRE	2 EA	985	1,970	
HM.DOUBLE DOOR FRAME	1 EA	275	275	
HM SINGLE DOOR FRAME	3 EA	200	600	
BORROWED LITES	2 EA	125	250	
DOOR CLOSERS	3 EA	135	405	
EXISTING DOUBLE LAB ENTRANCE DOOR			TO REMAIN	
ACCESS COORS	EA	225	225	
			6,430	
GLASS				
GLAZING PANELS AT DOORS	2 EA	175	350	
				$ 350

TETRAPHASE
480 ARSENAL STREET

Date 11/29/2006

WATERTOWN, MASSACHUSETTS
PRELIMINARY BUDGET ESTIMATE

DIVISION / DESCRIPTION	QTY	UNIT$	LINE SUM	DIV.SUM
DRYWALL				
WALL BLOCKING	1 LS	2,000	2,000	
INSTALL DOOR FRAMES	4 EA	80	320	
INSTALLATION OF ACCESS PANELS	1 EA	75	75	
INFILL WALL OPENINGS	2 EA	450	900	
FULL HEIGHT PARTITIONS	910 SF	9.50	8,645	
CUT IN DOOR OPENINGS	2 EA	450	900	
PATCH EXISTING WALLS	1 lS	1,800	1,800	
GYPSUM BOARD CEILINGS	160 SF	10.00	1,600	
INFILL DOOR OPENINGS	4 EA	500	2,000	
				$18,240
CEILINGS				
2'×4' VINYL FACED GYP BD W/ STAND SUSPENSION	2,756 SF	2.95	8,130	
2'×4' FISSURED CEILING W/ STANDARD GRID	828 SF	2.55	2,111	
				$10,242
FLOORING				
VCT FLOORING	4,122 SF	2.60	10,717	
EPOXY FLOORING	120 SF	12.50	1,500	
EPOXY BERMS AT DOORS	2 EA	150	300	
BASE	799 LF	2.65	2,117	
				$14,636
PAINTING				
PAINT WALLS	6,390 SF	0.90	5,751	
EPOXY WALL PAINT	650 SF	1.25	813	
PAINT DOORS	4 EA	100	400	
TOUCH UP	1 LS	900	900	
ELECTROSTATICALLY PAINT REUSED CASEWORK	1 LS	1,200	1,200	
PAINT EXISTING WALLS			NJC	$ 9,064
SPECIALTIES				
SIGNAGE			BY TETRAPHASE	
FIRE EXTINGUISHERS			EXISTING TO REMAIN	
				$ 0
LAB EQUIPMENT				
LAB EQUIPMENT			BY TETRAPHASE	$ 0

TETRAPHASE Date 11/29/2006

480 ARSENAL STREET
WATERTOWN, MASSACHUSETTS
PRELIMINARY BUDGET ESTIMATE

DIVISION / DESCRIPTION	QTY	UNIT$	LINESUM	DIV.SUM
LAB CASEWORK & CHEMICAL FUME HOODS				
RELOCATE 8’ CHEMICAL FUME HOOD	EA	950	950	
6’·0” CHEMICAL FUME HOODS	4 EA	7,200	28,800	
INSTALL 6’-0” CHEMICAL FUME HOODS	4 EA		INCLUDED	
6’·0” CHEMICAL FUME HOODS	5 EA	9,600	48,000	
INSTALL 8’-0” CHEMICAL FUME HOODS	5 EA		INCLUDED	
RELOCATE PENINSULA BENCHES	1 LS	2,800	2,800	
RECONFIGURE EXISTING BASE CABINETS	2 EA	1,250	2,500	
6’-0” EPOXY BENCHTOPS	26 LF	150	3,900	
3’·0” EPOXY BENCHTOPS	44 LF	95	4,180	
REAGENT SHELVING 2 HIGH	20 LF	150	3,000	
50% BASE CABINETS	48 LF	200	9,600	
25% BASEDRAWER UNITS	24 LF	260	6,240	
25% KNEE SPACES	24 LF	50	1,200	
NEW EPOXY SINKS	3 EA	450	1,350	
UTILITY RISERS	2EA	450	900	
REUSE 2 EXISTING PENINSULA ISLANDS & BENCHTOPS			INCLUDED	
INSTALL NEW CASEWORK	LS	9,500	9,500	
BUILD IWO (2)EA VENTED ALCOVES	ALW	0	0	
8’; WALK IN HOODS	2 EA	15,000	30,000	
ENCLOSE VENTED ALCOVES WI GLASS DOORS	0 SF	90	0	
LABORATORY TABLES			BY TETRAPHASE	
				$152,920
SPRINKLER				
SUPPLEMENTW/ NEW SPRINKLER HEADS AS REQ’D			INCL TRADES PERMITS	
INCL RELOCATIONS			INCL SPRINKLER	
BUDGET	1 LS	9,500	9,500	
				$ 9,600
PLUMBlNG				
CUT & CAP SERVICES AS REQ’D			INCL	
LAB SINK TRIM	4 EA		INCL	
RODIFAUCETS	4 EA		INCL	
6’ 0” FUME HOOD CONNECTS	4 EA		INCL	
8’·0” FUME HOOD CONNECTS	5 EA		INCL	
NITROGEN 180 DEG TURRETS	3 EA		INCL	
COMPRESSED AIR 180 DEG TURRETS	3 EA		INCL	
HOOKUP RELOCATED 8’-0” CFH	1 EA		INCL	
EMERGENCY EYEWASH DECK MOUNTED	4EA		INCL	
PLUMBING PERMIT			INCL	
ALCOVE GASSES	2 EA		INCL	
PROC CHILLED WATER PIPING TO 1 CHILLER	1 EA		INCL	
PLUMBING BUDGET	1 IS	105,132	105,132	
				$106,132

