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, 2019

Or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number: 001-35837

TETRAPHASE PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**20-5276217**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**

480 Arsenal Way
Watertown, Massachusetts 02472
(Address of Principal Executive Offices) (zip code)

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

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $.001 par value	**TTPH**	**Nasdaq Global Select Market**

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes ☒ No ☐

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

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

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

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

The aggregate market value of the registrant's common stock, $0.001 par value per share ("Common Stock"), held by non-affiliates of the registrant, based on the last reported sale price of the Common Stock on the Nasdaq Global Select Market at the close of business on June 28, 2019, was $17,578,294. For purposes hereof, shares of Common Stock held by each executive officer and director of the registrant and entities affiliated with such executive officers and directors have been excluded from the foregoing calculation because such persons and entities may be deemed to be affiliates of the registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares outstanding of the registrant's Common Stock as of March 9, 2020: 7,259,236

Documents incorporated by reference:

None.

TETRAPHASE PHARMACEUTICALS, INC.
Annual Report on Form 10-K
For the Fiscal Year Ended December 31, 2019

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References to Tetraphase

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

The Tetraphase Pharmaceuticals™ name and logo and the Xerava™ name and logo are registered trademarks of trade names of Tetraphase Pharmaceuticals, Inc. in the United States and/or other countries. Trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

Forward-Looking Information

This Annual Report on Form 10-K contains forward-looking statements regarding, among other things, our future discovery and development efforts, our future operating results and financial position, our business strategy, and other objectives for our operations. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "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 and the commercialization of pharmaceuticals, such as our ability to successfully commercialize Xerava, 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, adverse results in our drug discovery and clinical development activities, 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 biopharmaceutical company using our proprietary chemistry technology to create, develop and commercialize novel tetracyclines for serious and life-threatening conditions, including bacterial infections caused by multidrug-resistant, or MDR, bacteria. There is a medical need for new antibiotics as resistance to existing antibiotics increases. In recognition of this need, we developed our product, Xerava (eravacycline), a fully synthetic fluorocycline, as an intravenous, or IV antibiotic for use as a first-line empiric monotherapy for the treatment of MDR infections, including MDR Gram-negative infections, such as those found in complicated intra-abdominal infections, or cIAI.

On August 27, 2018, the United States Food and Drug Administration, or FDA, approved Xerava for the treatment of cIAI in adults. Approval of Xerava was based on our IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline) phase 3 program. In the first pivotal phase 3 trial in the IGNITE program in patients with cIAI, twice-daily IV Xerava met the primary endpoint by demonstrating statistical non-inferiority of clinical response compared to ertapenem, a carbapenem and a standard of care treatment for cIAI, and was well-tolerated. We refer to this trial as IGNITE1. In our other pivotal phase 3 clinical trial of Xerava in patients with cIAI, twice-daily IV Xerava met the primary endpoint by demonstrating statistical non-inferiority of clinical response compared to meropenem, another standard of care treatment, and was well-tolerated. We refer to this trial as IGNITE4. In both IGNITE1 and IGNITE4, Xerava achieved high cure rates in patients with poly-microbial infections (Gram-negative, Gram-positive, and anaerobic infections), including resistant isolates.

In October 2018, we commenced sales of Xerava in the United States. We are commercializing Xerava in the United States using a small, targeted commercial and medical affairs groups to build and promote access to Xerava. As a result, as of March 3, 2020, we have approximately 27 sales representatives. 3 regional business directors, 3 strategic market access executives and approximately 7 medical affairs personnel supporting Xerava in the United States.

On September 20, 2018, based on the results of IGNITE1, the European Commission, or EC, granted marketing authorization for Xerava for the treatment of cIAI in adults in all 28 countries of the European Union, or EU, plus Norway, Iceland and Liechtenstein. We plan to find a partner to commercialize Xerava in the EU. In February 2018 we entered into a license agreement with Everest Medicines Limited, or Everest Medicines, granting Everest Medicines commercialization rights to eravacycline in China and other Asian territories. In June 2018, Everest Medicines submitted an Investigational New Drug, or IND, application to the China National Medical Products Administration (formerly China FDA) for a phase 3 clinical trial of eravacycline in cIAI. The application was approved, and Everest Medicines began enrolling patients in this phase 3 trial in the second quarter of 2019.

We believe that the ability of Xerava to cover MDR Gram-negative bacteria, as well as MDR Gram-positive, anaerobic and atypical bacteria, may enable Xerava to become the drug of choice for first-line empiric treatment of patients with cIAI. In *in vitro* studies, Xerava has demonstrated the ability to cover a wide variety of MDR Gram-negative, Gram-positive, anaerobic and atypical bacteria, including MDR *Klebsiella pneumoniae* and MDR *Acinetobacter.* Multidrug-resistant *Klebsiella pneumoniae* (carbapenem-resistant Enterobacteriaceae [CRE]) and MDR Acinetobacter are listed as urgent threats and Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae is listed as serious threats by the Centers for Disease Control and Prevention, or CDC, in a 2019 report. They are also listed as “Priority 1; Critical Pathogens” in the World Health Organization’s priority pathogens list for R&D, published in February 2017. CREs were a confirmed area of great concern by the World Health Organization in an April 2014 global surveillance report. Gram-negative bacteria that are resistant to multiple available existing antibiotics are increasingly common and a growing threat to public health.

In addition to Xerava, we have also developed other fluorocycline antibiotic compounds, TP-6076 and TP-271, and TP-2846, a tetracycline for the treatment of acute myeloid leukemia. We developed TP-6076, a fully-synthetic fluorocycline derivative, as a lead candidate under our second-generation program to target unmet medical needs, including MDR Gram-negative bacteria such as carbapenem-resistant Enterobacteriaceae and carbapenem-resistant or pan-resistant *Acinetobacter baumanii*. To date, we have conducted phase 1 single-ascending and multiple-ascending dose studies evaluating the safety, tolerability and pharmacokinetics of IV TP-6076 in healthy volunteers. We also conducted a Phase 1 study to assess the bronchopulmonary disposition, pharmacokinetics, and safety of TP-6076 in healthy volunteers. TP-271 is a fully-synthetic fluorocycline that we developed for respiratory disease caused by bacterial biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia. To date, we have completed single-ascending and multiple-ascending dose trials for IV and oral formulations of TP-271. We have completed pre-clinical toxicology studies for TP-2846 and intend to file an IND with the FDA for TP-2846 upon identifying a partner. We are seeing to out-license each of these product candidates.

In June 2019, we announced a restructuring of our organization, including a 20% reduction in headcount, designed to focus our cash resources on commercializing Xerava primarily in the hospital setting. This reorganization included the elimination of our internal research function. As part of our restructuring, we decided not to engage in further product development, including conducting clinical trials of our product candidates, and are exploring out-licensing opportunities for all of our pipeline of early-stage antibiotics and oncology product candidates.

Going Concern

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2019, we had cash, cash equivalents and short-term investments of $21.2 million. Based on our recurring losses and cash outflows from operations since inception, expectation of continuing operating losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance our future operations, we have concluded that there is substantial doubt about our ability to continue as a going concern. For a further discussion of our liquidity, please refer to Part II, Item 7 of this report under the heading “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Liquidity and Capital Resources—Funding Requirements” and Note 1 to our consolidated financial statements in Part II, Item 8 of this Annual Report on Form 10-K.

Drug-Resistant Antibiotic Market

Physicians commonly prescribe antibiotics to treat patients with acute and chronic infectious diseases that are either presumed or known to be caused by bacteria. Inappropriate use of antibiotics and lack of new therapies has resulted in a rapid increase in bacterial infections that are resistant to multiple antibacterial agents. Global microbial resistance, including bacteria, viruses and fungi, now results in the death of at least 700,000 people each year, according to *The Review on Antimicrobial Resistance*, an analysis commissioned by the U.K. government in 2016. The report predicts that failing to develop effective treatments for drug-resistant bacteria by 2050 would lead to 10 million extra deaths a year. Further, in a 2019 report, the CDC estimated that every year in the United States, more than 2.8 million people acquire serious infections that are resistant to one or more of the antibiotics designed to treat those infections, with at least 35,000 dying as a result, and many more dying from other conditions that are complicated by the occurrence of an antibiotic-resistant infection. These antibiotic-resistant infections add considerable and avoidable costs to the United States healthcare system. In a September 2013 report, the CDC noted that the total economic cost of antibiotic-resistant infections to the United States economy has been estimated to be as high as $20 billion in excess direct healthcare costs. Over the last decade there has been an increase in antibiotics that target resistant Gram-positive bacteria, but there still remain limited therapeutic options for resistant Gram-negative infections. According to the CDC, among all of the bacterial resistance problems, Gram-negative pathogens are particularly worrisome because they are becoming resistant to nearly all drugs that would be considered for treatment, with the most serious Gram-negative infections being healthcare associated and the most common pathogens being *Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Acinetobacter*.

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

Broad-spectrum antibiotics are used to treat major hospital infections such as cIAI. Based on an analysis from a variety of industry sources, we estimate that the number of patients treated with antibiotics in the United States and European Union annually includes approximately 4.6 million cIAI patients with each patient being treated for an average of 7.6 days for a combined estimated 40 million annual average days of treatment. Of these patients, we believe that approximately 40% of cIAI patients require a change in therapy and 50% of patients with cIAI are receiving combination therapy.

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

Intra-abdominal infection is classified as uncomplicated or complicated based on the extent of the infection. cIAIs extend beyond the source organ into the peritoneal space (the space between the two membranes that separate the organs in the abdominal cavity from the abdominal wall) as a result of perforation or other damage to the gastrointestinal tract. cIAI diagnoses include intra-abdominal abscess, stomach or intestinal perforation, peritonitis, appendicitis, cholecystitis, or diverticulitis. Different bacterial pathogens are responsible for cIAI, including Gram-negative aerobic bacteria, Gram-positive bacteria, and anaerobic bacteria. Early detection, containment and appropriate antimicrobial treatment are essential to the successful treatment of IAI. This is even more critical with increasing rates of infections caused by drug-resistant bacteria, which limit the effectiveness of currently available antibiotics.

A nationwide electronic database looked at the prevalence of Gram-negative resistance from 2008-2015 in U.S. hospitals and it showed MDR rates continuing to increase. Out of the 3,158,349 isolates tested, 5.3% were considered MDR pathogens. Five bacteria accounted for 92.7% of all MDR isolates: *E coli* (39.4%), *P aeruginosa* (29.4%), *K pneumoniae* (13.2%), *A baumannii* (5.4%) and *Enterobacter* spp (5.2%). The highest rate of MDR was associated with the onset in hospital setting (11.4%), followed by the admission period (6.6%), and the ambulatory setting (3.5%). In the database, 42.9% of *A baumannii* were MDR isolates. The rate of MDR *A baumannii was* highest in the inpatient setting (58.6% of isolates from all body sources), followed by admission setting (43.2%), and ambulatory setting (24.8%).

Legislative initiatives have been approved as part of the 21st Century Cures Act, including the Antibiotic Development to Advance Patient Treatment Act which would provide a pathway for approval of antibiotics in limited populations of patients with few or no suitable treatment options. Other legislation still pending include the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms, or DISARM, Act which would remove certain novel antibiotics used to treat serious bacterial infections from the diagnosis-related group and receive a drug specific reimbursement.

Limitations of Available Treatment Options

When confronted with a new patient suffering from a serious infection, such as cIAI, 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 Against MDR Bacteria. A physician cannot risk prescribing an inappropriate antibiotic when initially treating a patient for a serious infection due to well-documented increased rates of morbidity and mortality associated with ineffective empiric therapy or where the pathogen has not yet been definitively identified. Frequently used products, such as linezolid and daptomycin, are limited to Gram-positive bacteria and thus are rarely used as a first-line empiric monotherapy if broad bacterial coverage is required. Recently approved products are limited to specific Gram-negative bacteria and thus are rarely used as a first-line empiric monotherapy if broad bacterial coverage is required. In addition, other popular antibiotics that have been used as first-line empiric monotherapies, such as levofloxacin and piperacillin/tazobactam have seen their utility as first-line empiric monotherapies diminished as the number of bacterial strains resistant to these therapies has increased. In response, utilization of broader-spectrum, higher potency antibiotics, such as carbapenems, has increased. This has been accompanied by an increase in resistance to these agents such that the utility of the entire carbapenem class is now threatened.

Carbapenem Overuse and Increased Resistance. Carbapenems, such as meropenem and ertapenem, are considered the empiric drugs of choice for the treatment of a suspected or document cIAI caused by extended-spectrum beta-lactamase, or ESBL, producing *Enterobacteriaceae*. Finding alternatives to carbapenems for treatment of infections caused by ESBL-producing *Enterobacteriaceae* is an urgent medical need. Because ESBL producers are frequently also resistant to fluoroquinolones and piperacillin/tazobactam the options are scarce. The use of carbapenems is growing, which has led to increased resistance. In 2010, carbapenems were used for more than 8 million patient days of therapy, or DOTs, a number which doubled to 16 million DOTs by 2015. In parallel with this increased utilization, carbapenem-resistant enterobacteriaceae, or CRE, has been observed. Increased use of carbapenems is also associated with a higher rate of carbapenem-resistant Pseudomonas aeruginosa and *Acinetobacter baumannii*.

Penicillin Allergies. It is estimated that 10% of individuals in the United States report having a penicillin allergy which may limit empiric treatment options for serious infections including cIAI. Commonly prescribed alternatives to penicillin include fluoroquinolones, aztreonam or an aminoglycoside. However, these agents do not routinely provide adequate *in vitro* activity against the common Gram-negative pathogens which cause cIAI. Fluoroquinolones, which are the most commonly prescribed class in patients with penicillin allergies, have a black boxed warning due to serious side effects and are also associated with developing *Clostridioides difficile* (formerly known as *Clostridium difficile), or C. difficile*, infection.

Poor Dose Optimization for Renally Impaired. With all beta-lactams, including carbapenems and piperacillin/tazobactam, it is necessary to adjust the dose for patients with renal impairment. This may cause problems with ensuring a patient is receiving an optimal dose when there are rapid changes in renal function associated with serious infections like cIAI. Xerava does not require dose adjustment for renal impairment, simplifying dosing in this setting.

Increased Risk of C. Difficile. Antibiotics are capable of disrupting the normal gut microflora, which can allow for *C difficile* to flourish and produce toxins. *C. difficile* is responsible for 20-30% of antibiotic-associated diarrhea cases and is the most common cause of infectious diarrhea in the healthcare setting. In general, a longer antibiotic duration and multiple antibiotics are two factors that increase the risk of antibiotic-associated *C difficile* diarrhea. Clindamycin carries the highest risk of *C difficile* infection, while fluoroquinolones, cephalosporins and carbapenems carry a fairly high risk,

Complicated and Expensive Multi-Drug Cocktails and Multi-Dose Regimens. Due to gaps in the spectrum of coverage of antibiotics, physicians are often confronted with the need to design complicated multi-drug cocktails for the first-line empiric treatment of patients with serious infections. The clinical situation is further complicated when each drug in the multi-drug cocktail has a different dosing regimen, such as three or four times a day, resulting in an added burden on the pharmacy and nursing staff, higher costs due to multiple drug administrations and an increased potential for medical errors or drug-drug interactions. We believe that, with the exception of Xerava, most of the antibiotics that are in development or have recently been approved by the FDA that are intended to cover a broad range of bacteria, including Gram-negative bacteria, or solely to address Gram-negative bacteria, are being developed or are approved for use in combination with one or more other antibiotics, and require the addition of a third drug such as metronidazole to address the presence of anaerobic bacteria. Multi-drug regimens may also be associated with toxicities not seen with the individual drugs, such as kidney injury, which has been reported when vancomycin and piperacillin/tazobactam are given together.

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, *C. difficile* colitis, nephrotoxicity and gastrointestinal disorders. Furthermore, allergies to beta-lactam antibiotics limit the utility of this class of antibiotics for up to 10% of patients.

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

- Potency and effectiveness against a broad range of bacteria, including MDR Gram-negative, Gram-positive, atypical and anaerobic bacteria;
- Offers an alternative to carbapenems;
- Capability of being used as a monotherapy in the majority of patients in the hospital with cIAI and other MDR infections;
- A convenient dosing regimen, such as once or twice-daily;
- A favorable safety and tolerability profile;
- No required dose adjustments for patients with impaired renal functions;
- No need for therapeutic drug monitoring for any patient group;
- Potent *in vitro* activity against *C. difficile;* and
- Ability to use in patients with penicillin and beta-lactam allergies

Based on our belief that Xerava has each of these characteristics, our goal is to develop Xerava to be the drug of choice for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including MDR Gram-negative infections such as those found in cIAI.

Xerava (Eravacycline)

Overview

We developed Xerava using our proprietary chemistry technology as an IV antibiotic for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including MDR Gram-negative infections such as those found in cIAI. On August 27, 2018, the FDA approved Xerava for the treatment of cIAI in adults. On September 20, 2018, the EC granted marketing authorization for Xerava for the treatment of cIAI in adults in all 28 countries of the EU, Norway, Iceland and Liechtenstein. Approval of Xerava in both the United States and in the EU was based on our IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline) phase 3 program in cIAI. We initiated sales of Xerava in the United States on October 15, 2018. For the year ended December 31, 2019, net sales of Xerava were $3.6 million. We plan to find a partner to commercialize Xerava in the EU.

We received approval for Xerava in the US and EU based on the results of our IGNITE1 and IGNITE4 phase 3 clinical trials evaluating the safety and efficacy of Xerava with IV administration for the treatment of cIAI. In each of IGNITE1 and IGNITE4, Xerava met the primary endpoint of statistical non-inferiority compared to the control therapy for the trial and those trials formed the basis of the approval of Xerava by the FDA for the treatment of cIAI.

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 Xerava, have been able to overcome bacterial resistance in *in vitro* studies.

Xerava is a novel, fully synthetic fluorocycline antibiotic. We selected Xerava for development from tetracycline derivatives that we generated using our proprietary chemistry technology. In designing Xerava, 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 Xerava to not be subject to tetracycline-specific mechanisms of drug resistance. As a result, we believe that Xerava is active against MDR bacteria in ways that tetracyclines currently on the market or in development are not.

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

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

Xerava has also demonstrated strong activity *in vitro* against Gram-positive pathogens, including both nosocomial and community-acquired methicillin susceptible or resistant *Staphylococcus aureus* strains, vancomycin susceptible or resistant *Enterococcus faecium* and *Enterococcus faecalis*, and penicillin-susceptible or resistant strains of *Streptococcus pneumoniae*. In *in vitro* studies of pathogens most prevalent in cIAI infections, Xerava consistently exhibited strong activity against *enterococci* and *streptococci*.

Key Differentiating Attributes of Xerava

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

- **Offers a broad range of activity against a wide variety of MDR Gram-negative, Gram-positive and anaerobic bacteria.** In our phase 2 and phase 3 clinical trials of the IV formulation of Xerava, Xerava demonstrated a high cure rate against a wide variety of MDR Gram-negative, Gram-positive and anaerobic bacteria. In addition, in *in vitro* studies, Xerava demonstrated potent antibacterial activity against Gram-negative bacteria, including ESBL-producing *enterobacteriaceae;* carbapenem-resistant *Enterobacteriaceae (CRE); MCR-1 gene expressing bacteria; Acinetobacter baumannii*, including *carbapenem resistant Acinetobacter (CRAB);* Gram-positive bacteria, including MRSA and vancomycin-resistant *enterococcus*, or VRE; and anaerobic pathogens. As a result, we believe that Xerava has the potential to be used as a first-line empiric monotherapy for the treatment of cIAI and potentially other serious and life-threatening infections.

- **Lower probability of drug resistance.** In the clinical trials and preclinical studies of Xerava that we have conducted for the treatment of cIAI, we have seen little decrease in susceptibility that would suggest increased resistance to Xerava. We believe that, as a fluorocycline, Xerava is not subject to tetracycline-specific mechanisms of drug resistance in certain MDR pathogens.
- **Favorable safety and tolerability profile.** Xerava has been evaluated in over 2,700 subjects in the phase 1, phase 2 and phase 3 clinical trials that we have conducted. In these trials, Xerava has demonstrated a favorable safety and tolerability profile. In our phase 2 and phase 3 clinical trials of Xerava in patients with cIAI, no patients suffered any drug-related serious adverse events, and safety and tolerability were comparable to the respective control therapies for the trials. In the phase 3 clinical trials of Xerava in patients with cUTI, safety and tolerability were comparable to the respective control therapies for these trials. In addition, in these phase 2 and phase 3 clinical trials, the rate at which gastrointestinal adverse events such as nausea and emesis occurred in the Xerava arms was low. Since Xerava is not a beta-lactam, it also offers an alternative treatment for patients with allergies to this commonly used antibiotic class.
- **Lower risk of *C. difficile* colitis.** Xerava, like other tetracycline class antibiotics, has shown activity against *C. difficile* in *in vitro* studies and, therefore, may be associated with a lower risk of *C. difficile* colitis compared with other broad-spectrum antibiotics.
- **Convenient dosing regimen.** In our clinical trials, we have dosed Xerava once or twice a day as a monotherapy. We believe that Xerava will be able to be administered as a first-line empiric monotherapy with 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.
- **No dosage adjustment required for impaired renal function.** Unlike other classes of antibiotics, such as beta-lactams, Xerava does not require dosage adjustment in patients with impaired renal function. In addition to convenience, this ensures that patients with rapidly fluctuating renal function do not have high drug levels, which could lead to toxicity, or low drug levels which could result in loss of efficacy.

Clinical Experience

We have studied IV and oral formulations of Xerava in over 2,700 subjects in 21 clinical trials completed from October 2009 to February 2018.

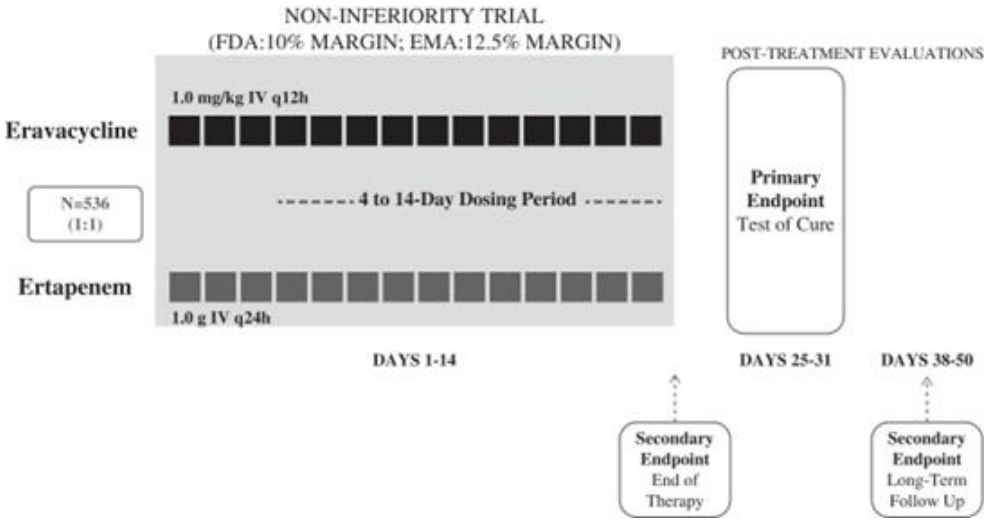
Phase 3 Clinical Program in cIAI

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

Our initial phase 3 clinical trial of Xerava for the treatment of patients with cIAI was our IGNITE1 trial. In December 2014, we announced that Xerava met the primary endpoint of statistical non-inferiority compared to ertapenem in IGNITE1 for the treatment of cIAI. In July 2017, we announced that Xerava met the primary endpoint of statistical non-inferiority compared to meropenem in IGNITE4 for the treatment of cIAI.

IGNITE1

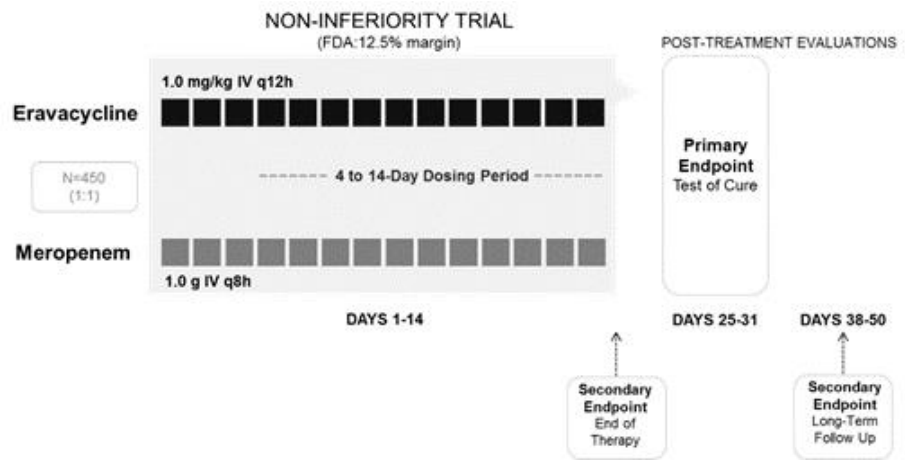
Eravacycline Phase 3 IGNITE1 Study Design



We designed IGNITE1 as a non-inferiority study. Under FDA guidance, the primary endpoint of the trial was clinical response at the test-of-cure, or TOC, visit in the microbiological intent-to-treat, or micro-ITT, population which consisted of all randomized patients in the trial who had baseline bacterial pathogens that cause cIAI and against which Xerava has antibacterial activity. Under EMA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the modified intent-to-treat, or MITT, population which consisted of all patients who received at least one dose of study drug, and in the clinically evaluable, or CE, patient population, which consisted of all randomized patients in the trial who meet key inclusion/exclusion criteria and follow other important components of the trial. We designed the trial to be consistent with the FDA's cIAI guidance, in which the FDA suggested that the primary efficacy endpoint for a trial of cIAI should be complete resolution of baseline signs and symptoms attributable to cIAI in the micro-ITT patient population 28 days after randomization and the absence of clinical failure including death and unplanned surgical procedures through the period ending 28 days following randomization.