TETRAPHASE
480 ARSENAL STREET

Date 11/29/2006

WATERTOWN, MASSACHUSETTS
PRELIMINARY BUDGET ESTIMATE

DIVISION / DESCRIPTION	QTY	UNIT$	LINE SUM	DIV.SUM
HVAC				
CUT AND DROP EXISTING UNUSABLE DUCTWORK			INCLUDED	
REUSE EXISTING MAINAIR HANDLER AND REBALANCE			INCLUDED	
MODIFY EXHAUST SYSTEM TO HANDLE ADDED HOODS & ROTO VAPS			INCLUDED	
NEW 6,000 CFM (5 HP) TRANSFER FAN W/COOLING (			INCLUDED	
REMOVE EXISTING SECONDARY AIR HANDLER			INCLUDED	
NEW 15 HP LAB EXHAUST FAN			INCLUDED	
ROTC VAP EXHAUST DROPS {150 CFM EA)	10 EA		INCLUDED	
REGISTER.DIFFUSERS, GRILLES			INCLUDED	
SUPPLY & EXHAUST BOXES FOR CHEM LAB & EQUIP RM			INCLUDED	
MODIFY SUPPLY DUCTWORK			INCLUDED	
BALANCING			INCLUDED	
STARTUP			INCLUDED	
HOOD MANAGEMENT	1 LS	109,000	109,000	
Delete Humidification in NMR Room	1 LS	-6,500	-6,500	
HVACBUDGET	1 LS	158,000	158,000	
				$260,600
ELECTRICAL				
SWITCHGEAR J DISTRIBUTION	1 LS	5,780	10,680	
.HVAC POWER WIRING	1 LS	2,875	3,975	
LIGHTING	1 LS	4,950	6,450	
EXIT / EMERGENCY LIGHTING	1 LS	475	755	
“FIRE ALARM	1 LS	1,130	1,980	
■ OUTLETS, WIREMOLD AND HOODS	1 LS	17,940	29,580	
TEL/DATA	1 LS	8,760	11,240	
JOB DIRECT EXPENSES & OTHER MATERIALS	1 LS	3,950	5,350	
UGHT & PWR TO SOLVENT, WASTE, NMR & MAT’LS			INCLUDED	
ELECTRICAL PERMIT			INCLUDED	
TEMPORARY SERVICES			INCLUDED	
ENGINEERING AND DOCS			INCLUDED	
				$ 69,910
SUPERVISION				
PROJECT SUPERINTENDENT	9 WKS	2,975	26,775	
PROJECT MANAGER (2 DAYS / WK)	8 WKS	1,190	9,520	
ESTIMATOR / PLANNER	1.5 WK	3,400	5,100	
ADMINISTRATIVE ASSISTANT	8 DAY	275	2,200	
ACCOUNTANT	8 DAY	350	2,800	
				$ 46,395

TETRAPHASE
480 ARSENAL STREET

Date 11/29/2006

WATERTOWN,MASSACHUSETTS
PRELIMINARY BUDGET ESTIMATE

DIVISION / DESCRIPTION	QTY	UNIT$	UNESUM	OIV.SUM
GENERAL CONDITIONS				
JOBSJTE TELEPHONE/FAX	2 MO	900	1,800	
CONSTRUCTION OFFICES				
USEEXISTING COURIER/ OVERNITE / POSTAGE	2 MO	450	900	
FIELD OFFICE SUPPLIES & COPIER RENTAL	2 MO	475	950	
MISC.TOOLS & SUPPLIES	2MO	600	1,200	
TEMP. TOILETS			USEEXISTING	
REPRODUCTION OF CONTRACT DOCUMENTS	1 LS	950	950	
WEEKLY CLEANING	9 DAYS	360	3,240	
DUMPSTER	5EA	675	3,375	
SAFETY & PROTECTION	1LS	1,500	1,500	
FINALCLEANING	1 LS	3,250	3,250	
				$ 17,165
ENGINEERING				
ARCHITECTURAL DESIGN & DRAWINGS	L.S	22,000	22,000	
MECHANICAUELECTRICAL ENGINEERING			*W/* SUBS	
STRUCTURAL	1 LS	2,500	W/SUBS	
				$ 22,000
INSURANCE & PERMITS				
GENERAL LIABILITY INSURANCE	1LS	$ 5,194	5,194	
BUILDING PERMITS	1LS	$ 7,752	7,752	
				$ 12,946
CONTINGENCY	1 LS	35,000	35,000	
				$ 35,000
OVERHEAD & PROFIT	6.5%	$53,305	53,305	
				$ 53,305
TOTAL BUDGET COST				$873,435

CLARIFICATIONS AND ALTERNATIVES

1 Pricing assumes that electric usage and Power Company Backcharges a1e paid for by the Landlord
2 Pricing assumes Haz Materials Handlirlg and DisposalIs by Landlord
3 Pricing assumes house HVAC system Is adequate to handle new loads.
4 Pricing assumes that existing electric service Is adequate to handle new work.

EXHIBIT C TO LEASE

WORK LETTER

EXHIBIT D TO LEASE

Rules and Regulations

1. The sidewalk, entries, and driveways of the Project shall not be obstructed by Tenant, or any Tenant Party, or used by them for any purpose other than ingress and egress to and from the Premises.

2. Tenant shall not place any objects, including antennas, outdoor furniture, etc., in the parking areas, landscaped areas or other areas outside of its Premises, or on the roof of the Project.

3. Except for animals assisting the disabled, no animals shall be allowed in the offices, halls, or corridors in the Project.

4. Tenant shall not disturb the occupants of the Project or adjoining buildings by the use of any radio or musical instrument or by the making of loud or improper noises.

5. If Tenant desires telegraphic, telephonic or other electric connections in the Premises, Landlord or its agent will direct the electrician as to where and how the wires may be introduced; and, without such direction, no boring or cutting of wires will be permitted. Any such installation or connection shall be made at Tenant's expense.

6. Tenant shall not install or operate any steam or gas engine or boiler, or other mechanical apparatus in the Premises, except as specifically approved in the Lease. The use of oil, gas or inflammable liquids for heating, lighting or any other purpose is expressly prohibited. Explosives or other articles deemed extra hazardous shall not be brought into the Project.

7. Parking any type of recreational vehicles is specifically prohibited on or about the Project. Except for the overnight parking of operative vehicles, no vehicle of any type shall be stored in the parking areas at any time. In the event that a vehicle is disabled, it shall be removed within 48 hours. There shall be no "For Sale" or other advertising signs on or about any parked vehicle. All vehicles shall be parked in the designated parking areas in conformity with all signs and other markings. All parking will be open parking, and no reserved parking, numbering or lettering of individual spaces will be permitted except as specified by Landlord.

8. Tenant shall maintain the Premises free from rodents, insects and other pests.

9. Landlord reserves the right to exclude or expel from the Project any person who, in the judgment of Landlord, is intoxicated or under the influence of liquor or drugs or who shall in any manner do any act in violation of the Rules and Regulations of the Project.

10. Tenant shall not cause any unnecessary labor by reason of Tenant's carelessness or indifference in the preservation of good order and cleanliness. Landlord shall not be responsible to Tenant for any loss of property on the Premises, however occurring, or for any damage done to the effects of Tenant by the janitors or any other employee or person.

11. Tenant shall give Landlord prompt notice of any defects in the water, lawn sprinkler, sewage, gas pipes, electrical lights and fixtures, heating apparatus, or any other service equipment affecting the Premises.

12. Tenant shall not permit storage outside the Premises, including without limitation, outside storage of trucks and other vehicles, or dumping of waste or refuse or permit any harmful materials to be placed in any drainage system or sanitary system in or about the Premises.

13. All moveable trash receptacles provided by the trash disposal firm for the Premises must be kept in the trash enclosure areas, if any, provided for that purpose.

14. No auction, public or private, will be permitted on the Premises or the Project.

15. No awnings shall be placed over the windows in the Premises except with the prior written consent of Landlord.

16. The Premises shall not be used for lodging, sleeping or cooking or for any immoral or illegal purposes or for any purpose other than that specified in the Lease. No gaming devices shall be operated in the Premises.

17. Tenant shall ascertain from Landlord the maximum amount of electrical current which can safely be used in the Premises, taking into account the capacity of the electrical wiring in the Project and the Premises and the needs of other tenants, and shall not use more than such safe capacity. Landlord's consent to the installation of electric equipment shall not relieve Tenant from the obligation not to use more electricity than such safe capacity.

18. Tenant assumes full responsibility for protecting the Premises from theft, robbery and pilferage.

19. Tenant shall not install or operate on the Premises any machinery or mechanical devices of a nature not directly related to Tenant's ordinary use of the Premises and shall keep all such machinery free of vibration, noise and air waves which may be transmitted beyond the Premises.

EXHIBIT E TO LEASE

TENANT'S PERSONAL PROPERTY

I. Existing (purchased from former tenant Protein Forest Inc. "PFI"):

Lab Equipment:
G7883 CD Glasswasher
GR Ext Ice Flaker MKS 400 Stor
Drum Cabinet w/Rollers for 2-55 Gal. Drums

Furniture:
Reception Area
2 Lounge Chairs w/Wood Arm Cap
Mojo Side Table 22" × 16"
Receptionist station

Conference Room:
Epson EMP720c LCD Projector
Virtu Board w/incl Doors, Glass Sh
16 Webb Chairs (Conf Room)
1 Rectangular Table 48" × 96" (Lg Conf Tbl)
Rectangular Table 48" × 72" (Sm Conf Table)
Virtu Server Cart 24" × 36" (Corner Table)

Executive Offices and Office Area:
All Workstations in 6 offices and all cubicle workstations in office Area, "area formerly marked on PFI floor plan as "Software Development RoomH and "Tech Station", OH Bins, Panels, etc.
27 lzzy Zachary Chairs (green office chairs)
12 Cache in Chairs (Side Chairs in Offices)

Cafeteria:
28 Zag Chairs (Cafe Chairs)
7 Square Table Tops & Bases (Cafe Tables)

II. To be purchased in the future (List is meant to be illustrative and not limited to these specific items):

Medicinal Chemistry:
400 MHzNMR
Agilent 1200 LC/MS
Agilent 1200 HPLCs
Lyophilizer
-20° Freezers
Fridges

Process Chemistry:
Large chiller/heater
Small chiller/heater
Large rotovap
Large vac.oven
SOL glass reactors
-20° Freezers
Fridges

Biology:

Microbiology:
-80° Freezers
Balances, analytical
Incubator, water jacketed, stacked
Water shaker
Microplate reader (plus microplate handling system)
Table top centrifuges
-20° Freezers
Fridges
Various rotors
Microscope
Balances
Magnetic stirrer
Orbital shaker
Electronic pipettor
Microcentrifuge
Vortex mixers

Cell Biology:
Cryogenic storage, liquid N2-based
Incubators (C02)
Microplate reader
Microscope fluorescence
Digital camera for microscope
Centrifuges

General Biology:
Autoclave
Sonicators (plus Sonicator tip)
Thermocyclers
Hybridization ovens
Shaking Incubators
Electroporation
Gyratory shakers
Western Blot

General[R&D equip. and Computers etc.]:
Rotovaps (for hoods)
Glasswasher
Ice machine
Chemical Storage cabinets
Computers - New hires -laptops
Computers - New Hires- desktops
IT - general network etc.
Telephone system and phones
Fax machines
Printers
Copier

EXHIBIT F TO LEASE

FORM OF LETTER OF CREDIT

IRREVOCABLE STANDBY LETTER OF CREDIT NO.SVBSF ____

DATE:NOVEMBER , 2006

BENEFICIARY:

ARE-480 ARSENAL STREET, LLC.
C/0 ALEXANDRIA REAL ESTATE EQUITIES, INC.
385 EAST COLORADO BLVD, SUITE 299
PASADENA, CA 91101

APPLICANT:

TETRAPHASE PHARMACEUTICALS INC
480 ARSENAL STREET, SUITE 110
WATERTOWN,MA 02472

AMOUNT:US $, AND 00/100 U.S. DOLLARS)

EXPIRATION DATE: , 2007 (ONE YEAR FROM LC ISSUE DATE)

LOCATION: AT OUR COUNTERS IN SANTA CLARA, CALIFORNIA

DEAR SIR/MADAM:

WE HEREBY ESTABLISH OUR IRREVOCABLE STANDBY LETTER OF CREDIT NO. SVBSF IN YOUR FAVOR AVAILABLE BY YOUR DRAFT DRAWN ON US AT SIGHT IN THE FORM OF EXHIBIT "A" ATTACHED AND ACCOMPANIED BY THE FOLLOWING DOCUMENTS:

1. THE ORIGINAL OF THIS LETTER OF CREDIT AND ALL AMENDMENT(S),IF ANY.

2. A DATED CERTIFICATION FROM THE BENEFICIARY, PURPORTEDLY SIGNED BY AN AUTHORIZED OFFICER, FOLLOWED BY HIS/HER DESIGNATED TITLE, STATING THE FOLLOWING:

(A) "THE BENEFICIARY HEREBY CERTIFIES THAT TETRAPHASE PHARMACEUTICALS INC OR ITS SUCCESSORS OR ASSIGNS UNDER THE LEASE HAS DEFAULTED IN ITS OBLIGATIONS UNDER THE LEASE AGREEMENT,DATED , 2006 [INSERT LEASE DATE] BY AND BETWEEN TETRAPHASE PHARMACEUTICALS INC AND ARE-480 ARSENAL STREET, LLC.(AS THE SAME MAY BE AMENDED AND ASSIGNED FROM TIME TO TIME, THE "LEASE") AND THAT BENEFICIARY IS DUE THE AMOUNT REQUESTED IN THIS DRAW REQUEST."

OR

(B) "THE BENEFICIARY HEREBY CERTIFIES THAT TETRAPHASE PHARMACEUTICALS INC OR ITS SUCCESSORS OR ASSIGNS UNDER THE LEASE HAS DEFAULTED IN ITS OBLIGATIONS UNDER THE LEASE, THAT BENEFICIARY IS BARRED BY APPLICABLE LAW FROM SENDING A NOTICE OF DEFAULT AND THAT BENEFICIARY IS DUE THE AMOUNT REQUESTED IN THIS DRAW REQUEST".

OR

(C) "THE BENEFICIARY IS IN RECEIPT OF SILICON VALLEY BANK NOTICE OF NON-EXTENSION OF LETTER OF CREDIT NO.SVBSF (THE "LETTER OF CREDIT) AND CERTIFIES THAT IT IS ENTITLED TO DRAW THE ENTIRE AMOUNT OF THE LETTER OF CREDIT."

OR

(D) “THE BENEFICIARY HEREBY CERTIFIES THAT BENEFICIARY IS DUE THE AMOUNT REQUESTED IN THIS DRAW REQUEST PURSUANT TO THE TERMS AND CONDITIONS OF THE LEASE.”