In December 2014, we announced top-line data from IGNITE1. In the trial, Xerava met the primary endpoint of statistical non-inferiority of clinical response at the TOC visit, under the guidance set by the FDA and the EMA. The primary analysis under the FDA guidance was conducted using a 10% non-inferiority margin in the micro-ITT population. In the micro-ITT population, the lower and upper bounds of the 95% confidence interval were -7.1% and 5.5%, respectively. Under the EMA guidance, the primary analysis was conducted using a 12.5% non-inferiority margin in the CE and MITT patient populations. In the CE population, the lower and upper bounds of the 95% confidence interval were -6.3% and 2.8%, respectively, and the lower and upper bounds of the 99% confidence interval were -7.9% and 4.4%, respectively. In the MITT population, the lower and upper bounds of the 95% confidence interval were -7.4% and 3.8%, respectively, and the lower and upper bounds of the 99% confidence interval were -9.2% and 5.6%, respectively. The most commonly reported drug-related adverse events for Xerava were gastrointestinal, including nausea (3.3%) and emesis (2.2%). This adverse event profile for Xerava was consistent with that seen in the phase 2 clinical trial of Xerava in cIAI. The spectrum of pathogens in this trial was similar to that seen in other pivotal trials of antibiotics in this patient population. The most common Gram-negative pathogens in the trial included *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas* and *Bacteroides.*

Eravacycline Phase 3 IGNITE4 Study Design



We designed IGNITE4 as a non-inferiority study. Under FDA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the micro-ITT population, which consisted of randomized patients in the trial who had baseline bacterial pathogens that cause cIAI and against which Xerava has antibacterial activity. Under EMA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the MITT population, which consisted of patients in the trial who received at least one dose of study drug, and in the CE patient population, which consisted of patients in the trial who met key inclusion/exclusion criteria and followed other important components of the trial. Secondary endpoints included clinical response at the end-of-treatment, TOC and follow-up visits in the intent-to-treat population, the CE population, the micro-ITT population and the microbiologically evaluable, or ME, population. The ME population consisted of all micro-ITT patients who met key inclusion/exclusion criteria and followed other important components of the trial. In the trial, we also studied microbiologic response at the end-of-treatment and TOC visits in the micro-ITT and ME populations, the safety and tolerability of Xerava in the safety population and pharmacokinetic parameters after Xerava administration.

On July 25, 2017, we announced top-line data from IGNITE4. In the trial, Xerava met the primary endpoint of statistical non-inferiority of clinical response at the TOC visit, under the guidance set by the FDA and the EMA. The primary efficacy analysis under the FDA guidance was conducted using a 12.5% non-inferiority margin in the micro-ITT population. Clinical cure rates in the micro-ITT population were 90.8% and 91.2% for Xerava (n=195) and meropenem (n=205), respectively (95% CI: -6.3%,5.3%). Under the EMA guidance, the primary analysis was conducted using a 12.5% non-inferiority margin of the MITT and CE patient populations. Clinical cure rates in the MITT population were 92.4% and 91.6% for Xerava (n=250) and meropenem (n=249), respectively (95% CI: -4.1%,5.8%). Clinical cure rates in the CE population were 96.9% and 96.1% for Xerava (n=225) and meropenem (n=231), respectively (95% CI: -2.9%,4.5%). The secondary analyses were consistent with, and supportive of, the primary outcome. The most commonly reported drug-related adverse events for Xerava were gastrointestinal, including nausea (2.4%) and emesis (1.6%). This adverse event profile for Xerava was consistent with that seen in the phase 2 clinical trial of Xerava in cIAI. The spectrum of pathogens in this trial was similar to that seen in other pivotal trials of antibiotics in this patient population. The most common Gram-negative pathogens in the trial included *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas* and *Bacteroides.*

Product Pipeline

We have developed three additional product candidates - TP-6076, a fully-synthetic fluorocycline derivative designed to target unmet medical needs, including MDR Gram-negative bacteria such as *Acinetobacter baumannii*; TP-271 is a fully-synthetic, broad-spectrum fluorocycline, for the treatment of respiratory diseases caused by bacterial biothreat pathogens; and TP-2846 a fully-synthetic tetracycline that we are developing for the treatment of AML. In June 2019, we determined to cease all work relating to these product candidates, including conducting any additional pre-clinical or clinical trials for any of these product candidates due to a lack of human and financial resources. We are seeking to outlicense each of these product candidates.

Sales and Marketing

We have established a targeted commercial organization in the United States to support the launch of Xerava in the United States. As of March 3, 2020, we had approximately 27 sales representatives, 3 regional business directors, 3 strategic market access executives and 7 medical affairs personnel supporting Xerava. Our sales force has on average 25 years of hospital sales experience and launching antibiotics. We also have tenured and focused marketing and sales operations teams located at our headquarters in Watertown, Massachusetts.

Our commercialization strategy is to develop Xerava into a first-line empiric monotherapy for the treatment of multidrug-resistant infections, including MDR Gram-negative infections such as those found in cIAI. We have retained worldwide commercial rights to all of our product candidates other than Xerava in China and other Asian territories. We exclusively licensed our commercial rights to Xerava in China and other Asian territories to Everest Medicines Limited in February 2018. In the future we may enter into additional regional licensing transactions similar to the Everest license agreement. We intend to retain control over the commercial execution of Xerava and any product candidate in the United States. We plan to seek a partner to commercialize Xerava in the EU.

Manufacturing and Supply

We do not own or operate manufacturing facilities for the production of Xerava or any of our product candidates, nor do we have plans to develop our own manufacturing operations in the foreseeable future. Xerava and our product candidates are organic compounds of low molecular weight, commonly referred to as small molecules. They are manufactured in a fully synthetic process from readily available starting materials.

We currently rely on a limited number of third-party contract manufacturers for all of our required raw materials, drug substance and finished product for our preclinical research and clinical trials. We do not have long-term agreements with any of these third parties other than with respect to our agreements with third-party contract manufacturers for the commercial production of Xerava. We currently employ internal resources to manage our third-party manufacturing relationships.

Patheon UK Limited Master Manufacturing Services Agreement

In June 2017, we and Patheon UK Limited and certain of its affiliates, or Patheon, entered into a master manufacturing services agreement, or the Patheon agreement. Under the Patheon agreement, we are responsible for supplying the active pharmaceutical ingredient for Xerava to Patheon, and Patheon is responsible for manufacturing Xerava, conducting quality control, quality assurance, analytical testing and stability testing and packaging. We entered into two related product agreements pursuant to the Patheon agreement that govern the terms and conditions of Patheon's manufacture of commercial supplies of Xerava at Patheon's Greenville, North Carolina and Ferentino, Italy manufacturing sites. Each product agreement is governed by the terms of the Patheon agreement, unless expressly modified in such product agreement. Pursuant to the Patheon agreement, we have agreed to order from Patheon at least a certain percentage of our annual commercial requirements for Xerava in the United States and European Union each year for the term of the Patheon agreement.

Under the Patheon agreement, we are required to submit to Patheon by a date in June of a calendar year the forecast for the following two years that sets forth the total quantity of Xerava commercial supply that we expect to order from Patheon during that period. Patheon has no obligation to manufacture the Xerava commercial supply in accordance with any forecast which is increased by a certain percentage above the previously forecast amount.

The Patheon agreement has an initial term ending December 31, 2022, and will automatically renew after the initial term for successive terms of two years each, unless either party gives notice of its intention to terminate at least 18 months prior to the end of the then current term. We may terminate a product agreement upon 30 days' prior written notice if any governmental agency takes any action that prevents us from importing, exporting, purchasing or selling Xerava. Either party may terminate the Patheon agreement or a product agreement (a) upon written notice if the other party has failed to remedy a material breach under the Patheon agreement or a product agreement within a specified time following receipt of written notice of such breach, and (b) immediately upon written notice to the other party in the event that the other party is declared insolvent or bankrupt, a voluntary petition of bankruptcy is filed in any court by such other party or the Pantheon agreement or a product agreement is assigned by such other party for the benefit of creditors. Patheon may terminate the Patheon agreement or a product agreement upon six months written notice if we assign the Patheon agreement to an assignee that, in the opinion of Patheon acting reasonably, is (i) not a creditworthy substitute for us or (ii) a competitor of Patheon.

The Patheon agreement contains, among other provisions, customary representations and warranties by the parties, a grant to Patheon of certain limited license rights to our intellectual property in connection with Patheon's performance of the services under the Patheon agreement, certain indemnification rights in favor of both parties, limitations of liability and customary confidentiality provisions.

Finorga SAS Commercial Supply Agreement

In October 2017, we and Finorga SAS, or Novasep, entered into a Commercial Supply Agreement, or the Novasep agreement. Under the Novasep agreement, Novasep will, pursuant to accepted purchase orders entered into under the Novasep agreement, manufacture for commercial supply the active pharmaceutical ingredient, or API, for Xerava for us.

Under the Novasep agreement, we will submit to Novasep on a periodic basis on or before the first business day of each calendar quarter a rolling forecast for a certain time period that sets forth the total quantity of the API for Xerava for commercial supply that we either have ordered, desire to order or expect to order from Novasep. A certain time period of each such forecast is binding on us and constitutes a "firm order". The remainder of each forecast will be for planning purposes only and will not be binding. Novasep has no obligation to manufacture the API for Xerava in accordance with any forecast that is not the subject of a firm order and which is increased by a certain percentage above the previously forecast amount.

The Novasep agreement has an initial term ending October 16, 2022, and will automatically renew after the initial term, unless either party gives notice of its intention to terminate at least 18 months prior to the end of the then current term. We may terminate the Novasep agreement upon 30 days' prior written notice (a) if any regulatory authority takes any action, or raises any objection, that prevents us from importing, exporting, purchasing or selling the API for Xerava, or (b) in the event that Novasep experiences a force majeure event. Either party may terminate the Novasep agreement (a) upon written notice if the other party has failed to remedy a material breach under the Novasep agreement within a specified time following receipt of written notice of such breach, and (b) immediately upon written notice to the other party in the event the other party makes a general assignment for the benefit of its creditors, or proceedings of a case are commenced in any court of competent jurisdiction by or against the other party seeking (i) such party's reorganization, liquidation, dissolution, arrangement or winding up, or the composition or readjustment of its debts, (ii) the appointment of a receiver or trustee for or over such party's property, or (iii) similar relief in respect of such party under any law relating to bankruptcy, insolvency, reorganization, winding up or composition or adjustment of debt, and such proceedings shall continue undismissed, or an order with respect to the foregoing shall be entered and continue unstayed, for a period of more than 60 days.

The Novasep agreement contains, among other provisions, customary representations and warranties by the parties, a grant to Novasep of certain limited license rights to the Company's intellectual property in connection with Novasep's performance of the services under the Novasep agreement, certain indemnification rights in favor of both parties, limitations of liability and customary confidentiality provisions.

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 25, 2020, we owned 12 U.S. patents, 81 foreign patents, eight pending U.S. patent applications, one pending application filed under the Patent Cooperation Treaty, or PCT, and 65 pending foreign patent applications in Europe and 20 other jurisdictions. The PCT is an international patent law treaty that provides a unified procedure for filing a single initial patent application for an invention simultaneously in each of the member states. Although a PCT application is not itself examined and cannot issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications. In addition, we have exclusively licensed from Harvard University rights under 12 U.S. patents, 34 foreign patents, two pending U.S. patent application and six pending foreign patent applications in Europe and ten other jurisdictions. Certain of our patents and patent applications are directed to the composition of matter and/or use of Xerava and patents have granted, or applications are pending in the United States, Europe, Japan and other countries.

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

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

We have filed applications for Supplementary Protection Certificates (SPCs) based on European Patent No. 2323972 directed to the composition of matter and use of Xerava. Some applications have granted and others are pending.

We have a pending U.S patent application and pending foreign patent applications directed to crystalline forms of Xerava. Any patents that may issue based on the pending applications will have an expiration date no earlier than 2037.

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 2037.

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 Xerava and other tetracycline derivatives. The key intermediates that enable our fully synthetic process are commonly referred to as enone intermediates. The licensed patents and patent applications are directed towards the composition of matter of enone intermediates and compounds used to make the enone intermediates, referred to as key precursors, as well as synthetic routes to those enone intermediates, precursors and our tetracycline derivatives under development.

Composition of matter for the enone intermediates and precursors used in preparing the enone intermediates, and methods of making the precursors and enone intermediates are covered by the U.S. patents we license from Harvard, which will expire no earlier than 2025, not 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 also expire or will expire no earlier than 2025.

Exclusively Licensed Intellectual Property Relating to Pentacycline and Tetracycline Derivatives

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

Patent Term and Patent Term Extensions

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

Trademark Applications Relating to the Company Nam, Logo and Xerava Product

As of February 19, 2020, TETRAPHASE PHARMACEUTICALS, our logo, and combinations of those are registered in the United States. TETRAPHASE PHARMACEUTICALS is either registered or pending in twelve other jurisdictions, the logo is pending or registered in the same twelve jurisdictions, the combination of the name and logo is pending in three of those jurisdictions, and two TETRAPHASE PHARMACEUTICALS Chinese character marks are registered in China. We own a trademark registration in the United States for Xerava, the proprietary name for the Xerava product.

Trade Secrets

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

Third-Party License Agreements

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 Xerava. Under the license agreement, we also have the right to expand the patent rights subject to the license to include improvement patents that may be owned by Harvard in the future and that meet specified criteria by paying to Harvard an additional license issuance fee in an amount to be agreed between Harvard and us. We also have a right of negotiation to expand the license to include additional patents relating to tetracycline chemistry within a specified category that may be owned by Harvard in the future, including patents covering inventions made by Andrew Myers, Ph.D., our scientific founder, under his consulting agreement with us. Since entering into the license agreement, we have entered into amendments to the license agreement pursuant to which we expanded the patent rights subject to the license in accordance with these rights. Under the license agreement, we are obligated to satisfy diligence requirements, including using commercially reasonable efforts to develop and commercialize licensed compounds and to implement a specified development plan, meeting specified development milestones and providing an update on progress on an annual basis. Our license grant from Harvard is subject to academic rights retained by Harvard and United States government rights and obligations that are customary in patent license agreements with universities in the United States.

In consideration for the rights granted to us by Harvard under the license agreement, as of December 31, 2019, we have paid Harvard an aggregate of $16.8 million in upfront license fees, sublicense fees and development milestone payments and issued 1,568 shares of our common stock to Harvard. We have also 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 ($12.6 million of which has already been paid with respect to Xerava), 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 in certain circumstances. We are also obligated to pay Harvard a specified share of non-royalty sublicensing and other revenues that we receive from sublicensees for the grant of sublicenses under the license in certain circumstances, and to reimburse Harvard for specified patent prosecution and maintenance costs.

The Harvard 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

Xerava

We received funding for Xerava under an award from 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 to CUBRC, Inc., or CUBRC, an independent, not-for-profit, research corporation that specializes in United States government-based contracts, with which we collaborated, a five-year contract that provided a total of up to $67.3 million in funding. The BARDA Contract contemplated that CUBRC would collaborate with us on the development, manufacturing and clinical evaluation of a novel tetracycline antibiotic with potential as an empiric countermeasure for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including *Francisella tularensis*, which causes tularemia, *Yersinia pestis*, which causes plague, and *Bacillus anthracis*, which causes anthrax disease, as well as bacterial pathogens associated with moderate-to-severe CABP and other serious hospital infections. The BARDA Contract also provided funding for certain activities in the development of Xerava to treat certain infections caused by life-threatening multidrug-resistant bacteria. In connection with the BARDA Contract, in February 2012, we entered into a cost-plus-fixed-fee subcontract with CUBRC under which we received $41.3 million to fund specific work performed by us related to Xerava.

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 served as lead technical experts on all aspects of the BARDA Contract and served as a subcontractor of CUBRC responsible for management of chemistry, manufacturing and control activities and clinical studies. The terms of the subcontract between us and CUBRC expired on December 31, 2019.

TP-6076

Our program to develop TP-6076 was partially covered by an award from Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, or CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance. In March 2017, CARB-X selected the Company to receive up to $4.0 million in research funding over eighteen months for TP-6076. In connection with this funding, the Company entered into a cost reimbursement Sub-Award Agreement with the Trustees of Boston University, the administrator of the program. The Sub-Award Agreement expired on June 30, 2019. The Company received payments totaling $3.2M during the life of this award. Our obligations under this Sub-Award Agreement have been met in full as of December 31, 2019.

TP-271

Our program to develop TP-271 was funded by the National Institute of Allergy and Infectious Diseases, or NIAID, a division of the National Institutes of Health, through the NIAID Contract, an agreement that provided $35.8 million in funding that NIAID awarded to CUBRC in October 2011. The NIAID Contract contemplated that CUBRC would collaborate with us on the development, manufacturing and clinical evaluation of a novel broad-spectrum tetracycline antibiotic for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, including *Francisella tularensis*, *Yersinia pestis* and *Bacillus anthracis*, as well as bacterial pathogens associated with CABP.

In connection with the NIAID Contract, in October 2011, we entered into a subcontract with CUBRC under which we received funding of $16.3 million, reflecting the portion of the NIAID Contract funding that was paid to us for our activities. The term of the NIAID subcontract expired on March 31, 2019. Our obligations under the NIAID Contract had been met in full as of December 31, 2019.

Collaborations

In February 2018, we entered into a license agreement, which we call the Everest license agreement, with Everest Medicines Limited, or Everest Medicines, whereby we granted Everest Medicines an exclusive license to develop and commercialize eravacycline, for the treatment of cIAI and other indications, in mainland China, Taiwan, Hong Kong, Macau, South Korea and Singapore, or the territory.

Under the terms of the Everest license agreement, we received from Everest Medicines an upfront cash payment of $7.0 million and are entitled to receive up to an aggregate of $16.5 million in clinical development and regulatory milestone payments and up to $20.0 million provided that certain sales thresholds are met. Through December 31, 2019, we have received $5.5 million from Everest Medicines in clinical development and regulatory milestones. There can be no guarantee that any such milestones or sales thresholds will in fact be met. We are obligated to make certain payments to Harvard based on amounts received from Everest Medicines under the Everest license agreement pursuant to the existing license agreement by and between Harvard and us.

In addition, on July 29, 2019, we amended our original agreement with Everest Medicines to extend Everest Medicines' exclusive license to develop and commercialize Xerava to the jurisdictions of the Malaysian Federation, the Kingdom of Thailand, the Republic of Indonesia, the Socialist Republic of Vietnam and the Republic of the Philippines. Under the terms of this amendment, we received from Everest Medicines an upfront, nonrefundable cash payment of $2.0 million in September 2019. As with the milestones discussed above, we were obligated to make certain payments to Harvard based on amounts received from Everest under this amendment pursuant to the existing license agreement by and between Harvard and us. During the fourth quarter of 2019, we paid Harvard $0.4 million related to this milestone.

We will also be entitled to receive double-digit tiered royalties on sales in the territory, if any, of products containing eravacycline. Royalties are payable with respect to each jurisdiction in the territory until the latest to occur of: (i) the last-to-expire of specified patent rights in such jurisdiction in the territory; (ii) expiration of marketing or regulatory exclusivity in such jurisdiction in the territory; or (iii) ten (10) years after the first commercial sale of a product in such jurisdiction in the territory. In addition, royalties payable under the Everest license agreement will be subject to reduction on account of generic competition and after patent expiry in a jurisdiction if required by applicable law, with any such reductions capped at certain percentages of the amounts otherwise payable during the applicable royalty payment period.

Under the terms and conditions of the Everest license agreement, Everest Medicines will be solely responsible for the development and commercialization of licensed products in the territory.

If either we or Everest Medicines materially breaches the Everest license agreement and does not cure such breach within 90 days (or fewer days in certain cases), the non-breaching party may terminate the Everest license agreement in its entirety. However, if the breach relates only to any jurisdiction other than mainland China, the non-breaching party may only terminate the Everest license agreement with respect to such jurisdiction. Either party may also terminate the Everest license agreement, effective immediately upon written notice, if the other party files for bankruptcy, is dissolved or has a receiver appointed for substantially all of its property. We may terminate the Everest license agreement if Everest Medicines, its affiliates or its sublicensees challenges the validity or enforceability of any of our patents covering any of the licensed compounds or products. In certain circumstances, if we materially breach the Everest license agreement Everest Medicines may reduce royalties owed to us in lieu of a termination. Moreover, if we materially breach the Everest license agreement and Everest Medicines terminates the Everest license agreement with respect to any jurisdiction and we then commercializes a licensed product in that jurisdiction, we will pay to Everest Medicines a low, single digit royalty on such sales of the licensed product in such jurisdiction for a minimum of five years after such termination.

Competition

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

We believe the key competitive factors that may affect the commercial success of Xerava for the treatment of cIAI are; efficacy, coverage of drug-resistant strains of bacteria, safety and tolerability profile, convenience of dosing, price, and the availability of reimbursement from governmental and other third-party payers. Outside factors that may affect the commercial success of Xerava are increased resistance trends, changes in the reimbursement landscape, and the approval/availability of rapid diagnostics.

We are selling Xerava as an IV antibiotic for use as a first-line empiric monotherapy for the treatment of cIAI. Xerava competes with a number of antibiotics that are currently marketed for the treatment of cIAI and other multidrug resistant infections, including meropenem, which is marketed by AstraZeneca as Merrem, imipenem/cilastatin, which is sold by Merck & Co., or Merck, as Primaxin, tigecycline, which was marketed by Pfizer as Tygacil, piperacillin/tazobactam, which is marketed by Pfizer as Zosyn, ceftolozane/tazobactam and imipenem/relebactam, which are marketed by Merck as Zerbaxa and Recarbrio, and ceftazidime/avibactam, which is marketed by Allergan, Inc. as Avycaz, meropenem and vaborbactam, which is marketed by Melinta Therapeutics as Vabomere, We also expect that Xerava will compete with future and current generic versions of marketed antibiotics.

We believe that Xerava may compete effectively against these compounds on the basis of:

- broad range of activity against a wide variety of resistant and MDR Gram-negative, Gram-positive and anaerobic bacteria;
- lower probability of drug resistance;
- a favorable safety and tolerability profile;
- effectiveness in patients with allergies to beta-lactam;
- a convenient dosing regimen with no need for adjustment for renal impairment;
- lower risk of *C. Difficile*;
- approval as a monotherapy; and
- no drug to drug interactions.

Government Regulation and Product Approval

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

U.S. Government Regulation

In the United States, the FDA regulates drugs and drug products 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 United States 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 new drug applications, or NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil and/or criminal penalties.

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA for a drug product which includes not only the results of the clinical trials but also detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- payment of user fees and FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

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

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

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an NDA. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides recommendations as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

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

Human Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial along with the requirement to ensure that the data and results reported from the clinical trials are credible and accurate. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the criteria for determining subject eligibility, the dosing plan, the parameters to be used in monitoring safety, the procedure for timely reporting of adverse events, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB representing each clinical site participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that site. The FDA may impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. 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 a limited number of healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness. During phase 1 clinical trials, sufficient information about the investigational drug's or biological product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid phase 2 clinical trials.
- Phase 2: The drug is administered to a larger, but still limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted indications and to determine dosage tolerance and optimal dosage. Phase 2 clinical trials are typically well-controlled and closely monitored.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product. Phase 3 clinical trials usually involve a larger number of participants than a phase 2 clinical trial.

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting phase 4 clinical trials could result in withdrawal of approval for products.

Progress reports detailing the status and a brief description of available results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, phase 2 and phase 3 clinical trials may not be completed successfully within any specified period or completed 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, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Marketing Approval

Assuming successful completion of the required clinical testing and other requirements, 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. 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.

Furthermore, the FDA is not required to complete its review within the established ten-month timeframe and may extend the review process by issuing requests for additional information or clarification.

In addition, under the Pediatric Research Equity Act of 2003, as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

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

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, 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 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 typically 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 or will be 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 GCP and the FDA is able to validate the data through an on-site inspection, if deemed necessary. The FDA also expects an explanation of how the foreign data are applicable to the United States population and United States medical practice.

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 a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications, and potentially subject to additional restrictions such as a REMS. A complete response letter generally contains a statement of specific deficiencies in the NDA and conditions that must be met in order to secure final approval of the NDA, which 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.

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, certain manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Special FDA Expedited Review and Approval Programs

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

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need, or if the drug qualifies as a QIDP under the recently enacted 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 in a number of different ways. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted.

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

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, meaning that it may be approved on (1) the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or (2) on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to expedited withdrawal procedures.

Moreover, under the provisions of the 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. The benefits of breakthrough therapy designation include much of the same benefits as fast track designation, plus intensive guidance from FDA to ensure an efficient drug development program and organizational commitment involving senior FDA managers.

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.

Limited Population Antibacterial Drug Pathway

With passage of the Cures Act, Congress authorized the FDA to approve an antibacterial or antifungal drug, alone or in combination with one or more other drugs, as a "limited population drug." To qualify for this approval pathway, the drug must be intended to treat a serious or life-threatening infection in a limited population of patients with unmet needs; the standards for approval of drugs and biologics under the FDCA and the Public Health Service Act, or PHSA, must be satisfied; and the FDA must receive a written request from the sponsor to approve the drug as a limited population drug pursuant to this provision. The FDA's determination of safety and effectiveness for such a product must reflect the benefit-risk profile of such drug in the intended limited population, taking into account the severity, rarity, or prevalence of the infection the drug is intended to treat and the availability or lack of alternative treatment in such a limited population.

Any drug or biologic approved under this pathway must be labeled with the statement "Limited Population" in a prominent manner and adjacent to the proprietary name of the drug or biological product. The prescribing information must also state that the drug is indicated for use in a limited and specific population of patients and copies of all promotional materials relating to the drug must be submitted to the FDA at least 30 days prior to dissemination of the materials. If the FDA subsequently approves the drug for a broader indication, the agency may remove any post-marketing conditions, including requirements with respect to labeling and review of promotional materials applicable to the product. Nothing in this pathway to approval of a limited population drug prevents sponsors of such products from seeking designation or approval under other provisions of the FDCA, such as accelerated approval.

Post-Approval Regulation

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 record keeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, many changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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

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

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

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

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

- restrictions on, or suspensions of, the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- interruption of production processes, including the shutdown of manufacturing facilities or production lines or the imposition of new manufacturing requirements;
- warning letters or other enforcement letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil penalties or criminal prosecution.

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

Abbreviated New Drug Applications for Generic Drugs

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

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

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval.

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

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

Hatch-Waxman Patent Certification and the 30-Month Stay

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

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

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

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

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

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

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. A sponsor must request such designation before submitting a marketing application. We obtained a QIDP designation for the IV formulation of Xerava for cIAI in July 2013, the oral formulation in March 2014, the IV formulation of TP-271 in September 2015, the oral formulation of TP-271 in February 2017, and expect to request QIDP designations for our other product candidates prior to submitting a marketing application for such product candidates, as appropriate.

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

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

Pediatric Studies and Exclusivity

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

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of an applicant, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, FDA will meet early in the development process to discuss pediatric study plans with sponsors and FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than 90 days after FDA's receipt of the study plan.

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

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

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

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials, marketing authorization, safety reporting 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 EU, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product authorization, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under EU regulatory systems, a company may submit an application for marketing authorization through several different procedures. These are the centralized, mutual recognition procedure, decentralized procedure, or national procedure (single EU Member State). The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases and designated orphan medicinal products. The centralized marketing authorization procedure is optional for medicinal products containing a new active substance that is not yet authorized in the EEA or for products that constitute a significant therapeutic, scientific or technical innovation or for which grant of centralized marketing authorization is in the interest of patients in the EU. Under the centralized procedure, an application for marketing authorization is submitted to the European Medicines Agency, or EMA, 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 and three of the four European Free Trade Association, or EFTA, countries (Iceland, Liechtenstein and Norway). The initial marketing authorization is valid for five years. The authorization may be renewed and remain valid for an unlimited period unless the national competent authority or the European Commission decides on justified grounds to proceed with one additional five-year renewal period. The renewal of a marketing authorization is subject to a re-evaluation of the risk-benefit balance of the product by the national competent authorities or the EMA. The decentralized authorization procedure permits companies to file identical applications for authorization simultaneously in several EU Member States for a medicinal product that has not yet been authorized in any EU Member State. The competent authorities of a single EU Member State, the reference member state, is appointed to review the application and provide an assessment report. The competent authorities of the other EU Member States, the concerned member states, are subsequently required to grant marketing authorization for their territories on the basis of this assessment. The only exception to this is where an EU Member State considers that there are concerns of potential serious risk to public health related to authorization of the product. In these circumstances, the matter is submitted to the Heads of Medicines Agencies, or CMDh for review. The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States.

In the EU, innovative medicinal products that are subject to marketing authorization on the basis of a full dossier qualify for eight years of data exclusivity from the data of marketing authorization and 10 years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the data of authorization of the innovative product. After this period an application for marketing authorization for a generic or biosimilar product may be submitted, and the innovator's data may be referenced. However, even if authorization is granted in relation to the generic product or biosimilar product this product cannot be marketed in the EU until 10 years after grant of authorization for the innovative product. The ten year market exclusivity period may be extended for a further year to a maximum of 11 years if, during the first eight years following authorization of the innovative product, authorization is granted for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

The holder of an EU marketing authorization for a medicinal product must comply with EU pharmacovigilance legislation. This includes requirements to conduct pharmacovigilance, and to assess and monitor the safety of medicinal products.

Various requirements apply to the manufacturing and placing of medicinal products on the EU market. Manufacture of medicinal products in the EU requires a manufacturing authorization. The manufacturing authorization holder must comply with requirements set out in the applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and APIs. These obligations extend to the manufacture of APIs outside of the EU for import into the EU. Similarly, the distribution of medicinal products into and within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of the EU Member States. Marketing authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

In the EU, the advertising and promotion of medicinal products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. Breaches of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of medicinal products to the general public and may also impose limitations on promotional activities with healthcare professionals.

Similar to the United States, the various phases of non-clinical and clinical research in the EU are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU Member States have transposed and applied the provisions of the Directive in a manner that is often not uniform. This has led to variations in the rules governing the conduct of clinical trials in the individual EU Member States. The EU legislator adopted Regulation (EU) No 536/2014, or the Clinical Trials Regulation in 2014. The new EU Clinical Trials Regulation, which will replace the EU Clinical Trials Directive, introduces a complete overhaul of the existing regulation of clinical trials for medicinal products in the EU, including a new coordinated procedure for authorization of clinical trials that is reminiscent of the mutual recognition procedure for marketing authorization of medicinal products, and increased obligations on sponsors to publish clinical trial results. The Clinical Trials Regulation is expected to start to apply in late 2019 or in 2020.

Clinical trials must currently be conducted in accordance with the requirements of the EU Clinical Trials Directive and applicable good clinical practice standards, as implemented into national legislation by EU Member States. Under the current regime, before a clinical trial can be initiated it must be approved in each of EU Member State where there is a site at which the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial must be reported to the NCA and ECs of the Member State where they occurred.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Pharmaceutical Insurance Coverage and Reimbursement

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

The containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The United States 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, the federal government provides health insurance for people who are 65 or older, and certain people with disabilities or certain conditions irrespective of their age, through the Medicare program, which is administered by the Centers for Medicare & Medicaid Services, or CMS. Coverage and reimbursement for products and services under Medicare are determined in accordance with the Social Security Act and pursuant to regulations promulgated by CMS, as well as the agency's subregulatory coverage and reimbursement guidance and determinations.

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

In the United States, there have been and continue to be a number of federal and state legislative and regulatory initiatives to expand health care coverage, improve health care quality, and contain health care costs, which could impact our ability to sell our products profitably. For example, the federal Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, known collectively as ACA, substantially changes the way health care is financed by United States governmental and commercial payors, and significantly affects the United States pharmaceutical industry. Among other things, the ACA establishes annual fees and taxes to be paid by manufacturers of certain branded prescription drugs; creates a new Medicare Part D coverage gap discount program, under which, as a condition of coverage of their products under Medicare Part D, manufacturers currently must agree to offer 70% point-of-sale discounts off of negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period; increases manufacturer rebate liabilities under the Medicaid Drug Rebate Program for outpatient drugs dispensed to Medicaid recipients; addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are injected, inhaled, infused, instilled, or implanted, and for line extensions of current drugs; and expands oversight and support for the federal government's comparative effectiveness research of services and products.

Some of the provisions of the ACA have yet to be fully implemented, and certain provisions have been subject to judicial or Congressional challenges. In addition, there have been efforts by the Trump Administration to repeal or replace certain aspects of the ACA, and to alter the implementation of the ACA and related laws. And legislation affecting implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed into law a continuing resolution on appropriations for fiscal year 2018 that, among other things, delayed the implementation of certain ACA-mandated fees, including the annual fee imposed on certain high-cost employer-sponsored health plans, commonly referred to as the "Cadillac" health plan tax; the annual fee imposed on certain health insurance providers based on market share; and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare prescription drug plans, commonly referred to as the "donut hole." Additional legislative changes, regulatory changes, and judicial challenges related to the ACA remain possible. It is unclear how the ACA and its implementation, as well as efforts to repeal or replace, or invalidate, the ACA, or portions thereof, will affect our business. We participate in and have certain price reporting obligations to the Medicaid Drug Rebate Program and other governmental pricing programs, and we have obligations to report the average sales price for certain of our drugs to the Medicare program. The Medicaid Drug Rebate Program and other governmental programs impose obligations to report pricing figures to the federal government and we are subject to these price reporting and other compliance obligations. Other programs impose limits on the price we are permitted to charge certain entities for our products. Statutory and regulatory changes or other agency action regarding these programs and their requirements could negatively affect the coverage and reimbursement by these programs of our products and could negatively impact our results of operations.

Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having federal funds being made available to the state for our drugs under Medicaid and Medicare Part B. Those rebates are based on pricing data reported by us on a monthly and quarterly basis to CMS, the federal agency that administers the Medicare and Medicaid programs. These data include the average manufacturer price and, in the case of innovator products, the best price for each drug, which, in general, represents the lowest price available from the manufacturer to any entity in the United States in any pricing structure, calculated to include all sales and associated rebates, discounts, and other price concessions. The ACA made significant changes to the Medicaid Drug Rebate program, and CMS issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate Program under the ACA. Our failure to comply with these price reporting and rebate payment options could negatively impact our financial results.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the Public Health Service's 340B drug pricing discount program in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B drug pricing program, which is administered by the Health Resources and Services Administration, or HRSA, requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. These 340B covered entities include a variety of community health clinics and other entities that receive health services grants from the Public Health Service, as well as hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. Changes to the definition of average manufacturer price and the Medicaid Drug Rebate amount under the ACA or otherwise also could affect our 340B ceiling price calculations and negatively impact our results of operations.

HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. HRSA also has announced that it will begin to implement a ceiling price reporting requirement related to the 340B program during the first quarter of 2019. It is currently unclear how HRSA will apply its enforcement authority under the new regulation. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Federal law also requires that a company that participates in the Medicaid Drug Rebate Program report average sales price information each quarter to CMS for certain categories of drugs that are paid under the Medicare Part B program. Manufacturers calculate the average sales price based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. CMS uses these submissions to determine payment rates for drugs under Medicare Part B. Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for our products and the resulting Medicare payment rate, and could negatively impact our results of operations. Also, the Medicare Part B drug payment methodology is subject to change based on potential demonstration projects undertaken by CMS or potential legislation enacted by Congress.

Pricing and rebate calculations vary across products and programs, are complex and are often subject to interpretation by us, governmental or regulatory agencies and the courts. The Medicaid rebate amount is computed each quarter based on our submission to CMS of our average manufacturer prices and best prices for the quarter. If we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations would increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price under the 340B program.

We could be held liable for errors associated with our submission of pricing data. Civil monetary penalties can be applied if we are found to have knowingly submitted any false price information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. Such conduct also could be grounds for CMS to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. We cannot assure you that our submissions will not be found by CMS to be incomplete or incorrect.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we participate in the U.S. Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. Under this program, we are obligated to make our innovative products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price to certain federal agencies that is no higher than the statutory Federal Ceiling Price, or FCP. The FCP is based on the non-federal average manufacturer price, or Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. Risks relating to price reporting and payment obligations under the foregoing programs are further discussed in the risk factor under the heading, "If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects."

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, in the EU, the sole legal instrument at the EU level governing the pricing and reimbursement of medicinal products is Council Directive 89/105/EEC, or the Price Transparency Directive. The aim of this Directive is to ensure that pricing and reimbursement mechanisms established in the EU Member States are transparent and objective, do not hinder the free movement of and trade in medicinal products in the EU, and do not hinder, prevent or distort competition on the market. The Price Transparency Directive does not provide any guidance concerning the specific criteria on the basis of which pricing and reimbursement decisions are to be made in individual EU Member States, nor does it have any direct consequence for pricing or reimbursement levels in individual EU Member States. The EU Member States are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement, and to control the prices and/or reimbursement levels of medicinal products for human use. An EU Member State may approve a specific price or level of reimbursement for the medicinal product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the medicinal product on the market, including volume-based arrangements, caps and reference pricing mechanisms.

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

On January 31, 2018, the European Commission adopted a proposal for a regulation on HTA. This legislative proposal is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The proposal provides that EU Member States will be able to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement. The European Commission has stated that the role of the draft HTA regulation is not to influence pricing and reimbursement decisions in the individual EU Member States. However, this consequence cannot be excluded.

Healthcare Fraud and Abuse Laws

Healthcare providers, physicians, distributors and third-party payors play a primary role in the distribution, recommendation and prescription of our products. Our arrangements with third-party payors and customers expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements through which we market, sell and distribute our products. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- The United States federal healthcare Anti-Kickback Statute prohibits any person from, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchasing, leasing, ordering or arranging for or recommending of any good or service for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute is subject to evolving interpretation and has been applied by government enforcement officials to a number of common business arrangements in the pharmaceutical industry. The government can establish a violation of the Anti-Kickback Statute without proving that a person or entity had actual knowledge of the statute or specific intent to violate it. There are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution; however, those exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. We seek to comply with the available statutory exemptions and safe harbors whenever possible, but our practices may not in all cases meet all of the criteria for safe harbor protection from anti-kickback liability. Moreover, there are no safe harbors for many common practices, such as educational and research grants or patient or product assistance programs.
- The federal civil False Claims Act prohibits, among other things, knowingly presenting, or causing to be presented, claims for payment of government funds that are false or fraudulent, or knowingly making, or using or causing to be made or used, a false record or statement material to a false or fraudulent claim to avoid, decrease, or conceal an obligation to pay money to the federal government. Private individuals, commonly known as "whistleblowers," can bring civil False Claims Act *qui tam* actions, on behalf of the government and such individuals and may share in amounts paid by the entity to the government in recovery or settlement. In recent years, several pharmaceutical and other healthcare companies have faced enforcement actions under the federal False Claims Act for, among other things, allegedly submitting false or misleading pricing information to government health care programs and providing free product to customers with the expectation that the customers would bill federal programs for the product. Federal enforcement agencies also have showed increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement and co-pay support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. Other companies have faced enforcement actions for causing false claims to be submitted because of the company's marketing the product for unapproved, and thus non-reimbursable, uses. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and significant mandatory penalties per false claim or statement for violations. Because of the potential for large monetary exposure, healthcare and pharmaceutical companies often resolve allegations without admissions of liability for significant and material amounts to avoid the uncertainty of treble damages and per claim penalties that may be awarded in litigation proceedings. Companies may be required, however, to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance. Criminal penalties, including imprisonment and criminal fines, are also possible for making or presenting a false, fictitious or fraudulent claim to the federal government.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, fraud provisions, among other things, impose criminal and civil liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors. HIPAA also prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement or representation, or making or using any false writing or document knowing the same to contain any materially false fictitious or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal healthcare Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

- The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program, requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the United States Department of Health and Human Services, Centers for Medicare and Medicaid Services, information related to payments and other transfers of value, directly or indirectly, to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. A manufacturer's failure to submit timely, accurately and completely the required information for all payments, transfers of value or ownership or investment interests may result in civil monetary penalties of up to an aggregate of $150,000 per year, and up to an aggregate of $1 million per year for "knowing failures." Manufacturers must submit reports by the 90th day of each calendar year.

Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payors, including private insurers or patients. Several states also require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products in those states and to report gifts and payments to individual health care providers in those states. Some of these states also prohibit certain marketing-related activities, including the provision of gifts, meals, or other items to certain health care providers, and restrict the ability of manufacturers to offer co-pay support to patients for certain prescription drugs. Some states require the posting of information relating to clinical studies and their outcomes. Some states and cities require identification or licensing of sales representatives. In addition, several states require pharmaceutical companies to implement compliance programs or marketing codes.

Employees

As of March 3, 2020, we had 67 employees, of which 67 are full-time employees, 38 of whom were primarily engaged in the commercialization and support of the commercialization of Xerava and none of whom were primarily engaged in research and development activities. A total of 9 employees have an M.D., PharmD or Ph.D. degree. None of our employees is represented by a labor union and we consider our employee relations to be good.

Available Information

We file reports and other information with the Securities and Exchange Commission as required by the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. You can review our electronically filed reports and other information that we file with the SEC on the SEC's web site at http://www.sec.gov.

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

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

Item 1A. Risk Factors

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

Risks Relating to Our Financial Position and Need for Additional Capital

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

We have incurred annual net operating losses in every year since our inception. Our net loss was $70.1 million for the year ended December 31, 2019 and $72.2 million for the year ended December 31, 2018. As noted below, we and our auditors have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, 2019, we had an accumulated deficit of $604.1 million. Prior to October 2018, when we commenced sales of Xerava in the United States, we had not generated any product revenues. For the year ended December 31, 2019, we generated $3.6 million in net product revenues from sales of Xerava. We have financed our operations primarily through the public offerings and private placements of our equity securities, debt financings, revenue from United States government grants and contract awards and milestone payments from our licensing agreement with Everest Medicines.

In the third quarter of 2018, we received marketing approval in the United States and in Europe for Xerava for the treatment of complicated intra-abdominal infections, or cIAI. Prior to the marketing approval of Xerava we had devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development. In June 2019, we determined to devote all of our financial resources and efforts to supporting the ongoing commercialization of Xerava and announced a restructuring of our organization, including a 20% reduction in headcount, designed to focus our cash resources on commercializing Xerava primarily in the hospital setting. As a result of the restructuring, we eliminated our internal research function and determined to explore out-licensing opportunities for our pipeline of early-stage antibiotics and oncology product candidates.

Notwithstanding the initiation of sales of Xerava and our 2019 restructuring, we expect to continue to incur significant expenses and operating losses for at least the next several years. The net losses we incur may fluctuate significantly from quarter to quarter. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect that our expenses will decrease in 2020 compared with 2019, as the cost savings associated with our June 2019 restructuring are expected to continue in 2020. Our expenses could increase if and as we:

- maintain, expand and protect our intellectual property portfolio; and
- in-license or acquire other products and technologies.

Our ability to become and remain profitable depends on our ability to generate revenue. Notwithstanding marketing approval of Xerava in the United States and Europe, we have not commenced sales of Xerava in Europe and do not expect to generate significant revenue from Xerava sales in the United States in the near future. The successful commercialization of Xerava will require us to be effective in a range of challenging activities, including:

- establishing and maintaining sales, marketing and distribution capabilities to effectively market, sell and be reimbursed for Xerava;
- contracting for the manufacture of sufficient commercial quantities of Xerava; and
- protecting and maintaining our rights to our intellectual property portfolio related to Xerava.

Because of the numerous risks and uncertainties associated with pharmaceutical product commercialization, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

We may be unable to successfully commercialize Xerava and, even if we do, we 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 will need additional funding to commercialize Xerava. 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.

We believe, based on our current operating plan, that our existing cash and cash equivalents as of December 31, 2019 and our projected revenues from sales of Xerava, together with the net proceeds of approximately $15.9 million from our registered direct offering and concurrent private placement of equity securities in January 2020, will be sufficient to fund our operations into the first quarter of 2021, however, we have based this estimate on assumptions that may prove to be wrong, and our capital resources may be utilized faster than we currently expect. As of December 31, 2019, management has further assessed this risk and, in accordance with the requirements of Accounting Standards Update No. 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, or ASC 205-40, determined that there is substantial doubt about our ability to continue as a going concern. There is no assurance that we will be successful in obtaining additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises or management plans to reduce costs that are not considered probable in their assessment of our ability to meet our obligations. If we are unable to obtain funding, we may be required to delay, reduce or eliminate our commercialization efforts, which could adversely affect our business prospects, and we may be unable to continue operations. We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund our expenses after that time. In light of our limited cash resources, we are exploring strategic alternatives to maximize shareholder value, including the potential sale or merger of us or our assets.

Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, although we are exploring out-licensing opportunities for our pipeline of early-stage antibiotics and oncology product candidates, there can be no assurance that we will be able to out-license these on a timely basis or on terms that are favorable to us, or at all. Our failure to raise capital through financing or a license of our pipeline as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We could be forced to significantly scale back or discontinue the commercialization of Xerava and reduce other expenditures, 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 Xerava and our other product candidates. In addition, in such circumstance, we would consider seeking protection under the bankruptcy laws in order to continue to pursue potential transactions and conduct a wind-down of our company. If we decide to seek protection under the bankruptcy laws, we would expect that we would file for bankruptcy at a time that is significantly earlier than when we would otherwise exhaust our cash resources. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders.

Our future funding requirements, both short-term and long-term, will depend on many factors, including, but not limited to:

- revenue received from commercial sales of Xerava;
- our ability to enter into collaborations, licensing, marketing, distribution or other arrangements with respect to Xerava and our product candidates, and the terms and timing of any such arrangements into which we enter;
- the timing and costs of manufacturing and other activities in connection with the commercialization of Xerava;
- 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 University, or Harvard, and other licenses under license agreements to which we may be a party;
- the costs of maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the extent to which we in-license or acquire other products and technologies; and
- our ability to continue as a going concern.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

We believe, based on our current operating plan, that our existing cash and cash equivalents as of December 31, 2019 and our projected revenues from sales of Xerava, together with the net proceeds of approximately $15.9 million from our registered direct offering and concurrent private placement of equity securities in January 2020, will be sufficient to fund our operations into the first quarter of 2021, however, we have based this estimate on assumptions that may prove to be wrong, and our capital resources may be utilized faster than we currently expect. The report from our independent registered public accounting firm for the year ended December 31, 2019 includes an explanatory paragraph stating that our recurring losses from operations, limited financial resources and the need to raise additional capital to finance our future operations raise substantial doubt about our ability to continue as a going concern. If we are unable to obtain sufficient funding, we may be forced to delay or reduce the scope of our commercialization efforts, our business, prospects, financial condition and results of operations will be materially and adversely affected, and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive

less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. Future reports from our independent registered public accounting firm may also contain statements expressing substantial doubt about our ability to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide funding to us on commercially reasonable terms, if at all.

We have 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 our product candidates, establishing a commercial infrastructure to launch Xerava in the United States and selling Xerava in the United States. We obtained marketing approval for Xerava in the United States and Europe in the third quarter of 2018 and commenced sales of Xerava in the United States in the fourth quarter of 2018. We have not yet demonstrated a long-term ability to 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.

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

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

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

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, products or product candidates or to grant licenses on terms that may not be favorable to us.

Risks Related to Product Development and Commercialization

We are dependent on the success of Xerava, and our ability to successfully commercialize Xerava. If we are unable to successfully commercialize Xerava or experience significant delays in doing so, our business could be materially harmed.

We have invested a significant portion of our efforts and financial resources in the development of Xerava for use as a first-line empiric monotherapy for the treatment of multidrug-resistant, or MDR, infections. We obtained marketing approval for Xerava for the treatment of cIAI in the United States and in Europe in the third quarter of 2018. Our prospects are substantially dependent on our ability to successfully commercialize Xerava for the treatment of cIAI. The success of Xerava will depend on several factors, including the following:

- continue growing sales of Xerava in the United States;
- acceptance of Xerava by the medical community, hospital formularies and patients;
- obtainment and maintenance of patent and trade secret protection and regulatory exclusivity;
- protection of our rights in our intellectual property portfolio;
- successful manufacturing of Xerava;

- favorable results of any additional clinical trials involving Xerava that we or others may conduct;
- competition with other therapies; and
- a continued acceptable safety profile of Xerava.

If we are unable to successfully commercialize Xerava for the treatment of cIAI our business could be materially harmed.

Xerava or any additional product candidate of ours that a future collaborator develops and commercializes 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 Xerava or the additional product candidates may be smaller than we estimated.

Prior to Xerava, we had never commercialized a product candidate for any indication. Efforts to educate the medical community and third-party payors on the benefits of Xerava may require significant resources and may not be successful. If Xerava does not achieve an adequate level of market acceptance, we may not generate significant product revenues. Therefore, we may not become profitable. We are exploring out-licensing opportunities for our pipeline of early-stage antibiotics and oncology product candidates. If any additional product candidate of ours that a future collaborator develops does not achieve market acceptance, the amounts we could receive under the licensing or collaboration agreement could be limited. The degree of market acceptance of Xerava, or any other product candidate that is approved for commercial sale, will depend on a number of factors, including, but not limited to:

- the efficacy and safety of the product;
- the potential advantages of the product compared to alternative treatments, including convenience and ease of administration;
- 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;
- our ability to offer the product for sale at competitive prices;
- the willingness 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;
- 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 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 Xerava or any product candidate is difficult to estimate. Our estimates of the potential market opportunity for Xerava are predicated on several key assumptions such as industry knowledge, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management and 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 Xerava could be smaller than our estimates of the potential market opportunity. If the actual market for Xerava 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 successfully establish and maintain sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing Xerava.

To achieve commercial success for Xerava, we must develop a successful sales and marketing organization. We have built a commercial organization in the United States and recruited experienced sales, marketing and distribution professionals. If we are unable to successfully operate the sales force and maintain marketing and distribution capabilities, our operating results may be adversely affected.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the ability of our sales personnel to obtain access to or persuade adequate numbers of physicians to appropriately prescribe any 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;
- the inability of our medical science group to educate physicians on the benefits to patients of Xerava; and
- unforeseen costs and expenses associated with maintaining an independent sales and marketing organization.

We plan to seek to commercialize Xerava outside the United States with the assistance of collaborators. If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of Xerava revenues to us may be lower than if we were to directly market and sell Xerava in those markets. As an example, if Everest Medicines Limited, or Everest Medicines, our collaboration partner for Xerava in certain Asian territories, is unsuccessful in developing and commercializing Xerava in the Chinese market, we may not receive any future milestone or royalty payments. 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 Xerava or any other future products.

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. Xerava and any product candidate of ours that we license to a third party will face competition from major pharmaceutical companies, specialty pharmaceutical companies, generic manufacturers and biotechnology companies worldwide. 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 MDR infections. Competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than Xerava or any of our product candidates that we license to a third party, which could impact the use of Xerava.

Xerava competes with a number of antibiotics that are currently marketed for the treatment of cIAI and other multidrug resistant infections, including meropenem, which is marketed by AstraZeneca as Merrem, imipenem/cilastatin, which is sold by Merck & Co., or Merck, as Primaxin, tigecycline, which is marketed by Pfizer as Tygacil, piperacillin/tazobactam, which is marketed by Pfizer as Zosyn, ceftolozane/tazobactam and imipenem/relebactam, which are marketed by Merck as Zerbaxa and Recarbrio, and ceftazidime/avibactam, which is marketed by Allergan, Inc., as Avycaz, meropenem and vaborbactam, which is marketed by Melinta Therapeutics as Vabomere, We also expect that Xerava will compete with future and current generic versions of marketed antibiotics.

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

Even if we are able to commercialize Xerava or a future collaborator is able to commercialize any product candidates that we license to it, 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 by country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or a future collaborator 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 directly or indirectly from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in Xerava and any of our product candidates that are commercialized, even if our product candidates obtain marketing approval.

Our and our future collaborators' ability to commercialize Xerava or any product candidate of ours that we license to a third party 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 the ability to sell Xerava or any such product candidates profitably.

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 Xerava or any of our product candidates that we license to a third party that is commercialized 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.

We do not plan to conduct any additional clinical registration trials of Xerava or any of our product candidates other than FDA required post approval Phase IV trials. However, if we determine to resume clinical development of any product candidates or license any product candidates to third parties for development, we or our collaborators will be subject to the risk that such 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, and we or our collaborators may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidate.

A company is 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 European Medicines Agency, or EMA, and may never receive such approvals. In addition, the company must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of its product candidates in humans before it 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.

The clinical development of any product candidate 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. Success may not be achieved in any future clinical trial of any product candidate.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of clinical trials warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval.