THE LEASE AGREEMENT MENTIONED ABOVE IS FOR IDENTIFICATION PURPOSES ONLY AND IT IS NOT INTENDED THAT SAID LEASE AGREEMENT BE INCORPORATED HEREIN OR FORM PART OF THIS LETTER OF CREDIT.

PARTIAL DRAWINGS ARE ALLOWED. THIS LETTER OF CREDIT MUST ACCOMPANY ANY DRAWINGS HEREUNDER FOR ENDORSEMENT OF THE DRAWING AMOUNT AND WILL BE RETURNED TO THE BENEFICIARY UNLESS IT IS FULLY UTILIZED.

DRAFT(S) AND DOCUMENTS MUST INDICATE THE NUMBER AND DATE OF THIS LETTER OF CREDIT.

THIS LETTER OF CREDIT SHALL BE AUTOMATICALLY EXTENDED FOR AN ADDITIONAL PERIOD OF ONE YEAR, WITHOUT AMENDMENT, FROM THE PRESENT AND/OR EACH FUTURE EXPIRATION DATE UNLESS AT LEAST SIXTY (60) DAYS PRIOR TO THE THEN CURRENT EXPIRATION DATE WE NOTIFY YOU BY OVERNIGHT COURIER SERVICE AT THE ABOVE ADDRESS THAT THIS LETTER OF CREDIT WILL NOT BE EXTENDED BEYOND THE CURRENT EXPIRATION DATE.IN NO EVENT SHALL THIS LETTER OF CREDIT BE AUTOMATICALLY EXTENDED BEYOND MARCH 31,2018 WHICH SHALL BE THE FINAL EXPIRATION DATE OF THIS LETTER OF CREDIT.

THIS LETTER OF CREDIT IS TRANSFERABLE BY THE ISSUING BANK AT THE REQUEST OF BENEFICIARY ONE OR MORE TIMES BUT IN EACH INSTANCE TO A SINGLE BENEFICIARY AND ONLY IN ITS ENTIRETY UP TO THE THEN AVAILABLE AMOUNT IN FAVOR OF ANY NOMINATED TRANSFEREE ASSUMING SUCH TRANSFER TO SUCH TRANSFEREE WOULD BE IN COMPLIANCE WITH THEN APPLICABLE LAW AND REGULATIONS, INCLUDING BUT NOT LIMITED TO THE REGULATIONS OF THE U.S. DEPARTMENT OF TREASURY AND U.S. DEPARTMENT OF COMMERCE.AT THE TIME OF TRANSFER,THE ORIGINAL LETTER OF CREDIT AND ORIGINAL AMENDMENT(S),IF ANY, MUST BE SURRENDERED TO US TOGETHER WITH OUR LETTER OF TRANSFER DOCUMENTATION (IN THE FORM OF EXHIBIT “B” ATTACHED HERETO).OUR TRANSFER FEE OF% OF 1% OF THE TRANSFER AMOUNT (MINIMUM $250.00) WILL BE PAID BY THE APPLICANT. ANY TRANSFER OF THIS LETTER OF CREDIT MAY NOT CHANGE THE PLACE OF EXPIRATION OF THE LETTER OF CREDIT FROM OUR ABOVE-SPECIFIED OFFICE. EACH TRANSFER SHALL BE EVIDENCED BY OUR ENDORSEMENT ON THE REVERSE OF THE ORIGINAL LETTER OF CREDIT AND WE SHALL FORWARD THE ORIGINAL LETTER OF CREDIT TO THE TRANSFEREE.

ALL DEMANDS FOR PAYMENT SHALL BE MADE BY PRESENTATION OF THE ORIGINAL APPROPRIATE DOCUMENTS ON A BUSINESS DAY AT OUR OFFICE (THE “BANK’S OFFICE”) AT: SILICON VALLEY BANK, 3003 TASMAN DRIVE, SANTA CLARA, CA 95054, ATTENTION: STANDBY LETTER OF CREDIT NEGOTIATION SECTION.

WE HEREBY AGREE WITH THE DRAWERS, ENDORSERS AND BONA FIDE HOLDERS THAT THE DRAFTS DRAWN UNDER AND IN ACCORDANCE WITH THE TERMS AND CONDITIONS OF THIS LETTER OF CREDIT SHALL BE DULY HONORED UPON PRESENTATION TO THE DRAWEE,IF NEGOTIATED ON OR BEFORE THE EXPIRATION DATE OF THIS CREDIT.

IF ANY INSTRUCTIONS ACCOMPANYING A DRAWING UNDER THIS LETTER OF CREDIT REQUEST THAT PAYMENT IS TO BE MADE BY TRANSFER TO YOURACCOUNTWITHANOTHER BANK, WE WILL ONLY EFFECT SUCH PAYMENT BY FED WIRE TO A U.S. REGULATED BANK, AND WE AND/OR SUCH OTHER BANK MAY RELY ON AN ACCOUNT NUMBER SPECIFIED IN SUCH INSTRUCTIONS EVEN IF THE NUMBER IDENTIFIES A PERSON OR ENTITY DIFFERENT FROM THE INTENDED PAYEE.

EXCEPT AS OTHERWISE PROVIDED HEREIN, THIS LETTER OF CREDIT IS SUBJECT TO THE UNIFORM CUSTOMS AND PRACTICES FOR DOCUMENTARY CREDITS, (1993 REVISION), INTERNATIONAL CHAMBER OF COMMERCE, PUBLICATION NO. 500.

SILICON VALLEY BANK

AUTHORIZED SIGNATURE

AUTHORIZED SIGNATURE

EXHIBIT “A” to LETTER OF CREDIT

DATE: _____ REF.NO. _____

__AT SIGHT OF THIS DRAFT

PAY TO THE ORDER OF US$ _____

US DOLLARS

_____

DRAWN UNDER SILICON VALLEY BANK, SANTA CLARA, CALIFORNIA, STANDBY LETTER OF CREDIT NUMBER NO. _____ DATED _____

TO: SILICON VALLEY BANK

_____

3003 TASMAN DRIVE
SANTA CLARA, CA 95054 (BENEFICIARY’S NAME)

Authorized Signature

GUIDELINES TO PREPARE THE DRAFT

1.DATE:ISSUANCE DATE OF DRAFT.
2.REF. NO.: BENEFICIARY’S REFERENCE NUMBER, IF ANY.
3. PAYTOTHE ORDER OF: NAME OF BENEFICIARY AS INDICATED IN THE LIC (MAKE SURE BENEFICIARY ENDORSES IT ON THE REVERSE SIDE).
4. US$: AMOUNT OF DRAWING IN FIGURES.
5. US DOLLARS: AMOUNT OF DRAWING IN WORDS.
6. LETTER OF CREDIT NUMBER:SILICON VALLEY BANK’S STANDBY *UC* NUMBER THAT PERTAINS TO THE DRAWING.
7.DATED:ISSUANCE DATE OF THE STANDBY UC.
8.BENEFICIARY’S NAME: NAME OF BENEFICIARY AS INDICATED IN THE UC.
9.AUTHORIZED SIGNATURE:SIGNED BY AN AUTHORIZED SIGNEROF BENEFICIARY.