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 addition, in the case of clinical trials of antibiotics such as Xerava, results may differ on the basis of the type of bacteria with which patients are infected. We cannot be certain that other clinical trials will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market product candidates.

Numerous unforeseen events may occur during, or as a result of, clinical trials that could delay or prevent us or our collaborators from obtaining regulatory approval for any of our product candidates, including:

- clinical trials may produce unfavorable or inconclusive results;
- we or our collaborators may decide, or regulators may require us or our collaborators, 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 anticipated, enrollment in these clinical trials may be slower than anticipated, or participants may drop out of these clinical trials at a higher rate than anticipated;
- 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 in a timely manner, or at all;
- regulators or institutional review boards may not authorize the commencement of a clinical trial or the conduct of a clinical trial at a prospective trial site;
- clinical trials may need to be suspended or terminated 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 clinical research be suspended or terminated 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 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 clinical data insufficient for approval.

If we or our collaborators are required to conduct additional clinical trials or other testing of any product candidate beyond the contemplated trials and testing or are unable to successfully complete clinical trials 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 our product candidates, we or our collaborators 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.

Serious adverse events or undesirable side effects or other unexpected properties of Xerava or any product candidate that we license to third parties 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 or our collaborators, an institutional review board, or regulatory authorities to interrupt, delay or halt 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 any product candidate is associated with serious adverse events or undesirable side effects or have properties that are unexpected, we or our collaborators 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 Xerava, some treatment-related adverse events were reported. The most common treatment-related adverse events observed in clinical trials of Xerava were nausea and emesis. Additional adverse events, undesirable side effects or other unexpected properties 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, trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order the cessation of further development of, or deny approval of, the product candidates. If such an event occurs with respect to Xerava or after an additional product candidate is approved, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such product;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more post-marketing 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 market acceptance of the affected product or 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.

Product liability lawsuits against us could divert our resources, cause us to incur substantial liabilities and limit commercialization of Xerava.

We face an inherent risk of product liability claims as a result of the commercialization of Xerava. For example, we may be sued if Xerava allegedly causes injury or is found to be otherwise unsuitable during 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 Xerava;
- 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 Xerava.

We maintain general liability insurance of $12 million in the aggregate and clinical trial liability insurance of $10 million in the aggregate for all product candidates, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. 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 Xerava, which could adversely affect our business, financial condition and 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 products and product candidates. Our prospects with respect to those products and product candidates will depend in part on the success of those collaborations.

Although we are commercializing Xerava ourselves in the United States, we intend to seek to commercialize Xerava outside the United States through collaboration arrangements. For instance, in February 2018, we entered into a license agreement with Everest Medicines under which we granted Everest Medicines an exclusive license to develop and commercialize Xerava for the treatment of cIAI and other indications, in mainland China and several other Asian territories and countries. In addition, we are exploring out-licensing opportunities for our pipeline of early-stage antibiotics and oncology 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 other than that with Everest Medicines.

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 or product candidate that we license to a third party.

Collaborations involving our products and product candidates, such as our license arrangement with Everest Medicines, 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 products and 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;
- collaborators 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 products and product candidates, might lead to additional responsibilities for us with respect to products and 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 products or 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 or product candidate licensed to it by us.

We contract with third parties for the manufacture of Xerava for commercialization. This reliance on third parties for manufacturing increases the risk that we will not have sufficient quantities of our product 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 Xerava or any product candidate for use in the conduct of clinical trials or for commercial supply. We currently rely on and expect to continue to rely on third-party contract manufacturers to manufacture commercial supplies of Xerava. Reliance on third-party manufacturers entails risks, including:

- delays in the manufacture of our clinical drug supply, registration and validation batches and commercial supply if our third-party manufacturers give greater priority to the supply of other products over Xerava or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- equipment malfunctions, power outages or other general disruptions experienced by our third-party manufacturers to their respective operations and other general problems with a multi-step manufacturing process;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us;
- the possible breach of the manufacturing agreement by the third party;
- the failure of the third-party manufacturer to comply with applicable regulatory requirements; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Third-party manufacturers are required to comply with current Good Manufacturing Processes, or cGMPs, and similar regulatory requirements outside the United States. Facilities used by our third-party manufacturers must be inspected by the FDA after we submit an NDA, and before potential approval of the product candidate. Similar regulations apply to manufacturers of our product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of our product candidates. If our manufacturers cannot successfully manufacture material that conforms to the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate as alternative qualified manufacturing facilities may not be

available on a timely basis or at all. In addition, our manufacturers are subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us or the contract manufacturer, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, interruptions in supply and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates and have a material adverse impact on our business, financial condition and results of operations.

Our current and anticipated future dependence upon others for the manufacture of Xerava may adversely affect our future profit margins and our ability to commercialize Xerava on a timely and competitive basis.

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

For Xerava outside the U.S. and for our product candidates, we intend to seek to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates. For example, we collaborate with Everest Medicines for commercialization of Xerava in certain countries outside the United States. We may not be able to enter into similar arrangements for any additional product candidates.

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

- the likelihood of approval by the FDA or comparable foreign regulatory authorities;
- the potential market for the subject product or product candidate;
- the costs and complexities of manufacturing and delivering such product or product candidate to patients;
- the potential for competing products;
- our patent position protecting the product or 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
- general industry and market conditions.

A collaborator may also consider alternative products, 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 or 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 for Xerava or any of our product candidates on a timely basis, on acceptable terms, or at all, we expect to curtail the development of Xerava or the product candidate, reduce or delay the development program for Xerava or the product candidate or one or more of our other development programs, delay its potential commercialization, 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 or product candidates or bring them to market and our business may be materially and adversely affected.

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 example, 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, and to pay royalties on sales of Xerava. 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.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain sufficient patent protection for our technology, products 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, products 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, products 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, products 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 products or product candidates, our ability to develop and commercialize those products or 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, products 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 notified and therefore are not able to be certain upon filing that we are the first to file for patent protection for any invention. Moreover, we may be subject to a third-party pre-issuance 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, products 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. For example, in August 2018 we received a Notice of Opposition from the European Patent Office notifying us that one of two European patents we own having claims directed to Xerava had been opposed by a third party. We filed a Response to the Opposition in November 2018 cancelling the opposed claims and maintaining the unopposed claims. Our other European patent covering Xerava is not impacted by the filing of this Opposition and cannot itself be opposed based on its grant date of July 3, 2013. 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 products and product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our products and 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 these 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, products or product candidates and Xerava. Other possible adversarial proceedings include interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be ordered by a court to cease developing, manufacturing, using, selling or offering for sale the infringing product. Alternatively, we may conclude that we need to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product or product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims that we or our employees have misappropriated the intellectual property of a third party, or claiming ownership of what we regard as our own intellectual property.

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

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Moreover, because we have licensed intellectual property from Harvard, we must rely on Harvard's practices with regard to the assignment of intellectual property to it. To the extent we or Harvard has 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, products and product candidates, 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 has executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

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

We own trademark registrations for TETRAPHASE PHARMACEUTICALS, our logo, and combinations of those in the United States. TETRAPHASE PHARMACEUTICALS is either registered or pending in twelve other jurisdictions, the logo is pending or registered in the same twelve jurisdictions, and the combination of the name and logo is registered or pending in three of those jurisdictions and two TETRAPHASE PHARMACEUTICALS Chinese character marks are registered in China. 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 own a trademark registration in the United States for Xerava, the proprietary name for the Xerava product.

We own two registrations and one application to register the Xerava trademark in three jurisdictions outside the United States and the availability of the proposed names for registration and use in foreign jurisdictions is not known. 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 seek to cancel registered trademarks. Cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. We have also obtained registration for our product design mark in four jurisdictions, including the United States.

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 any future product candidate that we develop in addition to Xerava, and our ability to generate additional revenue will be materially impaired.

The design, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, marketing, export, sale and distribution of product candidates 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 any such future product candidate will prevent the commercialization of such product candidate.

Product candidates may not be marketed in the United States until receipt of approval of an NDA from the FDA. 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 drug development and 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 data are insufficient for approval and require additional preclinical, clinical or other studies or additional information regarding chemistry, manufacturing and controls for the product candidate. Foreign regulatory authorities have differing requirements for approval of drug candidates which must be complied with prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that marketing approval will be received in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively impact the ability to obtain marketing approval in other jurisdictions. Delays in approvals or rejections of marketing applications in the United States or foreign countries may be based upon many factors, including regulatory requests for additional analyses, reports, data and studies, regulatory questions regarding, or different interpretations of, data and results, changes in regulatory policy during the period of product development and the emergence of new information regarding product candidates or related products. The FDA or equivalent foreign regulatory authorities may determine that a product candidate is not effective, or is only moderately effective, or has undesirable or unintended side effects, toxicities, safety profile or other characteristics that preclude marketing approval or prevent or limit commercial use. The FDA may also find during its pre-approval inspection that the facilities identified in the NDA fail to comply with cGMP requirements, thereby delaying or preventing approval. In addition, any marketing approval may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. Delays in obtaining approval or the failure to obtain approval of any product candidate would harm the commercial prospects for such product candidate.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad and may limit our ability to generate revenue from product sales.

In order to market and sell our products in the European Union and many other jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. We, and any future collaborators, may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and any future collaborators and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we or any future collaborators fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we or any future collaborators fail to comply with applicable non-U.S. regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the European Union.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the United Kingdom. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

We are subject to ongoing obligations and continuing regulatory review following the marketing approval of Xerava, which may result in significant additional expense. Xerava 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 Xerava or our product candidates, when and if approved.

Xerava is subject to, and any product candidate for which a future collaborator may obtain marketing approval will also be subject to, ongoing regulatory requirements, including for labeling, manufacturing, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements or requirements of equivalent foreign regulatory authorities, 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 are also required to report certain adverse reactions and production problems, if any, to the FDA or equivalent foreign authorities and to comply with requirements concerning advertising and promotion for our products.

In addition, even if marketing approval of a product candidate is granted to us or a future collaborator, 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 uses not described in the FDA-approved label, known as off-label uses, 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 promotion.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, it may impose restrictions on that product or us. In addition, if any product fails to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning or untitled letters;
- mandate modifications to promotional materials or require provision of corrective information to healthcare practitioners and patients;
- impose restrictions or requirements on the product or its manufacturers or manufacturing processes or suspension of manufacturing processes;
- impose restrictions on the labeling or marketing of the product;
- impose restrictions on product distribution or use;
- require post-marketing clinical trials;
- require withdrawal of the product from the market;
- refuse to approve pending applications or supplements to approved applications that we submit;
- require recall of the product;
- require entry into a consent decree, which can include imposition of various fines (including restitution or disgorgement of profits or revenue), reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- suspend, vary, modify or withdraw marketing approvals;

- refuse to permit the import or export of the product;
- seize or detain supplies of the product; or
- issue injunctions, levy fines or impose other civil penalties or bring criminal prosecution.

A recall of our products, or the discovery of serious safety issues with our products, could have a significant adverse impact on us.

The FDA and equivalent foreign authorities have the authority to require the recall of commercialized drugs in the event of material deficiencies, defects in design or manufacture, or stability failures. Manufacturers may, under their own initiative, recall a product if any material deficiency in a drug is found. A government-mandated or voluntary recall by us or one of our distributors could occur as a result of an unacceptable risk to health, component failures, manufacturing errors, stability failures, drug contamination or impurities, design or labeling defects or other deficiencies and issues. Recalls of any of our products would divert managerial and financial resources and have an adverse effect on our reputation, financial condition and operating results, which could impair our ability to produce our products in a cost-effective and timely manner. The FDA and equivalent foreign authorities require that certain classifications of recalls be reported to them within a defined period of time (within ten working days for the FDA) after the recall is initiated. Companies are required to maintain certain records of recalls, even if they are not reportable to the FDA or equivalent foreign authorities. We may initiate voluntary recalls involving our products in the future that we determine do not require notification of the FDA or equivalent foreign authorities. If the FDA or equivalent foreign authorities disagree with our determinations, they could require us to report those actions as recalls. A future recall announcement could harm our reputation with customers and negatively affect our sales. In addition, the FDA or equivalent foreign authorities could take enforcement action for failing to report the recalls when they were conducted.

An increase in the frequency or severity of adverse events, or repeated product complaints or malfunctions, may result in a voluntary or involuntary product recall, which could divert managerial and financial resources, impair our ability to manufacture our products in a cost-effective and timely manner and have an adverse effect on our reputation, financial condition, and operating results.

Any adverse event involving our products could result in future voluntary corrective actions, such as recalls or customer notifications, or regulatory agency action, which could include inspection, mandatory recall or other enforcement action. Any corrective action, whether voluntary or involuntary, will require the dedication of our time and capital, distract management from operating our business and may harm our reputation and financial results.

Our relationships with customers and third-party payors are 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 arrangements with third-party payors, healthcare professionals and customers who purchase, recommend or prescribe our products are 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 our products, and it is possible that our business activities could be subject to challenge or enforcement under one or more of these laws and regulations. These laws and regulations include the United States federal healthcare Anti-Kickback Statute, the federal civil False Claims Act, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, the federal Physician Payments Sunshine Act, and analogous state laws and regulations.

The shifting commercial compliance environment and the need to build and maintain robust and expandable systems to comply with different compliance or reporting requirements in multiple jurisdictions increase the possibility that we or our partners may fail to comply fully with one or more of these requirements, and 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. 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, any of which could adversely affect our ability to operate our business and our financial results. 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.

Similar restrictions are imposed on the promotion and marketing of medicinal products in the EU Member States and other foreign countries. These include restrictions prohibiting the promotion of a compound prior to its approval. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we may decide not to directly promote or market our products, inappropriate activity by our international distribution partners could have implications for us.

We also are subject to state and federal laws governing the collection, use, and disclosure and protection of health-related and other personal information, including state security breach notification laws, state health information privacy laws, and federal and state consumer protection laws. Failure to comply with these laws and regulations promulgated thereunder could result in government enforcement actions and create liability, private litigation, or adverse publicity. In addition, we may obtain health information from third parties, such as research institutions, that are subject to privacy and security requirements under HIPAA. Although we are not directly subject to HIPAA – other than with respect to providing certain employee benefits – we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly obtain or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In addition, HIPAA does not replace federal, state, or other laws that may grant individuals even greater privacy protections.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We have substantial reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental programs. Our failure to comply with these price reporting and rebate payment obligations could negatively impact our financial results.

The Centers for Medicare & Medicaid Services, or CMS, issued a final regulation, which became effective on April 1, 2016, to implement the changes to the Medicaid Drug Rebate Program under the Affordable Care Act. The issuance of the final regulation, as well as any other regulations and coverage expansion by various governmental agencies relating to the Medicaid Drug Rebate Program, has increased and will continue to increase our costs and the complexity of compliance, and could have a material adverse effect on our results of operations, particularly if CMS challenges the approach we take in our implementation of the final regulation.

We also participate in the 340B program. The U.S. Department of Health and Human Services' Health Resources and Services Administration, or HRSA, which administers the 340B program, issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities, which became effective on January 1, 2019. It is currently unclear how HRSA will apply its enforcement authority under the new regulation. Implementation of this regulation could affect our obligations and potential liability under the 340B program in ways we cannot anticipate.

We have obligations to report the average sales price for certain of our drugs to the Medicare program. Statutory or regulatory changes or CMS guidance could affect the average sales price calculations for our products and the resulting Medicare payment rate, and could negatively impact our results of operations.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program.

We participate in the U.S. Department of Veterans Affairs, or VA, and the Federal Supply Schedule, or FSS, pricing program. Pursuant to applicable law, knowing provision of false information in connection with price reporting under these programs can subject a manufacturer to civil monetary penalties. These program obligations also contain extensive disclosure and certification requirements. If we overcharge the government in connection with our FSS contract or Tricare Agreement, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We are subject to United States and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the United States domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

We have adopted a Code of Business Conduct and Ethics that mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. We cannot assure you, however, that our employees and third-party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws.

Our products and solutions are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, United States Customs regulations, and various economic and trade sanctions regulations administered by the United States Treasury Department's Office of Foreign Assets Controls. Exports of our products and solutions outside of the United States must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our products or solutions or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our products and solutions in international markets, prevent customers from using our products and solutions or, in some cases, prevent the export or import of our products and solutions to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our products and solutions could adversely affect our business, financial condition and results of operations.

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 harm our business.

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

We maintain workers’ compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, but this insurance may not provide adequate coverage against potential liabilities. We do not, however, 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. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Clinical development, including the conduct of clinical trials necessary to support an NDA, is a lengthy and expensive process with an uncertain outcome, and results of earlier preclinical studies and clinical trials may not be predictive of future trial results. Delays or failure can occur at any stage of clinical development and may adversely affect our business, operating results, and prospects.

Initiating and completing clinical trials necessary to support approval of products is time consuming and expensive and the outcome is uncertain. Clinical testing is expensive and can take many years to complete and its outcome is inherently uncertain. There is no guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. Failure can occur at any time and for any number of reasons during the clinical trial process. The results of preclinical studies and early clinical trials and evaluations of products may not be predictive of the results of later stage clinical trials. Similarly, the final results from a clinical trial may not be as favorable as interim results reported earlier in the same clinical trial. Products in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials.

Clinical trial failures may occur at any stage of development and may result from a multitude of factors both within and outside our control, including flaws in formulation or manufacturing, medical device design, adverse safety or efficacy profile and flaws in trial design, among others. If the trials result in negative or inconclusive results, we or our collaborators may decide, or regulators may require us, to discontinue trials of the products or conduct additional clinical trials or preclinical studies. In addition, data obtained from trials and studies are susceptible to varying interpretations, and we cannot guarantee that the FDA or foreign regulatory authorities will interpret data the same way that we or our collaborators do, which may delay, limit or prevent regulatory approval or clearance. The FDA or foreign regulatory authorities may also disagree with the design of clinical trials. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, we or our collaborators may be required to expend significant resources to conduct additional trials in support of potential approval of the products. Other potential reasons for clinical trial failures include, but are not limited to, inability to enroll sufficient patients, inability to engage sufficient clinical sites, inability to obtain or maintain institutional review board, or IRB, approval of the trial, or cessation of a trial for futility or safety concerns by us, or FDA, or foreign regulatory authorities, or an independent committee such as an independent data monitoring committee. As a result of any number of potential reasons, clinical trials may not be successful

Development of sufficient and appropriate clinical protocols to demonstrate safety and efficacy are required and we or our collaborators may not adequately develop such protocols to support clearance and approval or the results from such studies may not sufficiently demonstrate safety and efficacy. Further, the FDA or foreign regulatory authorities may, among other things, require the submission of data on a greater number of patients than originally anticipated and/or for a longer follow-up period or change the data collection requirements or data analysis applicable to clinical trials. Delays in patient enrollment or failure of patients to continue to participate in a clinical trial may cause an increase in costs and delays in the approval and attempted commercialization of the products or result in the failure of the clinical trial. In addition, despite considerable time and expense invested, the FDA or other regulatory authority may not consider the data adequate to demonstrate safety and efficacy. In addition, many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval.

Risks Related to Employee Matters

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 regulatory, commercialization and business development expertise of our executive management team, as well as the other principal members of our management, scientific and clinical team. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. For instance, in December 2017, our former chief medical officer terminated his employment with us, in March 2018, our former chief financial officer terminated her employment with us and in June 2019, our former chief medical officer terminated his employment with us. Also, in connection with our June 2019 restructuring, our board of directors appointed our then chief operating officer as our president and chief executive officer, effective August 1, 2019, with our then president and chief executive officer transitioning to a consulting role.

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 continue to commercialize Xerava will be limited.

We have reduced the size of our organization, and we may encounter difficulties in managing our business as a result of this reduction, or the attrition that may occur following this reduction, which could disrupt our operations. In addition, we may not achieve anticipated benefits and savings from the reduction.

In June 2019, we authorized the implementation of a restructuring of our organization, including a 20% reduction in headcount, designed to focus our cash resources on commercializing Xerava primarily in the hospital setting. The restructuring, and the attrition thereafter , resulted in the loss of longer-term employees, the loss of institutional knowledge and expertise and the reallocation and combination of certain roles and responsibilities across the organization, all of which could adversely affect our operations. Given the complexity and nature of our business, we must continue to implement and improve our managerial, operational and financial systems, manage our facilities and continue to recruit and retain qualified personnel. This will be made more challenging given the restructuring described above, ongoing attrition and additional measures we may take to reduce costs. As a result, our management may need to divert a disproportionate amount of its attention away from our day-to-day strategic and operational activities, and devote a substantial amount of time to managing these organizational changes. Further, the restructuring and possible additional cost containment measures may yield unintended consequences, such as attrition beyond our intended reduction in headcount and reduced employee morale. In addition, the restructuring may result in employees who were not affected by the reduction in headcount seeking alternate employment, which would result in us seeking contract support at unplanned additional expense. In addition, we may not achieve anticipated benefits from the restructuring. Due to our limited resources, we may not be able to effectively manage our operations or recruit and retain qualified personnel, which may result in weaknesses in our infrastructure and operations, risks that we may not be able to comply with legal and regulatory requirements, loss of business opportunities, loss of employees and reduced productivity among remaining employees. We may also determine to take additional measures to reduce costs, which could result in further disruptions to our operations and present additional challenges to the effective management of our company. If our management is unable to effectively manage this transition and restructuring and additional cost containment measures, our expenses may be more than expected, and we may not be able to implement our business strategy.

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

Although our operations are based in the United States, we plan to seek approvals to sell our products in foreign countries. Any business that we conduct outside the United States will be subject to additional risks that may materially adversely affect our ability to conduct business in international markets, including:

- potentially reduced protection for intellectual property rights;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting a product candidate being developed by a future collaborator 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.

Our internal computer systems, or those of any collaborators, contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs or overall business operations.

Our internal computer infrastructure and those of any collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. In June 2019, we experienced unauthorized access to an employee's e-mail. We investigated this security breach and believe it was contained to this one employee. While this event did not cause an interruption in our operations any future event could result in a material disruption of our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates by future collaborators could be delayed or halted.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately, or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to Our Common Stock

If we fail to meet the requirements for continued listing on the Nasdaq Global Select Market, our common stock could be delisted from trading, which would decrease the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed for quotation on the Nasdaq Global Select Market. We are required to meet specified requirements in order to maintain our listing on the Nasdaq Global Select Market, including, among other things, a minimum bid price of $1.00 per share. On June 24, 2019, we received a deficiency letter from the Listing Qualifications Department, or the Staff, of the Nasdaq Stock Market notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Select Market. On September 26, 2019 we affected a 1-for-20 reverse stock split for the purpose of regaining compliance with the minimum bid price rule. On October 11, 2019, we received notification from the Listing Qualifications Department of the Nasdaq Stock Market that for 10 consecutive business days, the closing bid price of our common stock had been at $1.00 per share or greater, confirming that we had regained compliance with the minimum bid price rule.

If in the future we fail to satisfy the Nasdaq Global Select Market's continued listing requirements, we may transfer to the Nasdaq Capital Market, which generally has lower financial requirements for initial listing, to avoid delisting, or, if we fail to meet its listing requirements, the OTC Bulletin Board. A transfer of our listing to the Nasdaq Capital Market or having our common stock trade on the OTC Bulletin Board could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

There are many factors that may adversely affect our minimum bid price, including those described throughout this section titled “Risk Factors”. Many of these factors are outside our control. As a result, we may not be able to sustain compliance with the minimum bid price rule in the long term. Any potential delisting of our common stock from the Nasdaq Global Select Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Global Select Market would also make it more difficult for our stockholders to sell our common stock in the public market.

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. Due to pricing pressures, slow commercial uptake for new antibiotics and general investor sentiment, antibiotic companies are presently experiencing significant volatility in their stock prices. For example, our stock traded within a range of a high price of $1,058.00 per share and a low price of $1.54 per share for the period beginning March 20, 2013, our first day of trading on the Nasdaq Global Select Market, through March 10, 2020. As a result of this volatility, you may not be able to sell your common stock at or above the public offering price. The market price for our common stock may be influenced by many factors, including:

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

We have been and may again be subject to class action litigation and have been and may again be subject to shareholder derivative litigation, which could distract our management and could result in substantial costs or large judgments against us.

The stock market frequently experiences extreme price and volume fluctuations. We have experienced significant declines in our stock price following our announcements that IGNITE2 and IGNITE3, our phase 3 clinical trials for Xerava for the treatment of patients with cUTI, did not meet the primary endpoints of those trials. In addition, the market prices of securities of companies in the biotechnology and pharmaceutical industry have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. These fluctuations could adversely affect the market price of our common stock. In the past, securities class action litigation has often been brought against companies following periods of volatility in the market prices of their securities. For instance, in January 2016 and March 2016, two class action lawsuits were filed against us, our chief executive officer and certain former executives in the United States District Court for the District of Massachusetts. These cases were subsequently consolidated. The court dismissed the consolidated cases in May 2017 and in November 2017, the plaintiffs withdrew a pending appeal in the United States Court of Appeals for the First Circuit. In addition, in May 2016, a shareholder derivative action was filed against our chief executive officer, certain former executive officers, all the members of our current board of directors, a former board member, and against us as nominal defendant, in Massachusetts Superior Court (Suffolk County). This case was subsequently dismissed by the court without prejudice due to the plaintiff's failure to properly perfect service of process. Furthermore, in July 2018 a class action lawsuit was filed against us, or chief executive officer, our chief scientific officer and other third parties in the United States District Court for the Southern District of New York in connection with the failure of IGNITE3 to meet its co-primary endpoints. This case was subsequently been moved to the United States District Court for the District of Massachusetts. In August 2019, the United States District Court for the District of Massachusetts (the "Massachusetts Federal Court") granted an unopposed motion for the appointment of a lead plaintiff. In October 2019, the lead plaintiff filed a motion to voluntarily dismiss the case and on October 16, 2019 the Massachusetts Federal Court entered an order dismissing the case. Due to the volatility in our stock price, we may be the target of similar litigation in the future.

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

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

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

The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity offerings.