IF YOU NEED FURTHER ASSISTANCE IN COMPLETING THIS DRAFT, PLEASE CALL OUR L/C PAYMENT SECTION AND ASK FOR:

ALICE DA LUZ:408-654-7120
EFRAIN TUVILLA: 408-654-6349

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BOS111 12079564.8

EXHIBIT “B” to Letter of Credit

DATE:

TO: SILICON VALLEY BANK 3003 TASMAN DRIVE RE: SANTA CLARA,.CA 95054
ATTN:INTERNATIONAL DIVISION. STANDBY LETTERS OF CREDIT

GENTLEMEN:

IRREVOCABLE STANDBY LETTER OF CREDIT NO. ISSUED BY SILICON VALLEY BANK, SANTA CLARA UCAMOUNT:

FOR VALUE RECEIVED,THE UNDERSIGNED BENEFICIARY HEREBY IRREVOCABLY TRANSFERS TO:

(NAME OF TRANSFEREE)
(ADDRESS)

ALL RIGHTS OF THE UNDERSIGNED BENEFICIARY TO DRAW UNDER THE ABOVE LEDER OF CREDIT UP TO ITS AVAILABLE AMOUNT AS SHOWN ABOVE AS OF THE DATE OF THIS TRANSFER.

BY THIS TRANSFER, ALL RIGHTS OF THE UNDERSIGNED BENEFICIARY IN SUCH LEDER OF CREDIT ARE TRANSFERRED TO THE TRANSFEREE. TRANSFEREE SHALL HAVE THE SOLE RIGHTS AS BENEFICIARY THEREOF,INCLUDING SOLE RIGHTS RELATING TO ANY AMENDMENTS, WHETHER INCREASES OR EXTENSIONS OR OTHER AMENDMENTS, AND WHETHER NOW EXISTING OR HEREAFTER MADE. ALL AMENDMENTS ARE TO BE ADVISED DIRECT TO THE TRANSFEREE WITHOUT NECESSITY OF ANY CONSENT OF OR NOTICE TO THE UNDERSIGNED BENEFICIARY.

THE ORIGINAL OF SUCH LETTER OF CREDIT IS RETURNED HEREWITH, AND WE ASK YOU TO ENDORSE THE TRANSFER ON THE REVERSE THEREOF, AND FORWARD IT DIRECTLY TO THE TRANSFEREE WITH YOUR CUSTOMARY NOTICE OF TRANSFER.

_____

_____

_____

SINCERELY, (BENEFICIARY’S NAME) (SIGNATURE OF BENEFICIARY) (NAME AND TITLE)

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BOS111 12079564.8

SIGNATURE AUTHENTICATED

The name(s}, title(s), and signature(s) conform to that/those on file with us for the company and the signature(s) is/are authorized to execute this instrument.

We further confirm that the company has·been identified applying the appropriate que diligence and enhanced due diligence as required by BSA and all its subsequent amendments.

_____
_____
_____
_____
(Name of Bank)
(Address of Bank)
(City, State, ZIP Code)

_____
_____
(Authorized Name and Title)
(Author-ized Signature)
(Telephone number)

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BOS111 12079564.8

EXHIBIT G TO LEASE

ENVIRONMENTAL REPORTS

1. Phase I Environmental Site Assessment Report, prepared by GZA GeoEnvironmental, Inc. (“GZA”), dated June 2001.

2. Watertown Materials Management Center Facility Exit Report Volume Iand Volume II,prepared by GZA, dated February 2002.

3. Tenant Exit Audit Review, prepared by ENVIRON International Corporation (“ENVIRON”), dated October 21, 2002.

4. Mold Investigation and Remediation Report,prepared by ENVIRON, dated December 29, 2003.

5. Decommissioning Plan Letter by Protein Forest, Inc. (“Protein Forest”},dated October 3, 2006.

6. Surrender Plan from Protein Forest to Tim White of ARE, dated November 3,2006.

7. Letter from the Commonwealth of Massachusetts to RusselGarlick of Protein Forest, dated September 27, 2005.

8. ChemicalList for Premise Surrender by Protein Forest, dated November 4, 2006.

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FIRST AMENDMENT TO LEASE

THIS FIRST AMENDMENT TO LEASE (this **"First Amendment"**) is made as of September 9, 2011 by and between **ARE-480 ARSENAL STREET, LLC** , a Delaware limited liability company **("Landlord"**), and **TETRAPHASE PHARMACEUTICALS, INC.** , a Delaware corporation (**"Tenant"**).

RECITALS

A. Landlord and Tenant are parties to that certain Lease Agreement dated as of November 16, 2006 (the **"Lease"**). Pursuant to the Lease, Tenant leases approximately 15,149 rentable square feet as more particularly described in Exhibit A to the Lease (the **"Original premises"**) in a building located at 480 Arsenal Street, Watertown, Massachusetts. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. Landlord and Tenant desire, subject to the terms and conditions set forth herein, to, among other things, amend the Lease to expand the Premises by adding approximately 750 rentable square feet to the Original Premises for a total of 15,899 as more particularly described on Exhibit A to this First Amendment (the **"Expansion Premises"**).

NOW, THEREFORE, in consideration of the foregoing Recitals, which are incorporated herein by this reference, the mutual promises and conditions contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

1. Delivery; Acceptance of Expansion Premises; Expansion Rent Commencement Date .

(a) Landlord shall use reasonable efforts to deliver the Expansion Premises to Tenant on or before November 1, 2011 (**"Delivery"** or **"Deliver"**) with Landlord's Work (defined below) substantially complete. Tenant acknowledges that there is currently a tenant occupying the Expansion Premises, and the parties agree that if Landlord fails to timely Deliver the Expansion Premises, including, without limitation, as a result of such existing tenant's failure to early vacate and surrender the Expansion Premises, Landlord shall not be liable to Tenant for any loss or damage resulting therefrom, and this Lease with respect to the Expansion Premises shall not be void or voidable. For the purposes of this Section 1 , **"Landlord's Work"** shall mean the following work items to be done within the Expansion Premises in conformance to Building standards and otherwise reasonable acceptable to Landlord and Tenant: the removal or a portion of the wall and the installation of a building-standard interior door between the Original Premises and the Expansion Premises as depicted on Exhibit A to this First Amendment. Other than Landlord's Work, Landlord shall have no obligation to perform any work at the Building in connection with Tenant's occupancy or obtain any permits, approvals or entitlements related to Tenant's specific use of the Premises or Tenant's business operations therein.

(b) The **"Expansion Premises Commencement Date"** shall be the date that Landlord Delivers the Expansion Premises to Tenant broom clean, free of all occupants with Landlord's Work substantially complete. Upon request of Landlord, Tenant shall execute and

deliver a written acknowledgement of the Expansion Premises Commencement Date when the same is established in the form attached hereto as Exhibit B ; provided, however, that Tenant's failure to execute and deliver such acknowledgement shall not affect Landlord's rights hereunder.

(c) Except for Landlord's Work: (i) Tenant shall accept the Expansion Premises in their condition as of the Expansion Premises Commencement Date, subject to all applicable Legal Requirements; (ii) Landlord shall have no obligation for any defects in the Expansion Premises; and (iii) Tenant's taking possession of the Expansion Premises were in good condition at the time possession was taken.

(d) Tenant agrees and acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the condition of all or any portion of the Expansion Premises, and/or the suitability of the Expansion Premises for the conduct of Tenant's business, and Tenant waives any implied warranty that the Expansion Premises are suitable for the Permitted Use.

2. Base Rent . Commencing on the Expansion Premises Commencement Date, the following amendments shall be deemed made to definitions contained on page 1 of the Lease:

3. Other Changes to Defined Terms . As of the Expansion Premises Commencement Date, Base Rent shall be increased to $47,569.22. Thereafter, Base Rent shall adjust in accordance with Section 5 of the Lease.

(i) The defined term **"Premises"** shall include the Original Premises and the Expansion Premises and shall comprise 15,889 rentable square feet. Exhibit A to this First Amendment shall be deemed added to Exhibit A to the Lease;

(ii) The defined term **"Tenant's Share of Operating Expenses"** shall be increased to 11.296%.

4. Early Termination . For avoidance of doubt, Section 3 of the Lease is hereby deleted in its entirely and is of no further force or effect.

5. OFAC . Tenant, and all beneficial owners of Tenant, are currently (a) in compliance with and shall at all times during the Term of the Lease remain in compliance with the regulations of the Office of Foreign Assets Control **("OFAC"**) of the U.S. Department of Treasury and any statute, executive order, or regulation relating thereto (collectively, the **"OFAC Rules"**), (b) not listed on, and shall not during the term of the Lease be listed on, the Specially Designated Nationals and Blocked Persons List maintained by OFAC and/or on any other similar list maintained by OFAC or other governmental authority pursuant to any authorizing statute, executive order, or regulation, and (c) not a person or entity with whom a U.S. person is prohibited from conducting business under the OFAC Rules.

6. Broker . Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, **"Broker"**) in connection with the

transaction reflected in this First Amendment and that no Broker brought about this transaction other than CBRE-NE. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than CBRE-NE, claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.

7. Miscellaneous .

(a) This First Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This First Amendment may be amended only by an agreement in writing, signed by the parties hereto.

(b) This First Amendment is binding upon and shall inure to the benefit of the parties hereto, their respective agents, employees, representatives, officers, directors, divisions, subsidiaries, affiliates, assigns, heirs, successors in interest and shareholders.

(c) This First Amendment may be executed in any number of counterparts, each of which shall be deemed an original, but all of which when taken together shall constitute one and the same instrument. The signature page of any counterpart may be detached therefrom without impairing the legal effect of the signature(s) thereon provided such signature page is attached to any other counterpart identical thereto except having additional signature pages executed by other parties to this First Amendment attached thereto.

(d) Except as amended and/or modified by this First Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this First Amendment. In the event of any conflict between the provisions of this First Amendment and the provisions of the Lease, the provisions of this First Amendment shall prevail. Whether or not specifically amended by this First Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this First Amendment.

[Signatures are on the next page.]

IN WITNESS WHEREOF , the parties hereto have executed this First Amendment as of the day and year first above written

LANDLORD:

ARE-480 ARSENAL STREET, LLC,
A Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS Corp.,
a Maryland corporation
general partner

By: /s/ Eric S. Johnson
Eric S. Johnson
Vice President
Real Estate Legal Affairs

TENANT:

TETRAPHASE PHARMACEUTICALS, INC.,
A Delaware corporation

By: /s/ Guy Macdonald
Its President & CEO

EXHIBIT A

EXPANSION PREMISES

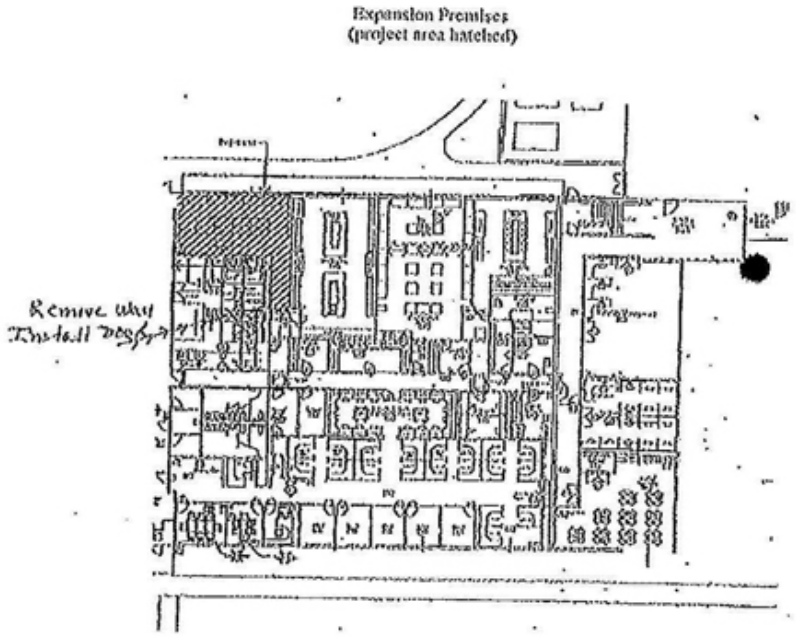

EXHIBIT B

ACKNOWLEDGMENT OF EXPANSION PREMISES COMMENCEMENT DATE

This **ACKNOWLEDGEMENT OF EXPANSION PREMISES COMMENCEMENT DATE** is made as of this day of , 20 , between **ARE-480 ARSENAL STREET, LLC,** a Delaware limited liability company (**"Landlord"**), and **TETRAPHASE PHARMACEUTICALS, INC.,** a Delaware corporation (**"Tenant"**), and is attached to and made a part of the Lease dated as of November 15, 2006, as amended by the First Amendment dated as of , 2011, (as amended, the **"Lease"**), by and between Landlord and Tenant. Any initially capitalized terms used but not defined herein shall have the meanings given them in the Lease.

Landlord and Tenant hereby acknowledge and agree, for all purposes of the Lease, that the **"Expansion Premises Commencement Date"** is , and the termination date of the Base Term of the Lease shall be midnight on November 30, 2012. In case of a conflict between this Acknowledgment of Expansion Premises Commencement Date and the Lease, this Acknowledgement of Expansion Premises Commencement Date shall control for all purposes.

IN WITNESS WHEREOF, Landlord and Tenant have executed this ACKNOWLEDGMENT OF EXPANSION PREMISES COMMENCEMENT DATE TO BE EFFECTIVE ON THE DATE FIRST WRITTEN ABOVE.