As part of our November 2019 registered direct offering, we issued (i) warrants to purchase an aggregate of 2,130,493 shares of our common stock at an exercise price of $3.62 per share, and (ii) pre-funded warrants to purchase an aggregate of 1,830,493 shares of our common stock at an exercise price of $0.01 per share. As part of our January 2020 private placement and registered direct offering, we issued (i) warrants to purchase an aggregate of 5,833,439 shares of our common stock at an exercise price of $2.87 per share, and (ii) pre-funded warrants to purchase 2,183,334 shares of our common stock at an exercise price of $0.001 per share. As of March 10, 2020, all of these warrants except for 400,000 pre-funded warrants exercised in November 2019, remained outstanding and, upon exercise in full of these, the shares issuable upon exercise would represent a significant portion of our outstanding common stock. The pre-funded warrants have no expiration, and the common warrants remain exercisable for five years from their respective dates of issuance. The 6,581,091 shares issuable upon exercise of the warrants sold in the registered direct offerings can be freely sold into the public market upon issuance, subject to volume limitations applicable to affiliates. We intend to file a registration statement registering the 5,396,668 shares of common stock issuable upon exercise of the warrants sold in the private placement. Sales of these shares could cause the market price of our common stock to decline significantly. Furthermore, if our stock price rises, the holders of these warrants may be more likely to exercise their warrants and sell a large number of shares, which could negatively impact the market price of our common stock and reduce or eliminate any appreciation in our stock price that might otherwise occur.

We may also find it more difficult to raise additional equity capital while these warrants are outstanding. At any time during which these warrants are likely to be exercised, we may be unable to obtain additional equity capital on more favorable terms from other sources. In addition, the exercise of these warrants would result in a significant increase in the number of our outstanding shares of common stock, which could have the effect of significantly diluting the interest of our current stockholders, and following such exercise the former holders of such warrants could have significant influence over our company as a result of the shares of common stock they acquire upon such exercise.

We have a significant securityholder, which could exert substantial influence over our business. In addition, in connection with any merger, consolidation or sale of all or substantially all of our assets, it would be entitled to receive consideration in excess of its reported beneficial ownership of our common stock and adversely impact the consideration our other securityholders would receive.

As of March 2, 2020, Armistice Capital, LLC, or Armistice, held 1,419,502 shares of our common stock, warrants to purchase up to 2,130,493 shares of our common stock at an exercise price of $3.62 per share, warrants to purchase up to 3,333,334 shares of our common stock at an exercise price of $2.87 per share, pre-funded warrants to purchase up to 1,430,493 shares of our common stock at an exercise price of $0.01 per share and pre-funded warrants to purchase up to 2,063,334 shares of our common stock at an exercise price of $0.001 per share. In addition, two members of our board of directors are affiliates of Armistice. Under the terms of the warrants and pre-funded warrants issued to Armistice, Armistice is not permitted to exercise such warrants to the extent that such exercise would result in Armistice (and its affiliates) beneficially owning more than 19.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants. After giving effect to the 19.99% beneficial ownership limitation currently in effect with respect to the warrants and pre-funded warrants held by Armistice, as of March 2, 2020, Armistice beneficially owned 19.6% of our outstanding common stock. If the warrants and pre-funded warrants held by Armistice could be exercised without this limitation, then as of March 2, 2020, Armistice would have beneficially owned 49.5% of our common stock. The information in this paragraph is based on a Schedule 13D filed with the SEC on January 23, 2020.

Although there are contractual limitations on the beneficial ownership of Armistice, if Armistice were to exercise its warrants for common stock, it could be able to exert substantial influence over our business. This concentration of voting power could delay, defer or prevent a change of control, entrench our management and the board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and Armistice on the other hand, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters. Furthermore, in the event of a sale of our company, whether by merger, sale of all or substantially all of our assets or otherwise, Armistice would be entitled to receive, with respect to each share of common stock issuable upon exercise of the warrants then held by it and without regard to the beneficial ownership limitations imposed on the conversion or exercise of such securities, the same amount and kind of securities, cash or property as it would have been entitled to receive if such securities had been converted into or exercised for shares of our common stock immediately prior to such sale of our company. Because Armistice would receive this sale consideration with respect to warrants not included in its reported beneficial ownership of our common stock, in the event of a sale of our company, it would be entitled to receive a significantly larger portion of the total proceeds distributable to the holders of our securities than is represented by its reported beneficial ownership of our common stock.

Moreover, the warrants that are exercisable for $3.62 and $2.87 per share that are held by Armistice provide that upon a fundamental transaction, which generally includes any merger with or into another entity, sale of all or substantially all of our assets, tender offer or exchange offer, or reclassification of our common stock, Armistice will have the right to require us to repurchase its warrants at their fair value using the Black Scholes value. As a result, in the event of a sale of our company, Armistice would be entitled to receive a significantly larger portion of the total proceeds distributable to the holders of our securities than they would if they exercised the warrants immediately prior to the transaction. In addition to these warrants, there are outstanding additional warrants to purchase up to an additional 2,500,105 shares of our common stock at an exercise price of $2.87 per share that contain similar fundamental transaction repurchase provisions. As a result, if Armistice and the holders of these other warrants exercise their right in connection with a fundamental transaction and have us repurchase their warrants at the Black Scholes value, the holders of our common stock could receive significantly less than they otherwise would in such a transaction.

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 products and product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value.

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

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

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation, development and growth of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

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

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

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;

- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or by-laws.

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

ITEM 1B. Unresolved Staff Comments

None.

ITEM 2. Properties

We lease our principal facilities, which consist of approximately 21,539 square feet of office, research and laboratory space located at 480 Arsenal Way, Watertown, Massachusetts. The leases covering this space expire on November 30, 2022. We believe that our existing facilities are sufficient for our current needs. In the third quarter of 2016, we entered into a sublease with respect to a portion of our principal facilities with an unrelated third party. This sublease was terminated in August 2019. In January 2020, we amended our lease to reduce the square feet of office, research and laboratory space from approximately 37,438 square feet to 21,539 square feet.

ITEM 3. Legal Proceedings

On February 7, 2020, DHL Supply Chain (Netherlands) B.V ("DHL") made an arbitration demand against the Company with Foundation UNUM. The arbitration demand alleges breach of contract by the Company under a letter of intent entered into between the parties in August 2018 between the parties, and DHL seeks full indemnification for all damages and costs resulting from the alleged breach by the Company, including but not limited to loss of profit, which DHL calculates at 2,335,000 Euros. We do not believe we have breached any contract with DHL and plan to engage in a vigorous defense against such claims.

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 Information

Our common stock began trading on the Nasdaq Global Select Market on March 20, 2013 under the symbol "TTPH". Prior to that date, there was no established public trading market for our common stock.

Holders

At March 9, 2020, there were approximately 8 holders of record of our common stock. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Dividends

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

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item is set forth in ITEM 12. "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" in this Annual Report on Form 10-K.

Purchase of Equity Securities

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

Unregistered Sales of Equity Securities

None

Comparative Stock Performance Graph

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

ITEM 6. Selected Financial Data

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

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 biopharmaceutical company using our proprietary chemistry technology to create, develop and commercialize novel tetracyclines for serious and life-threatening conditions, including bacterial infections caused by multidrug-resistant, or MDR, bacteria. There is a medical need for new antibiotics as resistance to existing antibiotics increases. In recognition of this need, we developed our product, Xerava (eravacycline), a fully synthetic fluorocycline, as an intravenous, or IV antibiotic for use as a first-line empiric monotherapy for the treatment of MDR infections, including MDR Gram-negative infections, such as those found in complicated intra-abdominal infections, or cIAI.

On August 27, 2018, the United States Food and Drug Administration, or FDA, approved Xerava for the treatment of cIAI in adults. Approval of Xerava was based on our IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline) phase 3 program. In the first pivotal phase 3 trial in the IGNITE program in patients with cIAI, twice-daily IV Xerava met the primary endpoint by demonstrating statistical non-inferiority of clinical response compared to ertapenem, a carbapenem and a standard of care treatment for cIAI, and was well-tolerated. We refer to this trial as IGNITE1. In our other pivotal phase 3 clinical trial of Xerava in patients with cIAI, twice-daily IV Xerava met the primary endpoint by demonstrating statistical non-inferiority of clinical response compared to meropenem, another standard of care treatment, and was well-tolerated. We refer to this trial as IGNITE4. In both IGNITE1 and IGNITE4, Xerava achieved high cure rates in patients with poly-microbial infections (Gram-negative, Gram-positive, and anaerobic infections), including resistant isolates.

In October 2018, we commenced sales of Xerava in the United States. We are commercializing Xerava in the United States using a small, targeted commercial and medical affairs groups to build and promote access to Xerava. As of March 3, 2020, we have approximately 27 sales representatives. 3 regional business directors, 3 strategic market access executives and approximately 7 medical affairs personnel supporting Xerava in the United States.

On September 20, 2018, based on the results of IGNITE1, the European Commission, or EC, granted marketing authorization for Xerava for the treatment of cIAI in adults in all 28 countries of the European Union, or EU, plus Norway, Iceland and Liechtenstein. We plan to seek a partner to commercialize Xerava in the EU. In February 2018 we entered into a license agreement with Everest Medicines Limited, or Everest Medicines, granting Everest Medicines commercialization rights to eravacycline in China and other Asian territories. In June 2018, Everest Medicines submitted an Investigational New Drug, or IND, application to the China National Medical Products Administration (formerly China FDA) for a phase 3 clinical trial of eravacycline in cIAI. The application was approved, and Everest Medicines began enrolling patients in this phase 3 trial in the second quarter of 2019.

We believe that the ability of Xerava to cover MDR Gram-negative bacteria, as well as MDR Gram-positive, anaerobic and atypical bacteria, may enable Xerava to become the drug of choice for first-line empiric treatment of patients with cIAI. In *in vitro* studies, Xerava has demonstrated the ability to cover a wide variety of MDR Gram-negative, Gram-positive, anaerobic and atypical bacteria, including MDR *Klebsiella pneumoniae* and MDR *Acinetobacter.* Multidrug-resistant *Klebsiella pneumoniae* (carbapenem-resistant Enterobacteriaceae [CRE]) and MDR Acinetobacter are listed as urgent threats and Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae is listed as serious threats by the Centers for Disease Control and Prevention, or CDC, in a 2019 report. They are also listed as "Priority 1; Critical Pathogens" in the World Health Organization's priority pathogens list for R&D, published in February 2017. CREs were a confirmed area of great concern by the World Health Organization in an April 2014 global surveillance report. Gram-negative bacteria that are resistant to multiple available existing antibiotics are increasingly common and a growing threat to public health.

In addition to Xerava, we have also developed other fluorocycline antibiotic compounds, TP-6076 and TP-271, and TP-2846, a tetracycline for the treatment of acute myeloid leukemia. We developed TP-6076, a fully-synthetic fluorocycline derivative, as a lead candidate under our second-generation program to target unmet medical needs, including MDR Gram-negative bacteria such as carbapenem-resistant Enterobacteriaceae and carbapenem-resistant or pan-resistant *Acinetobacter baumanii*. To date, we have conducted phase 1 single-ascending and multiple-ascending dose studies evaluating the safety, tolerability and pharmacokinetics of IV TP-6076 in healthy volunteers. We also conducted a Phase 1 study to assess the bronchopulmonary disposition, pharmacokinetics, and safety of TP-6076 in healthy volunteers. TP-271 is a fully-synthetic fluorocycline that we developed for respiratory disease caused by bacterial biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia. To date, we have completed single-ascending and multiple-ascending dose trials for IV and oral formulations of TP-271. We have completed pre-clinical toxicology studies for TP-2846 and intend to file an IND with the FDA for TP-2846 upon identifying a partner. We are seeking to out-license each of these product candidates.

In June 2019, we announced a restructuring of our organization, including a 20% reduction in headcount, designed to focus our cash resources on commercializing Xerava primarily in the hospital setting. This reorganization included the elimination of our internal research function. As part of our restructuring, we decided not to engage in further product development, including conducting clinical trials of our product candidates, and are exploring out-licensing opportunities for all of our pipeline of early-stage antibiotics and oncology product candidates.

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, undertaking preclinical studies and clinical trials of our product candidates and initiating commercial sales of Xerava. Prior to October 2018, when we commenced sales of Xerava in the United States, we had not generated any product revenues. We have financed our operations primarily through the public offerings and private placements of our equity securities, debt financings, revenue from United States government grants and contract awards and milestone payments from our licensing agreement. As of December 31, 2019, we had received an aggregate of $596.1 million in net proceeds from the issuance of equity securities and borrowings under debt facilities, an aggregate of $61.0 million from government grants and contracts and an aggregate of $14.5 million from licensing agreement milestone payments. As of December 31, 2019, our principal source of liquidity was cash and cash equivalents, which totaled $21.2 million.

As of December 31, 2019, we had an accumulated deficit of $604.1 million and cash and cash equivalents of $21.2 million. Our net losses were $70.1 million and $72.2 million for the years ended December 31, 2019 and 2018, respectively. We expect that our expenses will decrease in 2020 compared with 2019, driven by lower costs associated with development of Xerava, our 2019 reorganization and a gradual decrease in Xerava sales and marketing expenses.

In January 2020, we issued and sold (a) in a private placement, (i) 1,270,000 shares of common stock and accompanying warrants to purchase an aggregate of 1,270,000 shares of common stock, for a combined price of $3.00, and (ii) pre-funded warrants to purchase 2,063,334 shares of common stock and accompanying warrants to purchase 2,063,334 shares of common stock, for a combined price of $2.999, and (b) in a concurrent registered direct offering, (i) 2,380,105 shares of our common stock and accompanying warrants to purchase an aggregate of 2,380,105 shares of common stock, for a combined price of $3.00 and (ii) pre-funded warrants to purchase 120,000 shares of our common stock and accompanying warrants to purchase 120,000 shares of common stock, for a combined price of $2.999. The net proceeds from the concurrent January 2020 private placement and registered direct offering, after deducting the placement agent’s fees and other estimated offering expenses payable by us, were approximately $15.9 million.

We believe, based on our current operating plan, that our existing cash and cash equivalents as of December 31, 2019 and our projected revenues from sales of Xerava, together with the net proceeds of approximately $15.9 million from our registered direct offering and concurrent private placement of equity securities in January 2020, will be sufficient to fund our operations into the first quarter of 2021, however, we have based this estimate on assumptions that may prove to be wrong, and our capital resources may be utilized faster than we currently expect..

As of December 31, 2019, management has further assessed this risk and, in accordance with the requirements of Accounting Standards Update No. 2014-15, *Disclosure of Uncertainties about an Entity’s Ability to Continue as a Going Concern (Subtopic 205-40)*, or ASC 205-40, has determined that there is substantial doubt about our ability to continue as a going concern. There is no assurance that we will be successful in obtaining additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises or management plans to reduce costs that are not considered probable in their assessment of our ability to meet our obligations.

If we are unable to obtain funding, we may be required to delay, reduce or eliminate our commercialization efforts, which could adversely affect our business prospects, and we may be unable to continue operations. We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund our expenses after that time. In light of our limited cash resources, we are exploring strategic alternatives to maximize shareholder value, including the potential sale or merger of us or our assets.

Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, although we are exploring out-licensing opportunities for our pipeline of early-stage antibiotics and oncology product candidates, there can be no assurance that we will be able to out-license these on a timely basis or on terms that are favorable to us, or at all. Our failure to raise capital through financing or a license of our pipeline as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We could be forced to significantly scale back or discontinue the commercialization of Xerava and reduce other expenditures, 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 Xerava and our product candidates. In addition, in such circumstance, we would consider seeking protection under the bankruptcy laws in order to continue to pursue potential transactions and conduct a wind-down of our company. If we decide to seek protection under the bankruptcy laws, we would expect that we would file for bankruptcy at a time that is significantly earlier than when we would otherwise exhaust our cash resources. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders. See "—Liquidity and Capital Resources—Operating Capital Requirements."

Financial overview

Product Revenue

Xerava received approval on August 27, 2018 for the treatment of cIAI in adults. Following FDA approval of Xerava in the United States, we began selling Xerava in October 2018. We sell Xerava to a limited number of specialty distributors in the United States, who collectively represent our customers. These customers subsequently resell Xerava to hospitals or other treatment centers. In addition to the agreements with these distributors and the related discounts and fees, we are subject to government mandated rebates, chargebacks, and discounts with respect to the purchase of Xerava. Product revenue is recognized net of reserves for all variable consideration, including discounts, chargebacks, government rebates and product returns. For further discussion of our product revenue, see Note 2, *Summary of Significant Accounting Policies* to the consolidated financial statements.

Collaboration Revenue

In February 2018, we entered into a license agreement with Everest Medicines, whereby we granted Everest Medicines an exclusive license to develop and commercialize eravacycline, for the treatment of cIAI and other indications, in mainland China, Taiwan, Hong Kong, Macau, South Korea and Singapore. We amended this agreement in July 2019 to extend Everest Medicines' exclusive license to develop and commercialize Xerava to the jurisdictions of the Malaysian Federation, the Kingdom of Thailand, the Republic of Indonesia, the Socialist Republic of Vietnam and the Republic of the Philippines. Terms of this arrangement include various payment types, including upfront license fees, development, regulatory and commercial milestone payments, payments for clinical supply services and royalties on sales revenue. For further discussion of the Everest Medicines collaboration and the related revenue recognition, please see Note 2, *Summary of Significant Accounting Policies* and Note 3, *Significant Agreements and Contracts* to the consolidated financial statements.

Government Contract and Grant Revenue

Our government contract and grant revenue has been derived from funding provided under four awards. These awards included a contract from BARDA for the development of Xerava for the treatment of disease caused by bacterial biothreat pathogens, two separate awards from NIAID for the development of TP-271. These three awards were made to CUBRC. CUBRC served 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. The fourth award was from CARB-X. For further discussion of our government contract and grant revenue agreements and the related revenue recognition, please see Note 2, *Summary of Significant Accounting Policies* and Note 3, *Significant Agreements and Contracts* to the consolidated financial statements.

Cost of Revenue

Cost of revenue consists primarily of the manufacturing and distribution costs for Xerava, Xerava net sales-based royalties and the amortization of the intangible asset associated with certain milestones paid to Harvard University, or Harvard, related to Xerava. All manufacturing costs incurred prior to Xerava's approval in the United States on August 27, 2018 have been expensed in research and development and are not included in cost of revenue.

Research and Development Expenses

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

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

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

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and laboratory supplies, to each program based on the personnel resources allocated to such program. Expenses related to facilities, consulting, travel, conferences, stock-based compensation and depreciation are not allocated to a program and are separately classified as other research and development expenses. The following table identifies research and development expenses on a program-specific basis for our product candidates for the years ended December 31, 2019 and 2018:

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Xerava	$ 10,876	$ 31,542
TP-6076	1,293	2,092
BARDA Contract	1,023	1,399
CARB-X	460	2,048
NIAID Contract	88	2,525
Other development programs	3,040	3,276
Other research and development	6,005	11,997
Total research and development	$ 22,785	$ 54,879

Prior to our June 2019 reorganization, research and development activities were central to our business model. As part of our reorganization, we decided not to engage in further research and development, including conducting clinical trials of our product candidates. Instead, we intend to seek to out-license each of our pipeline candidates.

As of December 31, 2019, we had incurred an aggregate of $298.7 million in research and development expenses related to the development of Xerava, and $38.7 million in research and development expenses related to the development of Xerava that were funded under the BARDA Contract.

We have licensed our proprietary chemistry technology from Harvard University, or Harvard, on an exclusive worldwide basis under a license agreement that we entered into in August 2006. Under our license agreement, as of December 31, 2019, we have paid Harvard an aggregate of $16.8 million in upfront license fees, sublicense fees and development milestone payments for the licensed Harvard technology. We have also issued 1,568 shares of our common stock to Harvard under the license agreement. We have also 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 ($12.6 million of which has already been paid with respect to Xerava), 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 Company is obligated to make certain payments to Harvard based on amounts received under its license agreement with Everest Medicines Limited. During years ended December 31, 2019 and 2018, the Company paid $1.1 million and $9.7 million, respectively, related to the Everest Medicines license agreement and all other obligations under the Harvard agreement.

Selling, General and Administrative Expenses

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

We anticipate that our selling, general and administrative expenses will plateau or decrease for a number of reasons, including a decrease of infrastructure, including decreases in personnel-related costs, consulting, legal, and accounting costs.

Other Income (Expense)

Other income (expense) consists primarily of interest income, interest expenses and expenses related to the early payment of indebtedness under our term loan facility, which we paid off in August 2019. Interest income consists of interest earned on our cash and cash equivalents. The primary objective of our investment policy is capital preservation. 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 Solar Capital. We expect that our interest expense will decrease in future periods due to the early payment of the term loan facility in August 2019. During the year ended December 31, 2019 we recorded a one-time loss from debt extinguishment of $1.6 million as the difference between the net carrying amount of the indebtedness under the term loan facility and the amount paid.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including product revenue, inventory, estimates related to clinical trial accruals, stock-based compensation expense, government contract and grant revenues, and going concern considerations. We base our estimates on historical experience, known trends and events and various other factors that our management believes 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

Product Revenue

We sell Xerava to a limited number of specialty distributors in the U.S. These customers subsequently resell Xerava to hospitals or other treatment centers. In addition to the agreements with these distributors and the related discounts and fees, we are subject to government mandated rebates, chargebacks, and discounts with respect to the purchase of Xerava.

We recognize Xerava revenue at the time the performance obligation is satisfied, which is the point in time at which the goods are delivered to our customers' facilities, using a transaction price that represents the amount of consideration we expect to receive in exchange for the goods sold. Product revenue is recognized net of reserves for all variable consideration, including discounts, chargebacks, government rebates and product returns.

We evaluate our contracts with customers for all forms of variable consideration which may require an adjustment to the transaction price based on their estimated impact. We estimate variable consideration using the expected value method, which is the sum of probability-weighted amounts in a range of possible outcomes. These outcomes include market events and trends, forecasted product demand patterns, customer buying patterns and statutory requirements. The resulting reserves represent our best estimates of variable consideration we expect to occur.

Revenues from product sales are recorded at the gross sales price, net of reserves for variable consideration, as follows:

- *Trade Discounts and Allowances:* We offer our customers prompt pay discounts and service fees as stated in our customer contracts. The related reserves are set in the same period the corresponding revenue is recognized, resulting in a reduction of product revenue and receivables or recording of accrued liabilities. We employ the expected value method to estimate the impact of discounts and allowances, subject to any constraints.
- *Government Chargebacks and Rebates:* Under the terms of our master agreements, Customers may charge us back for reimbursement when they are contractually obligated to sell products to government entities or other end-users at a lower price than the wholesale acquisition cost, or WAC, at which those products were acquired from us. These rebates consist of Medicare, TriCare and Medicaid rebates as well as those related to other government drug pricing and reimbursement programs. We use the expected value method to estimate the variable consideration, subject to any constraints. Chargeback reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and receivables.
- *Product Returns:* We estimate the amount of product that may be returned and records this as a reduction in revenue in the relevant period. We currently estimate product return liabilities using available industry data, sales information and visibility into the inventory remaining in the distribution channel. We have not received any returns to date since launch. We use the expected value method to estimate the impact of product returns, subject to any constraints.

Collaboration Revenue Recognition

We entered into an out-licensing agreement that is evaluated under ASC 606, through which we license certain of our product candidates' rights to a third party. Any future out-license agreement entered into by us and additional third parties shall also be evaluated under ASC 606. Terms of these arrangements include various payment types, typically including one or more of the following: upfront license fees; development, regulatory and commercial milestone payments; payments for manufacturing supply services; and/or royalties on net sales of licensed products.

To determine the amount and timing of revenue to be recognized under each agreement, we evaluate the following criteria: (i) confirming the goods or services in the contract; (ii) defining the performance obligations under the agreement; (iii) determining the transaction price, including any constraint on variable consideration; (iv) allocating the transaction price to the performance obligations; and (v) defining how the revenue will be recognized for each performance obligation. In determining the accounting treatment for these arrangements, we develop assumptions to determine the stand-alone selling price for each performance obligation in the contract. These assumptions may include forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success.

Licenses of Intellectual Property: If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from upfront fees allocated to the license when the license is transferred to the licensee, including any associated know-how and the licensee can use and benefit from the license. For licenses that are bundled with other obligations, we use judgment to evaluate the combined performance obligation to determine whether it is satisfied over time or at a point in time and the appropriate method of measuring completion for purposes of recognizing revenue.

Milestone Payments: For arrangements that include development milestone payments, we evaluate whether the milestones are considered probable and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received.

Manufacturing Supply: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. We assess if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If we are entitled to additional payments when the licensee exercises these options, we recognize revenue when the licensee obtains control of the goods, which is upon delivery.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Going Concern Assessment

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

Based on our current operating plan, we expect that our cash and cash equivalents as of December 31, 2019, our projected revenues from sales of Xerava and the net proceeds from our concurrent private placement and registered direct offerings of equity securities completed in January 2020 will not be sufficient to fund our operations for more than one year beyond the filing date of this quarterly report, but only into the first quarter of 2021. This estimate is based on certain significant assumptions, which are uncertain and may turn out to be incorrect. In particular, the forecast assumes continued significant growth of Xerava revenue, for which we have limited historical experience to base our estimate. In addition, we have forecasted a continued reduction in expenses in 2020. If these estimates are incorrect, we may use our cash resources sooner than expected.

Results of Operations

Comparison of Years Ended December 31, 2019 and 2018

The following tables summarize the results of our operations for each of the years ended December 31, 2019 and 2018, together with the changes in those items in dollars and as a percentage:

	Year Ended December 31,		Increase/ (decrease)
	2019	2018	
		(in thousands)	
Revenue:			
Product revenue, net	$ 3,575	$ 178	$ 3,397
License and collaboration revenue	2,000	12,677	(10,677)
Government revenue	1,801	6,049	(4,248)
Total revenue	7,376	18,904	(11,528)
Expenses:			
Cost of revenue - product sales	2,687	130	2,557
Cost of revenue - intangible asset amortization	393	98	295
Research and development	22,785	54,879	(32,094)
Selling, general and administrative	49,043	37,078	11,965
Total expenses	74,908	92,185	(17,277)
Loss from operations	(67,532)	(73,281)	5,749
Other income (expense)	(2,553)	1,123	(3,676)
Net loss	$ (70,085)	$ (72,158)	$ 2,073

Product Revenue

We initiated sales of Xerava in the United States on October 15, 2018. For the year ended December 31, 2019, net sales of Xerava were $3.6 million.