LANDLORD:

ARE-480 ARSENAL STREET, LLC,
A Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS Corp.,
a Maryland corporation
general partner

By: _____

TENANT:

TETRAPHASE PHARMACEUTICALS, INC.,
A Delaware corporation

By: _____
Its _____

SECOND AMENDMENT TO LEASE

THIS SECOND AMENDMENT TO LEASE (this " **Second Amendment** ") is made as of March 15, 2012 by and between **ARE-480 ARSENAL STREET, LLC** , a Delaware limited liability company (" **Landlord** "), and **TETRAPHASE PHARMACEUTICALS, INC.** , a Delaware corporation (" **Tenant** ").

RECITALS

A. Landlord and Tenant are parties to that certain Lease Agreement dated as of November 16, 2006 as amended by that certain First Amendment to Lease dated as of September 9, 2011 (as amended, the " **Lease** "). Pursuant to the Lease, Tenant leases approximately 15,899 rentable square feet as more particularly described in the Lease in a building located at 480 Arsenal Street, Watertown, Massachusetts. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. The Base Term of the Lease expires on November 30, 2012.

C. Landlord and Tenant desire, subject to the terms and conditions set forth herein, to, among other things, amend the Lease to (i) extend the Base Term of the Lease for a period of 6 months commencing on December 1, 2012 and ending on May 31, 2013 (" **Interim Extension Term** "), (ii) provide for payment of Base Rent during the Interim Extension Term and (iii) amend Section 40 of the Lease.

NOW, THEREFORE , in consideration of the foregoing Recitals, which are incorporated herein by this reference, the mutual promises and conditions contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

1. Base Term . The Base Term of the Lease is hereby extended for a period of 6 months and shall expire on May 31, 2013.

2. Rent . Notwithstanding anything to the contrary in the Lease, Base Rent during the Interim Extension Term shall be $50,452.83 per month and Tenant shall continue to pay Tenant's Share of Operating Expenses and all other charges as set forth in the Lease.

3. Section 40/Right To Extend Term . The phrase "at least 12 months prior, and no earlier than 9 months prior, to expiration of the Base Term of the Lease or the expiration of any prior Extension Term" in the first paragraph of Section 40(a) of the Lease is hereby deleted in its entirety and replaced with "no earlier than June 1, 2012 and no later than August 31, 2012".

4. Broker . Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, " **Broker** ") in connection with the transaction reflected in this Second Amendment and that no Broker brought about this transaction other than CBRE-NE. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than CBRE-NE, claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.

5. Miscellaneous .

(a) This Second Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This Second Amendment may be amended only by an agreement in writing, signed by the parties hereto.

(b) This Second Amendment is binding upon and shall inure to the benefit of the parties hereto, their respective agents, employees, representatives, officers, directors, divisions, subsidiaries, affiliates, assigns, heirs, successors in interest and shareholders.

(c) This Second Amendment may be executed in any number of counterparts, each of which shall be deemed an original, but all of which when taken together shall constitute one and the same instrument. The signature page of any counterpart may be detached therefrom without impairing the legal effect of the signature(s) thereon provided such signature page is attached to any other counterpart identical thereto except having additional signature pages executed by other parties to this Second Amendment attached thereto.

(d) Except as amended and/or modified by this Second Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this Second Amendment. In the event of any conflict between the provisions of this Second Amendment and the provisions of the Lease, the provisions of this Second Amendment shall prevail. Whether or not specifically amended by this Second Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this Second Amendment.

[Signatures are on the next page.]

IN WITNESS WHEREOF , the parties hereto have executed this Second Amendment as of the day and year first above written.

LANDLORD:

ARE-480 ARSENAL STREET, LLC,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS CORP.,
a Maryland corporation,
general partner

By: /s/ Eric S. Johnson
Eric S. Johnson
Vice President
Real Estate Legal Affairs

TENANT:

TETRAPHASE PHARMACEUTICALS, INC.,
a Delaware corporation

By: /s/ David Lubner
Its: SVP, CFO

THIRD AMENDMENT TO LEASE

THIS THIRD AMENDMENT TO LEASE (this " **Third Amendment** ") is made as of September 18, 2012 by and between **ARE-480 ARSENAL STREET, LLC** , a Delaware limited liability company (" **Landlord** "), and **TETRAPHASE PHARMACEUTICALS, INC.** , a Delaware corporation (" **Tenant** ").

RECITALS

A. Landlord and Tenant are parties to that certain Lease Agreement dated as of November 16, 2006 as amended by that certain First Amendment to Lease dated as of September 9, 2011 and that certain Second Amendment to Lease dated as of March 15, 2012 (as amended, the " **Lease** "), Pursuant to the Lease, Tenant leases approximately 15,899 rentable square feet as more particularly described in the Lease in a building located at 480 Arsenal Street, Watertown, Massachusetts. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. The Base Term of the Lease expires on May 31, 2013.

C. Landlord and Tenant desire, subject to the terms and conditions set forth herein, to, among other things, amend the Lease to (i) extend the Base Term of the Lease for a period of one year commencing on June 1, 2013 and ending on May 31, 2014 (" **Extension Term** "), (ii) provide for payment of Base Rent during the Extension Term, (iii) delete Section 40 of the Lease and (iv) increase the Security Deposit.

NOW, THEREFORE , in consideration of the foregoing Recitals, which are incorporated herein by this reference, the mutual promises and conditions contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

1. Base Term . The Base Term of the Lease is hereby extended for a period of one year and shall expire on May 31, 2014.

2. Rent . Notwithstanding anything to the contrary in the Lease, Base Rent during the Extension Term shall be $52,996.66 per month and Tenant shall continue to pay Tenant's Share of Operating Expenses and all other charges as set forth in the Lease.

3. Section 40/Right To Extend Term . Section 40 of the Lease is hereby deleted in its entirety and Tenant shall have no further right to extend the Term.

4. Security Deposit . Notwithstanding anything to the contrary in the Lease, effective as of May 31, 2013, the Security Deposit amount shall be increased from $120,813.27 to $158,989.98 (" **Increased Security Deposit Amount** "). On or before May 31, 2013, Tenant shall deliver to Landlord (i) a substitute Letter of Credit or (ii) an amendment to the existing Letter of Credit, in compliance with Section 7 of the Lease and reflecting the Increased Security Deposit Amount.

5. Broker . Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, " **Broker** ") in connection with the transaction reflected in this Third Amendment and that no Broker brought about this transaction other than CBRE-NE. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than CBRE-NE, claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.

6. Miscellaneous .

(a) This Third Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This Third Amendment may be amended only by an agreement in writing, signed by the parties hereto.

(b) This Third Amendment is binding upon and shall inure to the benefit of the parties hereto, their respective agents, employees, representatives, officers, directors, divisions, subsidiaries, affiliates, assigns, heirs, successors in interest and shareholders.