License and Collaboration Revenue

In February 2018, we entered into a license agreement with Everest Medicines, whereby we granted Everest Medicines an exclusive license to develop and commercialize eravacycline, for the treatment of cIAI and other indications, in mainland China, and certain surrounding territories. During 2019, we recognized $2.0 million in license and collaboration revenue from the territory expansion payment received from Everest Medicines resulting from the July 2019 amendment of the license agreement. During 2018, we recognized $12.7 million related to the initial upfront payment, Chinese IND milestone and Phase 3 clinical trial milestone and from the sale of clinical trial material to Everest Medicines for the planned Chinese clinical trial. These payments were recognized as revenue as we had completed all of our performance obligations.

Revenue from U.S. Government Contracts and Grants

The following table sets forth our government contract and grant revenue for the years ended December 31, 2019 and 2018:

	Year Ended December 31,		Increase/
Revenue	**2019**	**2018**	**(decrease)**
		(in thousands)	
BARDA Contract	$ 1,254	$ 1,457	$ (203)
CARB-X Award	452	2,046	(1,594)
NIAID Contract	95	2,546	(2,451)
	$ 1,801	$ 6,049	$ (4,248)

Government contract and grant revenue was $1.8 million for the year ended December 31, 2019 compared to $6.0 million for the year ended December 31, 2018, a decrease of $4.2 million. This decrease was due to the scope and timing of activities conducted under our subcontract with respect to the BARDA and NIAID Contracts and the CARB-X Award. We do not expect to receive any government contract and grant revenue in 2020 from these contracts and awards, as all of these awards and related sub-awards have expired and all obligations have been satisfied as of December 31, 2019.

Cost of Revenue

Cost of product revenue was $3.1 million for the year ended December 31, 2019, compared to $0.2 million for the year ended December 31, 2018, consisting primarily of manufacturing and distribution costs for Xerava, Xerava net sales-based royalties and the amortization of the intangible asset associated with certain milestones paid to Harvard related to Xerava. All of our manufacturing costs incurred prior to Xerava's approval have been expensed in research and development expenses and are not included in cost of revenue. We expect cost of revenue to be variable during 2020 as these inventories are released over time and depleted.

Research and Development Expenses

Research and development expenses were $22.8 million for the year ended December 31, 2019 compared to $54.9 million for the year ended December 31, 2018, a decrease of $32.1 million. This decrease was primarily due to lower clinical trial costs associated with the IGNITE Phase 3 clinicals trials, which concluded in the first quarter of 2018 and license and milestone payments to Harvard that occurred in the first and second quarter of 2018. As a result of our determination in connection with the restructuring we announced in June 2019 to discontinue further product development, we expect future research and development costs to decrease significantly.

Selling, General and Administrative Expenses

Selling, general and administrative expenses for the year ended December 31, 2019 were $49.0 million compared to $37.1 million for the year ended December 31, 2018, an increase of $11.9 million. This increase was primarily due to an increase in commercial related expenses for Xerava.

Other Income (Expense)

Interest expense increased by $2.0 million for the year ended December 31, 2019 as compared to December 31, 2018 reflecting interest expense under our term loan facility. On August 30, 2019, we entered into a payoff letter with Solar Capital Ltd. as collateral agent and lender and the other lenders named under the Loan and Security Agreement, or the Loan Agreement (referred to collectively as the Lenders), pursuant to which the Company agreed to pay off and thereby terminate the Loan Agreement. Pursuant to the payoff letter, we paid a total of $30.7 million to the Lenders, representing the principal balance, accrued interest outstanding and a portion of the final fee under the Loan Agreement in repayment of our outstanding obligations under the Loan Agreement. We recorded a loss from debt extinguishment of $1.6 million as the difference between the net carrying amount of the indebtedness under the Loan Agreement and the amount paid. Interest income decreased by $0.5 million related to the year-over-year decrease in cash and cash equivalents. Other income increased by $0.3 million for the year ended December 31, 2019, related to an insurance reimbursement.

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 our total expenses to decrease but remain significant in 2020 and, as a result, we will need additional capital to fund our operations, which we may obtain from additional financings, research funding, collaborations, government 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, 2019, we had cash and cash equivalents of approximately $21.2 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, 2019, our funds were held in cash and money market funds.

On January 17, 2017, we entered into a Controlled Equity Offering Sales Agreement, or sales agreement, with Cantor Fitzgerald & Co., as sales agent, or Cantor. On July 7, 2017, we entered into an amendment to the sales agreement, or the amended sales agreement. In accordance with the terms of the sales agreement, we may offer and sell through Cantor, from time to time, shares of our common stock up to an aggregate offering price of $80,000,000 through an “at-the-market” offering program. As of December 31, 2019, we had sold 305,522 shares under the amended sales agreement at an average price of $129.80 per share and we had received aggregate cash proceeds of $38.2 million, after deducting the sales commissions and offering expenses. We made no sales under the amended sales agreement during 2019. Under the amended sales agreement, Cantor may sell shares of our common stock by methods deemed to be an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including sales made directly on The Nasdaq Global Select Market or on any other existing trading market for our common stock. We are not obligated to make any sales of shares of our common stock under the amended sales agreement. We or Cantor may suspend or terminate the offering of shares of our common stock upon notice to the other party and subject to other conditions and pay Cantor a commission rate equal to 3.0% of the gross proceeds per share sold.

On November 2, 2018, we entered into the Loan Agreement with the Lenders. The Lenders agreed to make available to us term loans in an aggregate principal amount of up to $75.0 million under the Loan Agreement. The Loan Agreement provided a term loan commitment of $50.0 million in two potential tranches: (i) a $30.0 million Term A loan facility funded on November 2, 2018 and (ii) a $20.0 million Term B loan facility to be funded at the request of the Company no later than October 31, 2020, subject to (a) the Company having unrestricted net cash proceeds of not less than $50 million from the issuance and sale of common stock and/or from other business activities and (b) the Company having product revenue greater than or equal to $14.0 million on a six month trailing basis prior to September 30, 2020. Both of these term loans had a maturity date of May 2, 2023. The Loan Agreement also provided access to an additional Term C loan facility in the amount of $25.0 million, to be funded at the Lenders’ sole discretion.

In connection with the Loan Agreement and the funding of the Term A facility, we issued to the Lenders warrants to purchase an aggregate of 20,718 shares of our common stock, equal to 3.00% of the term loan funded divided by the exercise price of $43.44. Each warrant will terminate 10 years from the date of its original issuance.

On August 30, 2019, we paid the Lenders a total of $30.7 million representing the principal balance, accrued interest outstanding and a portion of the final fee under the Loan Agreement in repayment of our outstanding obligations under the Loan Agreement. Upon the payment of the $30.7 million, all our outstanding indebtedness and obligations owing to the Lenders under the Loan Agreement were deemed paid in full. The Loan Agreement and the notes thereunder, as well as the security interests in the assets of the Company securing the Loan Agreement and note obligations, were terminated. The Lenders retained the warrants issued to them in connection with the origination of the Loan Agreement obligations.

On June 24, 2019, we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusions on the Nasdaq Global Select Market, referred to as the minimum bid price rule. On September 26, 2019 we affected a 1-for-20 reverse stock split for the purpose of regaining compliance with the minimum bid price rule.

On October 11, 2019, we received notification from the Listing Qualifications Department of the Nasdaq Stock Market that for 10 consecutive business days, the closing bid price of our common stock had been at $1.00 per share or greater, confirming that we had regained compliance with the minimum bid price rule.

On November 1, 2019, we completed a registered direct offering to Armistice Capital, LLC, a healthcare-focused institutional investor, or Armistice, priced at-the-market, of (i) 300,000 shares of common stock and accompanying warrants to purchase an aggregate of 300,000 shares of common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 1,830,493 shares of common stock and accompanying warrants to purchase an aggregate of 1,830,493 shares of common stock. Each share of common stock and accompanying common stock warrant were sold together at a combined price of $3.755, and each pre-funded warrant and accompanying common stock warrant were sold together at a combined price of $3.745. Each pre-funded warrant has an exercise price of $0.01 per share, is exercisable immediately and is exercisable until exercised in full. Each common stock warrant has an exercise price of $3.62 per share, is exercisable immediately and expires five years from the date of issuance. The net proceeds from the offering, after deducting the placement agent's fees and other offering expenses payable by us, are approximately $7.1 million.

On January 24, 2020, we completed a private placement with Armistice priced at-the-market of (i) 1,270,000 shares of common stock and accompanying warrants to purchase an aggregate of 1,270,000 shares of common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 2,063,334 shares of common stock and accompanying warrants to purchase up to an aggregate of 2,063,334 shares of common stock. Each share of common stock and accompanying common stock warrant were sold together at a combined price of $3.00, and each pre-funded warrant and accompanying common stock warrant were sold together at a combined price of $2.999, for gross proceeds of approximately $10 million. Each pre-funded warrant had an exercise price of $0.001 per share, was exercisable immediately and was exercisable until all of the pre-funded warrants are exercised in full. Each common stock warrant had an exercise price of $2.87 per share, was exercisable immediately and will expire five years from the date of issuance.

Also on January 24, 2020, we completed a registered direct offering to certain institutional investors priced at-the-market, of (i) 2,380,105 shares of common stock and accompanying warrants to purchase up to an aggregate of 2,380,105 shares of common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 120,000 shares of common stock and accompanying warrants to purchase up to an aggregate of 120,000 shares of common stock. Each share of common stock and accompanying common stock warrant were sold together at a combined price of $3.00, and each pre-funded warrant and accompanying common stock warrant were sold together at a combined price of $2.999, for gross proceeds of approximately $7.5 million. Each pre-funded warrant had an exercise price of $0.001 per share, was exercisable immediately and was exercisable until all of the pre-funded warrants are exercised in full. Each common stock warrant had an exercise price of $2.87 per share, was exercisable immediately and will expire five years from the date of issuance.

The net proceeds from the concurrent January 2020 private placement and registered direct offering, after deducting the placement agent’s fees and other estimated offering expenses payable by us, were approximately $15.9 million.

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

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Net cash used in operating activities	$ (63,670)	$ (59,628)
Net cash provided by (used in) investing activities	478	(4,954)
Net cash provided by (used in) financing activities	(23,345)	36,447
Net decrease in cash and cash equivalents	$ (86,537)	$ (28,135)

Cash Flows from Operating Activities. The $4.0 million increase in cash used in operating activities for the year ended December 31, 2019, compared to the year ended December 31, 2018, was primarily due to our increase in commercial spend for Xerava compared to the same period in 2018.

Cash Flows from Investing Activities. The $5.4 million decrease in cash used in investing activities for the year ended December 31, 2019, compared to the year ended December 31, 2018 was due to a $4.8 million payment to Harvard upon FDA approval of Xerava during the second half of 2018 together with cash proceeds from sales of lab equipment in 2019.

Cash Flows from Financing Activities. For the year ended December 31, 2019, the $23.3 million cash used in financing activities was due principally to the repayment of the Solar debt facility and related fees in August 2019 offset in part by net proceeds provided by the registered direct offering completed in November 2019. For the year ended December 31, 2019 the $36.4 million in cash provided by financing activities was primarily from the Solar debt facility plus sales of common stock under our amended sales agreement with Cantor.

Operating Capital Requirements

We expect to incur significant operating losses for at least the next several years as we commercialize Xerava and satisfy our obligations under our license agreement with Harvard.

We believe, based on our current operating plan, that our existing cash and cash equivalents as of December 31, 2019 and our projected revenues from sales of Xerava, together with the net proceeds of approximately $15.9 million from our registered direct offering and concurrent private placement of equity securities in January 2020, will be sufficient to fund our operations into the first quarter of 2021, however, we have based this estimate on assumptions that may prove to be wrong, and our capital resources may be utilized faster than we currently expect. In accordance with the requirements of ASC 205-40, based on our recurring losses and cash outflows from operations since inception, expectation of continuing operating losses and cash outflows from operations for the foreseeable future and the need to raise additional capital to finance our future operations, we have concluded that there is substantial doubt about our ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. There is no assurance that we will be successful in obtaining additional financing on terms acceptable to us, if at all, nor is it considered probable under the accounting standards. As such, under the requirements of ASC 205-40, management may not consider the potential for future capital raises or management plans to reduce costs that are not considered probable in their assessment of our ability to meet our obligations.

We will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund our operations beyond such time. If we are unable to obtain funding, we may be required to delay, reduce or eliminate our commercialization efforts, which could adversely affect our business prospects, and we may be unable to continue operations. In light of our limited cash resources, we are exploring strategic alternatives to maximize shareholder value, including the potential sale or merger of the Company or our assets.

We have based our projections of operating capital requirements and revenues on assumptions that may prove to be incorrect, and we may use all of our available capital resources sooner than we expect. However, because of the numerous risks and uncertainties associated with the commercialization of pharmaceutical products such as Xerava, our estimates of our operating capital requirements may be incorrect. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, although we are exploring out-licensing opportunities for our pipeline of early-stage antibiotics and oncology product candidates, there can be no assurance that we will be able to out-license these on a timely basis or on terms that are favorable to us, or at all. Our failure to raise capital through financing or a license of our pipeline as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. We could be forced to significantly scale back or discontinue the commercialization of Xerava and reduce other expenditures, 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 Xerava and our product candidates. In addition, in such circumstance, we would consider seeking protection under the bankruptcy laws in order to continue to pursue potential transactions and conduct a wind-down of our company. If we decide to seek protection under the bankruptcy laws, we would expect that we would file for bankruptcy at a time that is significantly earlier than when we would otherwise exhaust our cash resources. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether and to what extent any resources will be available for distributions to stockholders. Our future funding requirements, both short-term and long-term, will depend on many factors, including, but not limited to:

- revenues received from commercial sales of Xerava;
- our ability to enter into collaborations, licensing, marketing, distribution or other arrangements with respect to Xerava and our product candidates, and the terms and timing of any such arrangements into which we enter;
- the timing and costs of manufacturing and other activities in connection with the commercialization of Xerava;
- 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 University, or Harvard, and other licenses under license agreements to which we may be a party;

- the costs of maintaining and protecting our intellectual property rights and defending against intellectual property related claims;
- the extent to which we in-license or acquire other products and technologies; and
- our ability to continue as a going concern.

We will need to obtain substantial additional funding in order to successfully commercialize Xerava. 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, additional 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 or if our product revenue does not meet our current projections, or if, from our exploration of strategic alternatives, we are unable to consummate such a transaction or transactions on a timely basis or at all, we could be forced to significantly delay, scale back or discontinue the commercialization of Xerava or reduce other expenditures, 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 Xerava and our product candidates.

Contractual Obligations and Commitments

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2019:

	Payment due by period				
Contractual Obligations	**Total**	**Less than 1 Year**	**1 -3 Years**	**3-5 Years**	**More than 5 Years**
			(in thousands)		
Operating leases (1)	$ 5,573	$ 1,875	$ 3,698	$ -	$ —
Total contractual cash obligations	$ 5,573	$ 1,875	$ 3,698	$ -	$ —

(1) On November 29, 2018, we amended our existing operating lease to extend our lease term through November 30, 2022. In January 2020, we amended our lease to reduce the square feet of office, research and laboratory space from approximately 37,438 square feet to approximately 21,539 square feet. In third quarter of 2016, we entered into a sublease with respect to a portion of our principal facilities, which consist of office, research and laboratory space located at 480 Arsenal Way, Watertown, Massachusetts, with an unrelated third party. This sublease was terminated in August 2019. This amendment is expected to reduce the Company's lease expense related to its office lease by approximately $0.8 million annually.

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 a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

ITEM 8. Financial Statements and Supplementary Data

TETRAPHASE PHARMACEUTICALS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Tetraphase Pharmaceuticals, Inc. (the Company) as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company will require additional capital to fund its current operating plan and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Adoption of New Accounting Standard

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2019 as a result of the adoption of Accounting Standards Update (ASU) No. 2016-02, *Leases* (Topic 842), and the related amendments.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting 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.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2007.
Boston, Massachusetts
March 11, 2020

Tetraphase Pharmaceuticals, Inc.
Consolidated Balance Sheets

(In thousands, except par value amounts)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 21,239	$ 107,776
Accounts receivable, net	1,503	2,274
Contract asset	—	3,000
Assets held for sale	53	—
Inventory	1,595	748
Prepaid expenses and other current assets	2,103	2,674
Total current assets	26,493	116,472
Property and equipment, net	98	1,121
Intangible assets, net	4,259	4,652
Operating lease right-of-use assets	4,836	—
Restricted cash	699	699
Total assets	$ 36,385	$ 122,944
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,429	$ 3,210
Accrued expenses and other	5,794	11,761
Operating lease liabilities	1,547	—
Total current liabilities	9,770	14,971
Long-term operating lease liabilities	3,448	—
Loan payable	—	28,291
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, par value $0.001 per share; 5,000 shares authorized; no shares issued and outstanding	—	—
Common stock, par value $0.001 per share; 125,000 shares authorized; 3,466 and 2,684 shares issued and outstanding at December 31, 2019 and 2018, respectively	3	3
Additional paid-in capital	627,291	613,721
Accumulated deficit	(604,127)	(534,042)
Total stockholders' equity	23,167	79,682
Total liabilities and stockholders' equity	$ 36,385	$ 122,944

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except per share data)

	Years Ended December 31,	
	2019	**2018**
Revenue:		
Product revenue, net	$ 3,575	$ 178
License and collaboration revenue	2,000	12,677
Government revenue	1,801	6,049
Total revenue	7,376	18,904
Expenses:		
Cost of revenue - product sales	2,687	130
Cost of revenue - intangible asset amortization	393	98
Research and development	22,785	54,879
Selling, general and administrative	49,043	37,078
Total expenses	74,908	92,185
Loss from operations	(67,532)	(73,281)
Other income and expenses		
Loss on extinguishment of debt	(1,568)	-
Other income	333	-
Interest income	1,262	1,747
Interest expense	(2,580)	(624)
Net loss	$ (70,085)	$ (72,158)
Net loss per share-basic and diluted	$ (22.85)	$ (27.48)
Weighted-average common shares used in net loss per share-basic and diluted	3,067	2,626
Comprehensive loss	$ (70,085)	$ (72,158)

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
Consolidated Statements of Stockholders' Equity

(In thousands)

	Common Shares		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount			
Balance at December 31, 2017	2,573	$ 3	$ 592,291	$ (461,884)	$ 130,410
Issuance of common stock under stock plans	9	—	271	—	271
Issuance of common stock under "at-the-market" equity offering sales agreement, less issuance costs	98	—	7,039	—	7,039
Issuance of warrants to purchase common stock	—	—	803	—	803
Issuance of common stock under employee stock purchase plan	4	—	188	—	188
Stock-based compensation expense	—	—	13,129	—	13,129
Net loss	—	—	—	(72,158)	(72,158)
Balance at December 31, 2018	2,684	$ 3	$ 613,721	$ (534,042)	$ 79,682
Issuance of common stock under stock plans	68	—	—	—	-
Issuance of common stock and prefunded warrants under registered direct offering, less issuance costs	300	—	7,066	—	7,066
Issuance of common stock from warrant exercise	400	—	4	—	4
Issuance of common stock under employee stock purchase plan	14	—	65	—	65
Stock-based compensation expense	—	—	6,435	—	6,435
Net loss	—	—	—	(70,085)	(70,085)
Balance at December 31, 2019	3,466	$ 3	$ 627,291	$ (604,127)	$ 23,167

See accompanying notes to consolidated financial statements.

Tetraphase Pharmaceuticals, Inc.
Consolidated Statements of Cash Flows

(In thousands)

	Years Ended December 31,	
	2019	**2018**
Operating activities		
Net loss	$ (70,085)	$ (72,158)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization	633	576
Non-cash interest expense related to notes payable	621	145
Stock-based compensation expense	6,435	13,129
Loss on extinguishment of debt	1,568	—
Impairment of equipment related to restructuring	335	—
Gain on asset disposal	(83)	—
Changes in operating assets and liabilities:		
Accounts receivable	772	2,379
Contract asset	3,000	(3,000)
Inventory	(847)	(748)
Prepaid expenses and other assets	569	3,708
Accounts payable	(781)	(2,096)
Accrued expenses and other liabilities	(5,851)	(909)
Deferred revenue	(6)	(654)
Operating lease right-of-use assets	1,402	—
Operating lease liabilities	(1,352)	—
Net cash used in operating activities	(63,670)	(59,628)
Investing activities		
Acquisition of intangible assets	—	(4,750)
Proceeds from sale of property and equipment	586	—
Purchases of property and equipment	(108)	(204)
Net cash provided by (used in) investing activities	478	(4,954)
Financing activities		
Repayment of debt, including final payment	(30,480)	—
Proceeds from sale of common stock and prefunded warrants under registered direct offering, net of issuance costs	7,066	—
Proceeds from issuance of common stock under "at-the-market" equity offering sales agreement, net of issuance costs	—	7,039
Proceeds from exercise of warrant	4	—
Proceeds from issuance of debt, net of issuance costs	—	28,949
Proceeds from issuance of stock under stock plans	65	459
Net cash provided by (used in) financing activities	(23,345)	36,447
Net decrease in cash, cash equivalents and restricted cash	(86,537)	(28,135)
Cash, cash equivalents and restricted cash at beginning of period	108,475	136,610
Cash, cash equivalents and restricted cash at end of period	$ 21,938	$ 108,475
Supplemental cash flow information:		
Cash paid for interest on long-term debt	$ 1,955	$ 480

See accompanying notes to consolidated financial statements.

1. Organization and Operations

The Company

Tetraphase Pharmaceuticals, Inc. (the "Company") is a biopharmaceutical company using its proprietary chemistry technology to create, develop and commercialize novel tetracyclines for serious and life-threatening conditions, including bacterial infections caused by multidrug-resistant, or MDR, bacteria. There is a medical need for new antibiotics as resistance to existing antibiotics increases. In recognition of this need, the Company has developed its product, Xerava (eravacycline), a fully synthetic fluorocycline, as an intravenous, or IV antibiotic for use as a first-line empiric monotherapy for the treatment of MDR infections, including MDR Gram-negative infections, such as those found in complicated intra-abdominal infections, or cIAI.

On August 27, 2018, the United States Food and Drug Administration, or FDA, approved Xerava for the treatment of cIAI in adults. Approval of Xerava was based on its IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline) phase 3 program. In October 2018, the Company commenced sales of Xerava in the United States.

On September 20, 2018, based on the results of IGNITE1, the European Commission, or EC, granted marketing authorization for Xerava for the treatment of cIAI in adults in all 28 countries of the European Union, or EU, plus Norway, Iceland and Liechtenstein. The Company has not yet commenced sales outside of the U.S. In February 2018 the Company entered into a license agreement with Everest Medicines Limited, or Everest Medicines, granting Everest Medicines commercialization rights to eravacycline in China and other Asian territories.

In June 2019, the Company announced a restructuring of its organization, including a 20% reduction in headcount, designed to focus the Company's cash resources on commercializing Xerava primarily in the hospital setting. This reorganization included the elimination of the Company's internal research function. As part of our restructuring, the Company decided not to engage in further product development, including conducting clinical trials of its product candidates, and is exploring out-licensing opportunities for all of its pipeline of early-stage antibiotics and oncology product candidates.

Liquidity and Going Concern

Accounting Standards Update ("ASU"), 2014-15, *Presentation of Financial Statements-Going Concern (Subtopic 205-40)*, also referred to as Accounting Standards Codification ("ASC") 205-40 ("ASC 205-40"), requires the Company to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the financial statements are issued. This evaluation requires management to perform two steps. First, management must evaluate whether there are conditions and events that raise substantial doubt about the entity's ability to continue as a going concern. Second, if management concludes that substantial doubt is raised, management is required to consider whether it has plans in place to alleviate that doubt. Disclosures in the notes to the financial statements are required if management concludes that substantial doubt exists or that its plans alleviate the substantial doubt that was raised.

The Company has incurred annual net operating losses in every year since its inception. As of December 31, 2019, the Company had incurred losses since inception of $604.1 million and anticipates that it will continue to incur significant operating losses for the foreseeable future. The Company has financed its operations primarily through public offerings and private placements of equity securities, debt financings, revenue from United States government grants and contract awards and milestone payments from its licensing agreement. The Company will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund our operations including ongoing spending to commercialize Xerava.

As reflected in the consolidated financial statements, the Company had available cash and cash equivalents of $21.2 million at December 31, 2019. In addition, on January 24, 2020, the Company raised $15.9 million in net proceeds through a private placement and registered direct offering. The Company's forecasted cash required to fund operations, including its projected revenues from sales of Xerava, for a period of at least one year from the date of issuance of these consolidated financial statements, indicates that the Company has insufficient funds to continue operations through March 11, 2021, one year from the issuance of these financial statements. This estimate is based on certain significant assumptions, which are uncertain and may turn out to be incorrect. In particular, the forecast assumes continued significant growth of Xerava revenue, for which the Company has limited historical experience to base its estimate. In addition, the Company has forecast a continued reduction in expenses in 2020 as a result of the restructuring announced in June 2019. If these estimates are incorrect, the Company may use its cash resources sooner than expected. These factors raise substantial doubt about the Company's ability to continue as a going concern.

The Company will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund its operations including ongoing spending to commercialize Xerava, however, there can be no assurance that the Company will be able to obtain such funding or generate product revenue or revenues from collaborative partners, on terms acceptable to the Company, on a timely basis or at all. If the Company is unable to raise capital when needed or if its operating results fall short of its current projections, or if the Company determines to explore strategic alternatives but is unable to consummate such a transaction or transactions on a timely basis or at all, the Company could be forced to significantly delay, scale back or discontinue the commercialization of Xerava or reduce other expenditures, 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, the Company's rights to Xerava and its product candidates. The failure of the Company to obtain sufficient funds on acceptable terms when needed would have a material adverse effect on the Company's business, results of operations and financial condition. Because of the uncertainty in obtaining further funding, substantial doubt exists with respect to the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

Segment Information

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

Reverse Stock Split

On September 25, 2019, the Company's Board of Directors authorized a 1-for-20 reverse stock split and approved an amendment to the Company's Certificate of Incorporation (the "Amendment") to effect the 1-for-20 reverse split of the Company's common stock, which was effected on September 26, 2019. All of the share and per share amounts disclosed in these consolidated financial statements have been adjusted to reflect the reverse stock split.

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 product revenue, inventory, impairment of intangible assets, stock-based compensation expense, and going concern considerations. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Concentrations of Credit Risk and Off-Balance Sheet Risk

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

The Company is also subject to credit risk on its accounts receivable. The Company's trade receivables from product sales have payment terms ranging from 30 to 60 days. The Company has evaluated the creditworthiness of its customers and has determined each of them to be creditworthy. The Company has not experienced any trade receivable losses to date.