(c) This Third Amendment may be executed in any number of counterparts, each of which shall be deemed an original, but all of which when taken together shall constitute one and the same instrument. The signature page of any counterpart may be detached therefrom without impairing the legal effect of the signature(s) thereon provided such signature page is attached to any other counterpart identical thereto except having additional signature pages executed by other parties to this Third Amendment attached thereto.

(d) Except as amended and/or modified by this Third Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this Third Amendment. In the event of any conflict between the provisions of this Third Amendment and the provisions of the Lease, the provisions of this Third Amendment shall prevail. Whether or not specifically amended by this Third Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this Third Amendment.

[Signatures are on the next page.]

IN WITNESS WHEREOF , the parties hereto have executed this Third Amendment as of the day and year first above written.

LANDLORD:

ARE-480 ARSENAL STREET, LLC ,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership,
managing member

By: ARE-QRS CORP.,
a Maryland corporation,
general partner

By: /s/ Eric S. Johnson
Eric S. Johnson
Vice President
Real Estate Legal Affairs

TENANT:

TETRAPHASE PHARMACEUTICALS, INC.,
a Delaware corporation

By: /s/ David Lubner
Its: SVP, CFO

FOURTH AMENDMENT TO LEASE

THIS FOURTH AMENDMENT TO LEASE (this **" Fourth Amendment "**) is made as of November 20, 2013 by and between **ARE-480 ARSENAL STREET, LLC** , a Delaware limited liability company **("Landlord")** , and **TETRAPHASE PHARMACEUTICALS, INC.,** a Delaware corporation **("Tenant").**

RECITALS

A. Landlord and Tenant are parties to that certain Lease Agreement dated as of November 16, 2006, as amended by that certain First Amendment to Lease dated as of September 9, 2011, that certain Second Amendment to Lease dated as of March 15, 2012, and that certain Third Amendment to Lease dated as of September 18, 2012 (as amended, the **" Lease "**). Pursuant to the Lease, Tenant leases approximately 15,899 rentable square feet as more particularly described in the Lease in a building located at 480 Arsenal Street, Watertown, Massachusetts. Capitalized terms used herein without definition shall have the meanings defined for such terms in the Lease.

B. The Base Term of the Lease expires on May 31, 2014.

C. Landlord and Tenant desire, subject to the terms and conditions set forth herein, to, among other things, amend the Lease to (i) extend the Base Term of the Lease for a period of one year and two months commencing on June 1, 2014 and ending on July 31, 2015 **("Second Extension Term")** , and (ii) provide for payment of Base Rent during the Second Extension Term.

NOW, THEREFORE, in consideration of the foregoing Recitals, which are incorporated herein by this reference, the mutual promises and conditions contained herein, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

1. Base Term . The Base Term of the Lease is hereby extended to expire on July 31, 2015.

2. Rent .

(a) Tenant shall continue to pay Base Rent as set forth in the Lease through May 31, 2014. Notwithstanding anything to the contrary in the Lease, Base Rent during the Second Extension Term shall be as follows:

i) commencing on June 1, 2014, Base Rent shall be $54,586.56 per month; and

ii) commencing on June 1, 2015, Base Rent shall be $56,224.15 per month

(b) Tenant shall continue to pay Tenant's Share of Operating Expenses and all other charges as set forth in the Lease.

3. Broker . Landlord and Tenant each represents and warrants that it has not dealt with any broker, agent or other person (collectively, **" Broker "**) in connection with the transaction

reflected in this Fourth Amendment and that no Broker brought about this transaction other than CBRE-NE. Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker, other than CBRE-NE, claiming a commission or other form of compensation by virtue of having dealt with Tenant or Landlord, as applicable, with regard to this leasing transaction.

4. Miscellaneous .

(a) This Fourth Amendment is the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior and contemporaneous oral and written agreements and discussions. This Fourth Amendment may be amended only by an agreement in writing, signed by the parties hereto.

(b) This Fourth Amendment is binding upon and shall inure to the benefit of the parties hereto, their respective agents, employees, representatives, officers, directors, divisions, subsidiaries, affiliates, assigns, heirs, successors in interest and shareholders.

(c) This Fourth Amendment may be executed in any number of counterparts, each of which shall be deemed an original, but all of which when taken together shall constitute one and the same instrument. The signature page of any counterpart may be detached therefrom without impairing the legal effect of the signature(s) thereon provided such signature page is attached to any other counterpart identical thereto except having additional signature pages executed by other parties to this Fourth Amendment attached thereto.

(d) Except as amended and/or modified by this Fourth Amendment, the Lease is hereby ratified and confirmed and all other terms of the Lease shall remain in full force and effect, unaltered and unchanged by this Fourth Amendment. In the event of any conflict between the provisions of this Fourth Amendment and the provisions of the Lease, the provisions of this Fourth Amendment shall prevail. Whether or not specifically amended by this Fourth Amendment, all of the terms and provisions of the Lease are hereby amended to the extent necessary to give effect to the purpose and intent of this Fourth Amendment.

[Signatures are on the next page.]

IN WITNESS WHEREOF, the parties hereto have executed this Fourth Amendment as of the day and year first above written.

LANDLORD:

ARE-480 ARSENAL STREET, LLC,
a Delaware limited liability company

By: ALEXANDRIA REAL ESTATE EQUITIES, L.P.,
a Delaware limited partnership, managing member

By: ARE-QRS CORP.,
a Maryland corporation,
general partner

By: 

Eric S. Johnson
Vice President
Real Estate Legal Affairs

TENANT:

TETRAPHASE PHARMACEUTICALS, INC.,
a Delaware corporation

By: 

Its: SVP, CFO

EXHIBIT 21.1

SUBSIDIARIES OF THE REGISTRANT

Name	Jurisdiction of Organization	Percentage Ownership
Tetraphase Securities Corporation	Massachusetts	100%

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-194125) pertaining to the 2013 Stock Incentive Plan of Tetraphase Pharmaceuticals, Inc. and the Registration Statement (Form S-8 No. 333-189361) pertaining to the 2006 Stock Incentive Plan and the 2013 Stock Incentive Plan of Tetraphase Pharmaceuticals, Inc., of our report dated March 6, 2014, with respect to the consolidated financial statements of Tetraphase Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2013.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 6, 2014

Exhibit 31.1

CERTIFICATION

I, Guy Macdonald, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 6, 2014

/s/ Guy Macdonald
Guy Macdonald
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, David Lubner, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 6, 2014

/s/ David C. Lubner
David C. Lubner
Senior Vice Present and Chief Financial Officer

EXHIBIT 32.1

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

In connection with the Annual Report on Form 10-K of Tetraphase Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Guy Macdonald, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

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

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

Date: March 6, 2014

/s/ Guy Macdonald
Guy Macdonald
Chief Executive Officer

EXHIBIT 32.2

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

In connection with the Annual Report on Form 10-K of Tetraphase Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David Lubner, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

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

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

Date: March 6, 2014

/s/ David C. Lubner
David C. Lubner
Senior Vice President and Chief Financial Officer