Principles of Consolidation

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

Cash and Cash Equivalents

The Company considers all highly liquid investments with maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents at December 31, 2019 and 2018 consisted of cash and money market funds.

Fair Value Measurements

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

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

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

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

Financial instruments measured at fair value as of December 31, 2019 and 2018 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, 2019				
Cash and money market funds	$ 21,239	$ 21,239	$ —	$ —
December 31, 2018				
Cash and money market funds	$ 107,776	$ 107,776	$ —	$ —

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 which is materially consistent with its cost.

Accounts Receivable

Accounts receivable at December 31, 2019 and December 31, 2018 represent amounts due from two main sources: (1) Trade accounts receivable of $0.8 million and $0.1 million, respectively, consisting of payments to be received from customers for sales of Xerava, net of prompt payment discounts, chargebacks, rebates and certain fees and (2) contract accounts receivable of $0.7 million and $2.2 million, respectively, related to the Company's government-related agreements.

Contract accounts receivable relate to payments from entities administering the Company's government-related agreements which include unbilled contract accounts receivable of $0.7 million and $0.7 million at December 31, 2019 and 2018, respectively.

Contract Balances

The Company recognizes a contract asset when the Company transfers goods or services to a customer before the customer pays consideration or before payment is due, excluding any amounts presented as a receivable (i.e., accounts receivable). A contract asset represents the Company's right to consideration in exchange for goods or services that the Company has transferred to a customer.

As of December 31, 2018, such contract assets were $3.0 million in relation to milestone payments to be received under the terms of the Everest Medicines License Agreement. For the twelve-month period ended December 31, 2018, the Company recognized license revenue included in such contract assets of $3.0 million. See Note 3 for further details.

Inventory

Inventory is stated at the lower of cost or net realizable value on a first-in, first-out (FIFO) basis. Prior to the regulatory approval of Xerava, given the uncertainty of approval, the Company recognized as research and development expense costs related to the manufacture of Xerava. Upon approval of Xerava, the Company began to capitalize such costs as inventory.

During each quarter, the Company performs an assessment quantifying any potential excess or obsolete inventory and writes down any such inventory to its net realizable value in the period in which the impairment is identified. These adjustments are based upon multiple factors, including inventory levels at the company and at its specialty distributors, projected demand and product shelf life. These impairment charges, if required, are recorded as a cost of revenue. As of December 31, 2019 and 2018, there was no excess or obsolete inventory.

Inventory consisted of the following at December 31:

	December 31, 2019	December 31, 2018
Raw Materials	$ -	$ -
Work-in-process	115	655
Finished goods	1,480	93
Total Inventory	$ 1,595	$ 748

Inventory is related to commercial product, Xerava. There were no reserves or write downs for excess and obsolete inventory during the years ended December 31, 2019 and 2018.

Leases

Effective January 1, 2019, the Company adopted Accounting Standards Codification, or ASC, Topic 842, *Leases*. The Company adopted the new guidance as of January 1, 2019 using the modified retrospective adoption method in which it did not restate prior periods. Prior periods are presented in accordance with ASC 840, *Leases.*

The Company's review and approval process for new leases, contracts, amendments and renewals includes an evaluation at the inception of each agreement to determine whether the contract is within the scope of ASC Topic 842, or other areas of accounting guidance. The Company's contracts are determined to contain a lease within the scope of ASC Topic 842 when all of the following criteria based on the specific circumstances of the agreement are met: (1) there is an identified asset for which there are no substantive substitution rights; (2) the Company has the right to obtain substantially all of the economic benefits from the identified asset; and (3) the Company has the right to direct the use of the identified asset.

Upon transition to ASC 842, an operating lease asset is valued at the amount of the lease liability adjusted for prepaid or accrued lease payments, the remaining balance of any lease incentives received, unamortized initial direct costs and impairment of the operating lease asset. Once the Company assesses a contract for a lease, it will only reassess whether a contract is or contains a lease if the terms and conditions of the contract are amended. Leases with a greater than one-year duration are categorized on the balance sheet as operating lease assets, lease liabilities, and if applicable, long-term lease liabilities. Leases with a duration of less than one year are not presented on the balance sheet.

The Company records the operating lease asset and related lease liability based upon the present value of the lease payments not yet paid using the discount rate for the lease established at the commencement date. The discount rate associated with each lease agreement is based upon either (i) the rate implicit in the lease or (ii) the Company's incremental borrowing rate if the rate implicit in the lease is indeterminable.

Although separation of lease and non-lease components is required, certain practical expedients are available to entities. The Company's facilities operating leases have lease and non-lease components which the Company has elected to account for as one single lease component. The lease component results in an operating lease asset being recorded on the balance sheet and amortized as lease expense on a straight-line basis to the statements of operations.

Property and Equipment, Net

Property and equipment are stated at cost. Costs of major additions and betterments are capitalized; maintenance and repairs which do not improve or extend the life of the respective assets are charged to expense. Upon disposal, the related cost and accumulated depreciation or amortization is removed from the accounts and any resulting gain or loss is included in the consolidated statements of operations and comprehensive loss. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, which range from three to five years. Leasehold improvements are amortized over the estimated useful lives of the assets or related lease terms, whichever is shorter.

Assets Held-for-Sale

The Company classifies assets as held-for-sale when the following conditions are met: (1) management has committed to a plan to sell, (2) the assets are available for immediate sale in their present condition, (3) the Company has initiated an active program to identify a buyer, (4) it is probable that a sale will occur within one year, (5) the assets are actively marketed for sale at a reasonable price in relation to their current fair value, and (6) there is a low likelihood of significant changes to the plan or that the plan will be withdrawn. If all of the criteria are met as of the balance sheet date, the assets are presented separately in the balance sheet as held-for-sale at the lower of the carrying amount or fair value less costs to sell. The assets are then no longer depreciated or amortized while classified as held-for-sale.

During 2019, the Company disposed of property and equipment with a gross carrying amount of $0.1 million and accumulated depreciation of $0.1 million. The Company did not dispose of any property and equipment during 2018. Depreciation and amortization expense amounted to $0.2 million and $0.5 million in the periods ended December 31, 2019 and December 31, 2018, respectively.

The Company initially recorded certain laboratory equipment asset impairments in the second quarter of 2019 in accordance with ASC 360 *Property, Plant and Equipment* for assets held-and-used, as the criteria to classify the laboratory equipment as held-for-sale had not been met. The Company identified an indicator of impairment related to this held-and-used laboratory equipment as it was more likely than not that some of its laboratory equipment would be sold or otherwise disposed of significantly before the end of its previously estimated useful life primarily as a result of the restructuring described in Note 14. For the laboratory equipment where its fair value did not exceed its carrying amount, an impairment was recognized. Fair value was an estimate of the sales price less cost to sell. In the third quarter of 2019, the Company committed to a plan to actively sell certain of its laboratory equipment. Having met all other criteria, the laboratory equipment met the criteria to classify that equipment as held-for-sale. At December 31, 2019, $0.1 million of laboratory equipment was classified as held-for-sale as reflected in the consolidated balance sheet. Laboratory equipment held-for-sale is reflected at the lower of its carrying amount or fair value less the cost to sell, with any excess recorded as an impairment. In aggregate, impairment losses recognized in connection with laboratory equipment was $0.3 million and included in research and development costs in the consolidated statement of operations for the year ended December 31, 2019.

Long-Lived Assets

The Company evaluates the recoverability of its property, equipment and intangible assets when circumstances indicate that an event of impairment may have occurred. The Company recognizes an impairment loss only if the carrying amount of a long-lived asset is not recoverable based on its undiscounted future cash flows. Impairment is measured based on the difference between the carrying value of the related assets or businesses and the fair value of such assets or businesses.

Restricted Cash

At December 31, 2019 the Company had $699,000 in restricted cash deposits with a bank, of which $500,000 is serving as security for our field force corporate credit card program and $159,000 is collateral for a letter of credit issued to the landlord of the Company's leased facility. If the Company defaults on its rental obligations, $159,000 will be payable to the landlord. In addition, the Company has $40,000 in restricted cash to secure the Company's corporate purchasing credit card.

Intangible Assets

The Company maintains definite-lived intangible assets related to certain capitalized milestone payments to Harvard University (Harvard). These assets are amortized over their remaining useful lives, which are estimated based on the shorter of the remaining patent life or the estimated useful life of the underlying product. Intangible assets are amortized using the economic consumption method if anticipated future revenues can be reasonably estimated. The straight-line method is used when future revenues cannot be reasonably estimated.

The Company assesses its intangible assets for impairment if indicators are present or changes in circumstance suggest that impairment may exist. Events that could result in an impairment, or trigger an interim impairment assessment, include the receipt of additional clinical or nonclinical data regarding one of the Company's drug candidates or a potentially competitive drug candidate, changes in the clinical development program for a drug candidate, or new information regarding potential sales for the drug. If impairment indicators are present or changes in circumstance suggest that impairment may exist, the Company performs a recoverability test by comparing the sum of the estimated undiscounted cash flows of each intangible asset to its carrying value on the consolidated balance sheet. If the undiscounted cash flows used in the recoverability test are less than the carrying value, the Company would determine the fair value of the intangible asset and recognize an impairment loss if the carrying value of the intangible asset exceeds its fair value.

The Company capitalized milestone payments of $4.75 million related to regulatory approval of Xerava in the US and EU, which will be amortized over their estimated useful lives of approximately 12 years. Amortization expense for each of the following five years is expected to be $0.4 million.

During the year ended December 31, 2019, management identified impairment indicators related to the intangible assets for the Harvard milestones. As result, an interim test of recoverability of the intangible asset was performed based on the estimated undiscounted future cash flows related to the intangible asset, and concluded the intangible asset was recoverable. The Company's quantitative assessment considered significant assumptions related to estimates of future Xerava sales, offset by direct costs to derive the sales. The estimates of future Xerava sales include estimates of significant growth as the product was recently launched in the fourth quarter of 2018. Given the limited history of sales and the inherent difficulty in making a long-range forecast, such estimates contain significant uncertainty. If the assumptions regarding forecasted revenue or the costs to derive such revenues are not achieved, we may be required to perform future impairment analyses and record an impairment charge for the intangible asset in future periods. It is not possible at this time to determine if any such future impairment charge would result or, if it does, whether such charge would be material.

Revenue Recognition

Product Revenue

Revenue recognition under ASC 606 is applied through a five-step model as follows: (1) identify the contract(s) with the customer; (2) identify performance obligations in the contract; (3) determine the transaction price; (4) allocate transaction price to the performance obligation; and (5) recognize revenue when (or as) each performance obligation is satisfied.

The Company's arrangements with its distributors are determined to be contracts within the scope of ASC 606 when all five criteria in ASC 606 are met. These five criteria were assessed at the inception of each arrangement. Since the criteria were met during this initial assessment, the Company will not reassess the criteria unless there is an indication of a significant change in facts and circumstances. In order to meet the definition of a contract, it must also be probable that the Company will collect the consideration to which it is entitled for goods or services to be transferred. Once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services to be delivered with each contract, determines whether those are performance obligations and the related transaction price. The Company then recognizes revenue based on the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied.

The Company's product revenue consists of the sales of Xerava, which the Company began selling to customers in October 2018. The Company sells Xerava to specialty distributors. These customers resell Xerava to hospitals or other treatment centers. In addition to these distributor agreements and the related discounts and allowances, the Company is subject to government mandated rebates, chargebacks, and discounts with respect to the purchase of the Company's product. Product revenue is recognized net of reserves for all variable consideration, including discounts, chargebacks, government rebates and product returns. The Company is expensing the costs of obtaining and fulfilling these contracts when incurred. The Company has opted to immediately expense the incremental cost of obtaining a contract when the underlying related asset would have been amortized over one year or less.

The performance obligation from the sale of Xerava is satisfied and revenue is recognized when the specialty distributor customer obtains control of the product, which typically occurs upon delivery to the Customer.

Revenues from product sales are recorded at the net sales price, or transaction price, which includes estimates of variable consideration for which reserves are established and result from contractual adjustments, government rebates, returns and other allowances that are offered within the contracts with our Customers, healthcare providers, payors and other indirect customers relating to the sale of our products.

Reserves for Variable Consideration

The Company evaluates its contracts with customers for forms of variable consideration which may require an adjustment to the transaction price based on their estimated impact. Revenues from product sales are recorded at the gross sales price, net of variable consideration, as described above.

The Company estimates variable consideration using the expected value method, which is the sum of probability-weighted amounts in a range of possible outcomes. These outcomes include market events and trends, forecasted product demand patterns, customer buying patterns and statutory requirements. The resulting reserves represent the Company's best estimates of variable consideration it expects to occur.

Before it can include an amount of variable consideration in the transaction price, the Company must consider whether the amount of variable consideration is constrained. The Company includes estimates of variable consideration in revenue only when it has a "high degree of confidence" that revenue will not be reversed in a subsequent reporting period. To include variable consideration in the estimated transaction price, the entity has to conclude that it is "probable" that a significant revenue reversal will not occur in future periods, considering both the likelihood and magnitude of a revenue reversal to apply the constraint. Based on the above, the Company applies the constraint to variable consideration included in its contracts if it cannot conclude that it is probable that a significant revenue reversal will not occur in future periods.

Trade and Group Purchasing Discounts and Allowances: The Company offers its customers prompt pay discounts and service fees as stated in its customer and group purchasing organization contracts. The Company pays these service fees to its customers and group purchasing organizations in exchange for their performance of various product distribution, marketing and promotional services targeted at advancing end-user sales of the Company's product. The related reserves are set in the same period the corresponding revenue is recognized, resulting in a reduction of product revenue.

Government Chargebacks and Rebates: Under the terms of the Company's master agreements, customers may charge back the Company for reimbursement when they are contractually obligated to sell products to government entities or other end-users at a lower price than the wholesale acquisition cost, or WAC, at which those products were acquired from the Company. These rebates consist of Medicare, TriCare and Medicaid rebates as well as those related to other government drug pricing and reimbursement programs.

Product Returns: Products are eligible for return by the Customers in various scenarios under the Company's returns policies included as part of its master distribution agreements. Return options are provided for expired merchandise, short-dated merchandise, products damaged in transit, or any discontinued, withdrawn, or recalled products. The Company estimates the amount of product that may be returned and records this as a reduction in revenue in the relevant period. The Company currently estimates product return liabilities using available industry data, sales information and visibility into the inventory remaining in the distribution channel. The Company has not received any returns to date since launch.

Total product revenue allowances and reserves as of December 31, 2019 were $0.1 million.

The Company will continue to assess its estimates of the various components of variable consideration as it accumulates additional historical data and make adjustments to these estimates and allowances accordingly.

Collaboration Revenue

The Company has entered into an out-licensing agreement that is evaluated under Accounting Standards Codification, Topic 606 ("Topic 606"), *Revenue from Contracts with Customers*, through which the Company licenses certain of its product candidates' rights to a third party. Any future out-licensing agreements entered into by the Company and additional third parties shall also be evaluated under Topic 606. Terms of these arrangements include various payment types, typically including one or more of the following: upfront license fees; development, regulatory and commercial milestone payments; payments for manufacturing supply services; and/or royalties on net sales of licensed products.

To determine the amount and timing of revenue to be recognized under each agreement, the Company evaluates the following criteria: (i) confirming the goods or services in the contract; (ii) defining the performance obligations under the agreement; (iii) determining the transaction price, including any constraint on variable consideration; (iv) allocating the transaction price to the performance obligations; and (v) defining how the revenue will be recognized for each performance obligation. In determining the accounting treatment for these arrangements, the Company develops assumptions to determine the stand-alone selling price for each performance obligation in the contract. These assumptions may include forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success.

Licenses of Intellectual Property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from upfront fees allocated to the license when the license, including any associated know-how, is transferred to the licensee and the licensee can use and benefit from the license. For licenses that are bundled with other obligations, the Company uses judgment to evaluate the combined performance obligation to determine whether it is satisfied over time or at a point in time and the appropriate method of measuring completion for purposes of recognizing revenue.

Milestone Payments: For arrangements that include development milestone payments, the Company evaluates whether the milestones are considered probable and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are not considered probable of being achieved until those approvals are received.

Manufacturing Supply: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. If the Company is entitled to additional payments when the licensee exercises these options, the Company recognizes revenue when the licensee obtains control of the goods, which is upon delivery.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

Government Contract Revenue

The Company's government contract revenue has been derived from its subcontracts with CUBRC under the BARDA Contract, and the NIAID Contract, its subaward under the NIAID Grant and its cost reimbursement Sub-Award Agreement with the Trustees of Boston University, the administrator of the CARB-X program (Note 3). The Company recognized revenue under these best-efforts, cost-reimbursable and cost-plus-fixed-fee subcontracts and subaward as the Company performed services under the subcontracts and subaward so long as a subcontract and subaward had been executed and the fees for these services were fixed or determinable, legally billable and reasonably assured of collection. Recognized amounts reflected the Company's partial performance under the subcontracts and subaward and equal direct and indirect costs incurred plus fixed fees, where applicable. The Company did not recognize revenue under these arrangements for amounts related to contract periods where funding was 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 were presented gross on the consolidated statements of operations and comprehensive loss as the Company determined it was the primary obligor under these arrangements relative to the research and development services it performed as lead technical expert.

Revenue under the Company's subcontracts under both the NIAID Contract and the BARDA Contract and under the CARB-X Award were earned under a cost-plus-fixed-fee arrangement in which the Company was reimbursed for direct costs incurred plus allowable indirect costs and a fixed-fee earned. Billings under these arrangements were based on approved provisional indirect billing rates, which permitted recovery of allowable fringe benefits, allowable overhead and general and administrative expenses and a fixed fee.

Revenue under the Company's subaward under the NIAID Grant was earned under a cost-reimbursable arrangement in which the Company was reimbursed for direct costs incurred plus allowable indirect costs. Billings under the NIAID Grant were based on approved provisional indirect billing rates, which permitted recovery of fringe benefits and allowable general and administrative expenses.

Cost of Revenue

Cost of revenue consists primarily of the manufacturing and distribution costs for Xerava, Xerava net sales-based royalties and the amortization of the intangible asset associated with certain milestones paid to Harvard related to Xerava. All manufacturing costs incurred prior to Xerava's approval in the United States on August 27, 2018 have been expensed in research and development and are not included in cost of revenue. Manufacturing costs at contract manufacturing sites not yet approved by the US FDA for commercial production have also been expensed in research and development and are not included in cost of revenue.

Research and Development Expenses

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

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

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

Comprehensive Loss

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

Income Taxes

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

Stock-Based Compensation

The Company determines stock-based compensation at the grant date using the Black-Scholes option pricing model to estimate fair value for employee and non-employee equity awards. The Company recognizes the value of the award as an expense on a straight-line basis over the requisite service period using the estimated fair market value of the stock and accounts for forfeitures as they occur. For employee awards with performance conditions, the Company assesses whether the condition is probable of achievement, in which case, the fair value of the award is recognized over the requisite service period.

Recently Adopted Accounting Pronouncements

In June 2018, the FASB issued ASU 2018-07, Compensation – "Stock Compensation (Topic 718), Improvements to Nonemployee Share-based Payment Accounting, which addresses aspects of the accounting for nonemployee share-based payment transactions. This pronouncement is effective for annual reporting periods and interim periods within those annual periods beginning after December 15, 2019. The Company early adopted ASU 2018-07 on April 1, 2019 and there was no impact on adoption.

In February 2016, the Financial Accounting Standards Board, or FASB, issued ASU No. 2016-02, *Leases* (Topic 842), which among other things, results in the recognition of lease assets and lease liabilities by lessees on the Company's balance sheets for virtually all leases. ASU 2016-02 supersedes most previous lease accounting guidance and is effective for interim and annual periods beginning after December 15, 2018. The Company adopted the new guidance as of January 1, 2019 using the modified retrospective adoption method in which it did not restate prior periods. The Company has elected the transition relief package of practical expedients permitted within Topic 842. Accordingly, the Company has not reassessed the classification of its existing leases as the transition date, whether existing contracts at the transition date contain a lease, or whether unamortized initial direct costs before the transition adjustments would have met the definition of initial direct costs at lease commencement. The Company does not allocate consideration in its leases to lease and non-lease components and does not record leases on its balance sheet with terms of 12 months or less.

The Company uses its estimated incremental borrowing rate, which is derived from information available at the lease commencement date, in determining the present value of lease payments. The Company's incremental borrowing rate represents the rate of interest that the Company would have to pay to borrow over a similar term an amount equal to the lease payments in a similar economic environment. The Company considers its recent debt issuances and publicly available data for instruments with similar terms and characteristics when calculating its incremental borrowing rates.

The adoption had a material impact on the consolidated balance sheet related to the recognition of operating lease assets of $6.2 million and lease liabilities of $6.3 million as of January 1, 2019, along with derecognition of deferred rent originally accounted for under the legacy guidance. The adoption did not have a material impact on the consolidated statement of operations. The Company has implemented changes to related processes, controls and disclosures upon adoption of the standard.

There have been no other significant changes to the Company's significant accounting policies since the beginning of this fiscal year.

Recent Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU No. 2016-13, "Financial Instruments – Credit Losses (Topic 326): *Measurement of Credit Losses on Financial Instruments*, or ASU 2016-13. ASU 2016-13 will change how companies account for credit losses for most financial assets and certain other instruments. For trade receivables, loans and held-to-maturity debt securities, companies will be required to recognize an allowance for credit losses rather than reducing the carrying value of the asset. ASU 2016-13 is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2016-13 will have on the Company's consolidated financial position and results of operations.

In December 2019, the FASB issued ASU 2019-12, *Simplifying the Accounting for Income Taxes*, or ASU 2019-12, which includes amendments to simplify the accounting for income taxes by removing certain exceptions to the general principles in ASC 740, *Income Taxes*, or ASC 740. The amendments also improve consistent application of and simplify U.S. GAAP for other areas of ASC 740 by clarifying and amending existing guidance. The new guidance is effective for the Company for annual periods beginning after December 15, 2021 and interim periods within fiscal years beginning after December 15, 2022. Early adoption of the amendments is permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2019-12 will have on the Company's consolidated financial statements.

Net Loss per Common Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration for common stock equivalents. Pre-funded warrants of are considered outstanding as of their issuance date and are included in the basic net loss per share calculation. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, warrants, stock options, and restricted stock units are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

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

	Year Ended December 31,	
	2019	**2018**
Warrants	2,151,211	20,718
Outstanding stock options	177,768	366,020
Unvested restricted stock units	91,981	54,035
Total	2,420,960	440,773

3. Significant Agreements and Contracts

License Agreement

Harvard University

In August 2006, the Company entered into a license agreement for certain intellectual property with Harvard. Under the license agreement, as of December 31, 2019, the Company has paid in aggregate $16.9 million in upfront license fees, sublicense fees, development and regulatory milestone payments and royalties on net sales of such product, for the licensed Harvard technology, and has issued 1,568 shares of common stock to Harvard.

For each product covered by the license agreement, the Company is obligated to make certain payments totaling up to approximately $15.1 million upon achievement of certain development and regulatory milestones and to pay additional royalties on net sales of such product. The Company is also obligated to make certain payments to Harvard based on amounts received under its license agreement with Everest Medicines Limited. For the years ended December 31, 2019 and 2018, the Company paid Harvard $1.1 million and $9.7 million, respectively.

Paratek

On March 18, 2019, the Company and Paratek Pharmaceuticals, Inc., or Paratek, entered into a license agreement, or the Paratek License Agreement. Under the terms of the Paratek License Agreement, Paratek granted to Tetraphase a non-exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses, under certain Paratek patents.

The terms of the Paratek License Agreement provide for the Company to pay Paratek royalties at a low single digit percent on net sales of Xerava sold in the United States. The Company’s obligation to pay royalties with respect to the licensed product is retroactive to the date of the first commercial sale of Xerava and shall continue until there are no longer any valid claims of the Paratek patents which will expire in October 2023.

Everest Medicines License Agreement

In February 2018, the Company entered into a license agreement (the “Everest License Agreement”) with Everest Medicines Limited (“Everest Medicines”), whereby the Company granted Everest Medicines an exclusive license to develop and commercialize eravacycline, for the treatment of complicated intra-abdominal infections and other indications, in mainland China, Taiwan, Hong Kong, Macau, South Korea and Singapore (the “Territory”).

Under the terms of the Everest License Agreement, the Company received from Everest Medicines an upfront cash payment of $7.0 million in the first quarter of 2018 and a cash payment of $2.5 million related to Everest Medicines’ submission of an Investigational New Drug Application, or IND, with the Chinese Food and Drug Administration in June 2018. In 2019, the Company received an additional cash payment of $3.0 million related to Everest Medicine’s initiation of a Phase 3 clinical trial.

The Company is also eligible to receive up to an aggregate of $11.0 million in future clinical development milestone payments and up to an aggregate of $20.0 million in sales milestone payments. There can be no guarantee that any such milestones or sales thresholds will in fact be met. The Company is obligated to make certain payments to Harvard based on amounts received from Everest Medicines under the Everest License Agreement pursuant to the existing license agreement by and between Harvard and the Company.

The Company will also be entitled to receive low double-digit tiered royalties on sales in the Territory, if any, of products containing eravacycline. Royalties are payable with respect to each jurisdiction in the Territory until the latest to occur of: (i) the last-to-expire of specified patent rights in such jurisdiction in the Territory; (ii) expiration of marketing or regulatory exclusivity in such jurisdiction in the Territory; or (iii) ten (10) years after the first commercial sale of a product in such jurisdiction in the Territory. In addition, royalties payable under the Everest License Agreement will be subject to reduction on account of generic competition and after patent expiry in a jurisdiction if required by applicable law, with any such reductions capped at certain percentages of the amounts otherwise payable during the applicable royalty payment period.

In addition, on July 29, 2019, the Company amended its original agreement with Everest Medicines to extend Everest Medicines' exclusive license to develop and commercialize Xerava to the jurisdictions of the Malaysian Federation, the Kingdom of Thailand, the Republic of Indonesia, the Socialist Republic of Vietnam and the Republic of the Philippines. Under the terms of this amendment, the Company received from Everest Medicines an upfront, nonrefundable cash payment of $2.0 million in September 2019. As with the milestones discussed above, the Company is obligated to make certain payments to Harvard based on amounts received from Everest under this amendment pursuant to the existing license agreement by and between Harvard and the Company. During the year ended December 31, 2019, the Company incurred expense of $0.4 million related to this milestone.

Under the terms and conditions of the Everest License Agreement, Everest Medicines will be solely responsible for the development and commercialization of licensed products in the Territory. The Company agreed to manufacture clinical material, which will be paid by Everest at the Company's cost, as well as commercial supply, which will be paid by Everest at cost plus a reasonable margin.

In evaluating the recognition of revenue under the Agreement, the Company identified the following three performance obligations under the Agreement: (i) exclusive license to develop and commercialize eravacycline for the treatment of complicated intra-abdominal infections and other potential, future indications, in the Territory, (ii) provision of information and technical assistance related to the know-how transfer for the development of eravacycline; and (iii) provision of clinical supply to Everest Medicines.

The Company evaluated the Everest License Agreement under Topic 606 at the time of execution of the arrangement. Based on that evaluation, the upfront fee of $7.0 million represented the amount of the consideration to be included in the transaction price, which was allocated to the identified performance obligations. Subsequent to execution, the Company determined that the milestones for the Chinese IND and Phase 3 clinical trial were probable to be achieved and that a significant revenue reversal would not occur, and included the payment amounts of $2.5 and $3.0 million, respectively, in the transaction price.

The Company recognized the $2.0 million territory expansion upfront payment associated with the July 2019 amendment as collaboration revenue during the year ended December 31, 2019, as the Company has no further performance obligations pursuant to the arrangement.

No other clinical milestones, regulatory milestones, sales-based milestones or sales royalties have been included in the transaction price, as these milestones were not considered probable at execution or each reporting period thereafter given Everest Medicines relatively short operating history, the uncertainty of regulatory processes in China and that commercial sales have not commenced. The Company determined that the license and related know-how were a combined performance obligation as the license is not distinct without the provision of the related know-how transfer. The Company's requirement to manufacture clinical supply for Everest Medicines is dependent on Everest Medicines' future purchases, the payment for which was determined to be at cost and therefore potentially represents a material right. However, based on the amount of clinical supply expected to be ordered by Everest Medicines, the Company estimated that the value of this right was immaterial.

Other Material Agreements

Patheon UK Limited Master Manufacturing Services Agreement

In June 2017, the Company and Patheon UK Limited and certain of its affiliates ("Patheon") entered into a master manufacturing services agreement. Under the Patheon agreement, the Company is responsible for supplying the active pharmaceutical ingredient for eravacycline to Patheon, and Patheon is responsible for manufacturing eravacycline, conducting quality control, quality assurance, analytical testing and stability testing and packaging. The Company and Patheon entered into two related product agreements pursuant to the Patheon agreement that govern the terms and conditions of Patheon's manufacture of commercial supplies of eravacycline at Patheon's Greenville, North Carolina and Ferentino, Italy manufacturing sites. Pursuant to the Patheon agreement, the Company has agreed to order from Patheon at least a certain percentage of its annual commercial requirements for eravacycline in the United States and European Union each year for the term of the Patheon agreement. The Patheon agreement has an initial term ending December 31, 2022, and will automatically renew after the initial term for successive terms of two years each, unless either party gives notice of its intention to terminate at least 18 months prior to the end of the then current term. The Company may terminate a product agreement upon 30 days' prior written notice under certain circumstances.

Finorga SAS Commercial Supply Agreement

In October 2017, the Company and Finorga SAS ("Novasep") entered into a commercial supply agreement. Under the agreement, Novasep will, pursuant to accepted purchase orders entered into under the agreement, manufacture for commercial supply the active pharmaceutical ingredient for eravacycline. This agreement has an initial term ending October 16, 2022, and will automatically renew after the initial term, unless either party gives notice of its intention to terminate at least 18 months prior to the end of the then current term. The Company may terminate the Novasep agreement upon 30 days' prior written notice under certain circumstances.

Government Grant and Contracts

BARDA Contract for Eravacycline

The Company received funding for the development of Xerava under an award to CUBRC from BARDA, an agency of the is U.S. Department of Health and Human Services. In January 2012, BARDA awarded a five-year contract, which was subsequently extended, that provided for up to a total of $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens (or BARDA Contract). The funding under the BARDA Contract was also used for the development, manufacturing and clinical evaluation of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria.

In connection with the BARDA Contract, in February 2012, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC, an independent, not for profit, research corporation that specializes in U.S. government-based contracts, which was also the direct recipient of the BARDA Contract. The BARDA Contract and the Company's subcontract with CUBRC under the BARDA Contract had terms which expired on December 31, 2019. Committed funding from CUBRC under the Company's BARDA subcontract was for up to approximately $41.3 million through December 31, 2019, the current contract end date. Total funds of $40.7 million have been received by the Company through December 31, 2019 under this contract. During the years ended December 31, 2019 and 2018, the Company recognized revenue of $1.3 million and $1.5 million, respectively, from the Company's subcontract under the BARDA Contract.

NIAID Grant and Contract for TP-271

The Company received funding for its phase 1 compound TP-271 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 Contract was awarded in September 2011, provided up to a total of approximately $35.8 million and expired on March 31, 2019.

In connection with the NIAID Contract, in October 2011, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC, the direct recipient of the NIAID Contract, which subcontract expired on March 31, 2019 under which the Company could originally receive funding of up to approximately $16.9 million (which was subsequently reduced to $16.3 million based on actual work performed), reflecting the portion of the NIAID Contract funding that could be paid to the Company for its activities. As of December 31, 2019, the Company had received $16.2 million under this agreement. The Company has not received any additional funds under this agreement since that date. Our obligations under the NIAID Contract had been met in full as of December 31, 2019. During the years ended December 31, 2019 and 2018, the Company recognized revenue of $0.1 million and $2.5 million, respectively, from the Company's subcontract under the NIAID Contract.

CARB-X Award for TP-6076

In March 2017, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) selected the Company to receive up to $4.0 million in research funding over eighteen months for TP-6076. In connection with this funding, the Company entered into a cost reimbursement Sub-Award Agreement, or the Sub-Award Agreement, with the Trustees of Boston University, the administrator of the program. The Company began recognizing revenue from the Sub-Award Agreement in April 2017. During the years ended December 31, 2019 and 2018, the Company recognized revenue of $0.5 million and $2.0 million, respectively, under this Sub-Award Agreement and does not expect to receive any additional revenue under the award. As of December 31, 2019, the Company had received $3.2 million. Our obligations under this Sub-Award Agreement have been met in full as of December 31, 2019.

4. Property and Equipment, net and Assets Held-for-Sale

Property and equipment, net and assets held-for-sale at December 31, 2019 and 2018 consisted of the following (in thousands):

Depreciation and amortization expense related to property and equipment for the years ended December 31, 2019 and 2018 was $0.2 million and $0.5 million, respectively.

	December 31,		
	2019	**2018**	**Depreciable lives**
Leasehold improvements	$ 923	$ 923	shorter of assets life or lease term
Furniture and fixtures	234	509	5 years
Office and computer equipment	135	217	3 years
Laboratory equipment	-	3,278	5 years
Property and equipment, gross	1,292	4,927	
Less accumulated depreciation and amortization	(1,194)	(3,806)	
Property and equipment, net	$ 98	$ 1,121	
Assets held-for-sale	$ 53	$ -	

5. Accrued Expenses

Accrued expenses at December 31, 2019 and 2018 consisted of the following (in thousands):

	December 31, 2019	**December 31, 2018**
Salaries and benefits	$ 1,825	$ 3,801
Drug supply and development	2,608	3,901
Professional fees	573	1,178
Commercial	516	910
Clinical trial related	111	146
License payments	-	617
Other	161	1,208
Total	$ 5,794	$ 11,761

The Company has $0.9 million of employee bonuses that are payable contingent, which have not been accrued as of December 31, 2019.

6. Stockholder's Equity

In January 2017, the Company entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement"), with Cantor Fitzgerald & Co. as sales agent ("Cantor"). In July 2017, the Company entered into an amendment to the Sales Agreement to increase the maximum aggregate offering price of the shares of common stock that it may issue and sell from time to time under the Sales Agreement from $40,000,000 to $80,000,000.

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

The Company is not obligated to make any sales of shares of its common stock under the Amended Sales Agreement. The Company or Cantor may suspend or terminate the offering of shares of the Company's common stock upon notice to the other party and subject to other conditions. The Company pays Cantor a commission rate equal to 3.0% of the gross proceeds per share sold.

As of December 31, 2019, the Company had sold an aggregate of 305,522 shares of common stock under the Sales Agreement, at an average selling price of approximately $129.80 per share for aggregate gross proceeds of $39.6 million and net proceeds of $38.2 million after deducting sales commissions and offering expenses. The Company did not sell any shares of Common Stock under the Sales Agreement during 2019. As of March 9, 2020, $40.4 million of common stock remained available to be sold under the Amended Sales Agreement.

On November 1, 2019 the Company completed a registered direct offering to a healthcare-focused institutional investor priced at-the-market, of (i) 300,000 shares of common stock and accompanying warrants to purchase an aggregate of 300,000 shares of common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 1,830,493 shares of common stock and accompanying warrants to purchase an aggregate of 1,830,493 shares of common stock. Each share of common stock and accompanying common stock warrant were sold together at a combined price of $3.755, and each pre-funded warrant and accompanying common stock warrant were sold together at a combined price of $3.745. Each pre-funded warrant has an exercise price of $0.01 per share, is exercisable immediately and is exercisable until exercised in full. Each common stock warrant has an exercise price of $3.62 per share, is exercisable immediately and expires five years from the date of issuance. The net proceeds to the Company from the offering, after deducting the placement agent's fees and other estimated offering expenses payable by the Company, was approximately $7.1 million. The fair value allocated to the common stock, warrants and pre-funded warrants, less issuance costs, was $0.6 million, $2.9 million and $3.6 million, respectively. 400,000 of the pre-funded warrants were exercised during November 2019.

Also, on January 24, 2020 the Company completed a private placement and registered direct offering of common stock and warrants, which raised $15.9 million in net proceeds. Refer to Note 16 for further information.

7. Stock-based Compensation

In February 2013, the Company's board of directors and stockholders approved, effective upon the closing of the IPO, the 2013 Stock Incentive Plan (the "2013 Plan"). Under the 2013 Plan, the Company may grant incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards for the purchase of that number of shares of Common Stock equal to the sum of (i) 84,438 shares of Common Stock, (ii) 12,913 shares of Common Stock that were reserved for issuance under the 2006 Plan that remained available for issuance under the 2006 Plan upon the closing of the IPO, (iii) any shares of Common Stock subject to awards under the 2006 Plan which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company without having been fully exercised or resulting in any Common Stock being issued. In addition, the number of shares of Common Stock that may be issued under the 2013 Plan is subject to automatic annual increases, to be added on January 1 of each year from January 1, 2014 through and including January 1, 2023, equal to the number of shares that is the lesser of (a) 150,000, (b) 4% of the then outstanding shares of Common Stock or (c) an amount determined by the Company's board of directors. In January 2020, the number of shares authorized for issuance under the 2013 Plan increased by 138,642 shares.

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

Stock Options

Stock option activity at December 31, 2019 and changes during the year then ended are presented in the table and narrative below (in thousands, except share and per share data):

	Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Options outstanding at December 31, 2018	366,020	$ 223.11	7.45	$ 5
Granted	9,200	17.72		
Exercised	-	-		
Canceled	(197,452)	213.15		
Options outstanding at December 31, 2019	177,768	$ 223.53	5.62	$ -
Options exercisable at December 31, 2019	126,517	$ 277.42	4.92	$ -

The aggregate intrinsic value in the table above represents the difference between the Company's closing common stock price on the last trading day during the year ended December 31, 2019 and the exercise price of the options, multiplied by the number of in-the-money options. As of December 31, 2019, there was $3.1 million of total unrecognized stock-based compensation cost related to employee and director unvested stock options granted under the 2006 Plan and the 2013 Plan. The Company expects to recognize that cost over a remaining weighted-average period of 1.9 years.

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

	Years Ended December 31,	
	2019	2018
Volatility factor	98.80%-100.42%	91.45%-97.39%
Expected life (in years)	5.78-6.11	5.31-6.11
Risk-free interest rate	1.43%-2.52%	2.41%-3.04%
Dividend yield	0%	0%

For grants in 2019, expected volatility is based on the historic volatility of the Company's common stock and expected term is estimated based on the Company's historical data. For grants in 2018, the Company did not have sufficient historical data to support a calculation of volatility and expected life. As such, the Company used a weighted-average volatility considering he Company's own volatility and the volatilities of a representative group of publicly traded companies and used the simplified method to estimate expected life of the stock option. The risk-free interest rate used for each grant in 2019 and 2018 is based on a zero-coupon U.S. Treasury instrument with a remaining term of the share-based award.

Compensation cost for stock options and restricted stock units granted to employees and directors is based on the estimated grant-date fair value and is recognized over the vesting period of the applicable option on a straight-line basis. Stock-based compensation expense related to stock options and restricted stock units granted to employees and directors was $6.4 million and $13.0 million during the years ended December 31, 2019 and 2018, respectively.

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, 2019 and 2018 was $13.75 and $83.54, respectively.

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

	Year Ended December 31,	
	2019	2018
Research and development	$ 1,872	$ 5,721
General and administrative	4,563	7,408
Total	$ 6,435	$ 13,129

	Year Ended December 31,	
	2019	2018
Stock options	$ 4,848	$ 10,925
Restricted stock units	1,526	2,089
Employee stock purchase plan	61	115
Total	$ 6,435	$ 13,129

Restricted Stock Units and Performance Stock Units

During 2019 and 2018, the Company awarded employees 127,742 and 32,671 restricted stock units, respectively. These restricted stock units vest in annual increments over one to two years, subject to continued employment with the Company.

During 2019 and 2018, , the Company issued to certain employees 16,650 and 14,200 performance stock units, respectively, which vest based on service and performance conditions. During the year ended December 31, 2019, 6,650 awards fully vested. Vesting of these awards is contingent on the occurrence of certain milestone events and fulfillment of any remaining service condition. As a result, the related compensation cost is recognized as an expense when achievement of the milestone is considered probable over the remaining requisite service period.

The following table summarizes the restricted stock and performance stock units activity for the year ended December 31, 2019:

	Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2018	54,035	$ 60.10
Granted	144,392	22.99
Cancelled	(38,783)	33.76
Vested/Released	(67,663)	38.79
Unvested at December 31, 2019	91,981	$ 28.62

As of December 31, 2019, there was $1.0 million of total unrecognized stock-based compensation expense related to restricted stock units and performance stock units granted under the Plan. The expense is expected to be recognized over a weighted-average period of 1.5 years.

8. Employee Stock Purchase Plan

The ESPP was approved by the Company's stockholders on June 12, 2014 and allows the Company to sell an aggregate of 30,000 shares of common stock. The ESPP allows eligible employees to purchase common stock at a price per share equal to 85% of the lower of the fair market value of the common stock at the beginning or end of each period during the term of the ESPP. The offering periods are six months each from May to November and from November to May of each calendar year. Pursuant to the ESPP, the Company sold a total of 14,421 shares of common stock during the year ended December 31, 2019 under the ESPP at purchase prices of $2.09, and $15.05, respectively, which represented 85% of the closing price of the Company's common stock on May 14, 2019, and November 14, 2019, respectively. Pursuant to the ESPP, the Company sold a total of 4,307 shares of common stock during the year ended December 31, 2018 under the ESPP at purchase prices of $63.00, and $32.40, respectively, which represented 85% of the closing price of the Company's common stock on May 12, 2018, and November 14, 2018, respectively. The Company records stock-based compensation expense under the ESPP based on the fair value of the purchase rights using the Black-Scholes option pricing model. The total stock-based compensation expense recorded as a result of the ESPP was $61,000 and $115,000 during the years ended December 31, 2019 and 2018, respectively.

9. Debt Facility

On November 2, 2018, the Company entered into a loan and security agreement (the Loan Agreement) with Solar Capital Ltd., as collateral agent and lender, and the other lenders named therein (Solar Capital Ltd. and the other lenders are collectively referred to as the Lenders). On August 30, 2019, the Company entered into a payoff letter with the Lenders, pursuant to which the Company agreed to pay off and thereby terminate the Loan Agreement. Pursuant to the payoff letter, the Company paid a total of $30.7 million to the Lenders, representing the principal balance, accrued interest outstanding and a portion of the final fee under the Loan Agreement in repayment of the Company's outstanding obligations under the Loan Agreement. The Company recorded a loss from debt extinguishment of $1.6 million as the difference between the net carrying amount of the indebtedness under the Loan Agreement and the amount paid.

In connection with the Loan Agreement and the funding of the initial loan facility, the Company issued to the Lenders warrants to purchase an aggregate of 20,718 shares of the Company's common stock, equal to 3.00% of the term loan funded divided by the exercise price of $43.44. The warrants will terminate 10 years from the date of its original issuance. The warrants were equity classified with a fair value of $0.8 million at issuance and recorded to additional paid in capital.

The Company recorded interest expense related to the loan facility of $2.6 million and $0.6 million for the years ended December 31, 2019 and 2018, respectively.

10. Income Taxes

The Company accounts for income taxes under ASC 740, *Accounting for Income Taxes*. Deferred income tax assets and liabilities are determined based upon differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse.

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

	Year ended December 31,	
	2019	**2018**
United States	$ (67,960)	$ (61,046)
Foreign	(2,125)	(11,112)
Total loss before income taxes	$ (70,085)	$ (72,158)

For the years ended December 31, 2019 and 2018 the Company did not have a current or deferred income tax expense or benefit.

A reconciliation of the Federal statutory tax rate of 21% to the Company's effective income tax rate follows:

	Year ended December 31,	
	2019	**2018**
Federal statutory tax rate	(21.00)%	(21.00)%
State taxes, net of federal benefits	(1.70)%	(5.20)%
State tax rate change	2.00%	1.10%
Permanent differences	0.10%	—
Credits	(0.90)%	(1.80)%
Intellectual property transfer	—	(3.80)%
Change in valuation allowance	14.40%	25.20%
Foreign rate differential	0.60%	3.20%
Equity-based compensation	6.40%	2.30%
Other	0.10%	—
Effective tax rate	—%	—%

As of December 31, 2019, the Company had federal net operating loss carryforwards, or NOLs, of approximately $489.1 million and state net operating loss carryforwards of $418.3 million, which are available to reduce future taxable income. Federal net operating loss carryforwards of $383.1 million will expire on various dates through 2037. $106.0 million of the federal net operating loss carryforwards can be carried forward indefinitely. The state net operating loss carryforwards of $418.3 million will expire at various dates through 2039.

As of December 31, 2019, the Company has a carryforward of disallowed interest expense of $2.9 million, which can be carried forward indefinitely.

The Company also had federal tax credits of $8.8 million and state tax credits of $3.1 million, which may be used to offset future tax liabilities. The federal and state tax credit carryforwards will expire at various dates through 2039 and 2034, respectively.

The NOL, tax credit and disallowed interest 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. In addition, 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. Any adjustment as a result of such study would be fully offset by a decrease in the Company's valuation allowance.

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

	Year ended December 31,	
	2019	**2018**
Deferred tax assets:		
Net operating loss carryforwards	$ 128,773	$ 114,097
Research and development credits and carryforwards	11,270	10,649
Equity-based compensation	4,104	8,836
Accrued expenses and other	414	270
Intangibles	3,243	4,578
Interest limitation carryforward	657	-
Lease liability	1,136	-
Deferred tax assets	149,597	138,430
Deferred tax liabilities:		
Right-of-use asset	(1,100)	-
Deferred tax liabilities	(1,100)	-
Less valuation allowance	(148,497)	(138,430)
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, 2019 and 2018, respectively, because the Company's management has determined that is it more likely than not that these assets will not be realized. The $10.1 million increase in the valuation allowance in 2019 primarily relates to the loss incurred by the Company in this period.

ASC 740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statement by prescribing the minimum recognition threshold and measurement of a tax position taken or expected to be taken in a tax return. The Company had gross tax-effected unrecognized tax benefits of $1.4 million and $1.3 million at December 31, 2019 and 2018, respectively. Unrecognized tax benefits represent tax positions for which reserves have been established. A full valuation allowance has been provided against the Company's deferred tax assets, so that the effect of any unrecognized tax benefits would simply be to reduce the gross amount of the deferred tax asset and the corresponding valuation allowance. The Company anticipates that the amount of unrecognized tax benefits recorded will not change in the next twelve months.

As of December 31, 2019 and 2018, the Company had no accrued interest or penalties related to uncertain tax positions.

The aggregate changes in gross unrecognized tax benefits during the years ended December 31, 2019 and 2018 were as follows (in thousands):

	Year ended December 31,	
	2019	2018
Balance at beginning of year	$ 1,291	$ 1,107
Increases for tax positions taken during current period	73	130
Increases for tax positions taken in prior periods	—	54
Decreases for tax positions taken during current period	—	—
Decreases for tax positions taken in prior periods	—	—
Balance at end of year	$ 1,364	$ 1,291

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 2016 through 2018. 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.

11. Commitments and Contingencies

Lease Commitments

The Company's leases consist of office equipment and office and laboratory space in Watertown, MA. On March 24, 2015, the Company amended its existing operating lease to expand its existing premises by an additional 13,711 square feet of office and laboratory space for a total of 29,610 square feet.

On June 18, 2015, the Company further amended its existing operating lease to expand its leased premises by an additional 7,828 square feet of office and laboratory space for a total of 37,438 square feet.

In the third quarter of 2016, the Company entered into a sublease with respect to a portion of its principal facilities with an unrelated third party. This sublease was terminated in August 2019.

On November 29, 2018, the Company amended its existing operating lease to extend the lease term through November 30, 2022 for all of its existing operating leases.

On January 31, 2020, the Company amended its lease of office and laboratory space in Watertown, MA to reduce the square feet from approximately 37,438 square feet to approximately 21,539 square feet.

On January 1, 2019, the Company adopted ASU 2016-02, *Leases*. Refer to Note 2, "*Summary of Significant Accounting Policies*" herein for additional disclosures.

The Company identified and assessed significant assumptions in recognizing the right-of-use asset and lease liability as follows:

- *Incremental borrowing rate* - The Company's lease agreements do not provide implicit rates. The Company has one outstanding loan facility which was utilized to derive the Company's incremental borrowing rate for its existing leases at the transition date. The Company estimated its incremental borrowing rate based on its credit quality indicators from its outstanding loan facility. The Company compared its incremental borrowing rate to rates available in the market for similar borrowings, and adjusted these rates based on the impact of collateral over the term of the lease to substantiate the incremental borrowing rate applied to its leases at the transition date.
- *Lease and non-lease components* – The Company is required to pay fixed fees for operating expenses in addition to monthly base rent for certain operating leases. The amounts of additional rent associated with these fees are considered non-lease components. The Company has elected the practical expedient which allows non-lease components to be combined with lease components and will therefore include these additional rent amounts in its lease payments. Any variable components of these operating costs are excluded from lease payments and are recognized in the period incurred.

The components of lease expense were as follows:

	Year ended December 31, 2019
Operating lease cost	$ 1,897
Variable lease cost	1,203
Total lease cost	$ 3,100
Weighted-average remaining lease term (years)	2.90
Weighted-average discount rate	9.25%

Cash paid for amounts included in the measurement of the lease liabilities included in the operating cash flows were $1.8 million and $1.4 million for the years ended December 31, 2019 and 2018 respectively.

As of December 31, 2019, the aggregate minimum future rent payments under the lease agreement are as follows (in thousands):

	Total
2020	$ 1,916
2021	1,950
2022	1,785
Thereafter	—
Less: Imputed interest	(656)
Present value of lease payments	$ 4,995

The Company recorded $1.5 million and $1.4 million in rent expense for the years ended December 31, 2019 and 2018, respectively

12. Employee Benefit Plan

In 2007, the Company established the Tetraphase Pharmaceuticals, Inc. 401(k) Plan (the “401(k) Plan”) for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue Code. Eligible employees are permitted to contribute to the 401(k) Plan within statutory and 401(k) Plan limits. During 2014, the Company began to make matching contributions of 50% of the first 6% of employee contributions. The Company made matching contributions of $0.5 million and $0.4 million for the years ended December 31, 2019 and 2018, respectively.

13. Legal Proceedings

On February 7, 2020, DHL Supply Chain (Netherlands) B.V (“DHL”) made an arbitration demand against the Company with Foundation UNUM. The arbitration demand alleges breach of contract by the Company under a letter of intent entered into between the parties in August 2018 between the parties, and DHL seeks full indemnification for all damages and costs resulting from the alleged breach by the Company, including but not limited to loss of profit, which DHL calculates at 2,335,000 Euros. The Company does not believe it has breached any contract with DHL and plans to engage in a vigorous defense against such claims. No amounts have been accrued for this matter at December 31, 2019.

14. Corporate Restructuring Charges

On June 10, 2019, the Company announced a restructuring of its organization, including a 20% reduction in headcount, designed to focus its cash resources on commercializing Xerava. This reorganization included the elimination of its internal research function and an exploration of out-licensing opportunities for all of its pipeline of early-stage antibiotics and oncology product candidates. The Company incurred total costs associated with the restructuring of $2.4 million, all of which the Company incurred during 2019. The restructuring charges consist primarily of severance costs and asset impairment costs, offset in part by stock-based compensation adjustments associated with award modifications.

The restructuring charges recorded during the year ended December 31, 2019 and the related liability balance as of December 31, 2019 for each major type of cost associated with this restructuring plan are as follows:

	Restructuring Expense	Cash payments	Non-cash expense	Restructuring Liability at December 31, 2019
Employee severance and related costs	$ 2,130	$ (1,549)	$ —	$ 581
Asset impairments	335	-	(335)	-
Compensation expense	(97)	-	97	-
	$ 2,368	$ (1,549)	$ (238)	$ 581

15. Quarterly Results (Unaudited)

	Three Months Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
	(in thousands, except per share data) (unaudited)			
Revenues:				
Product revenue, net	$ 341	$ 796	$ 978	$ 1,460
License and collaboration revenue	—	—	2,000	—
Government revenue	932	277	362	230
Total revenue	1,273	1,073	3,340	1,690
Expenses:				
Cost of revenue - product sales	164	307	882	1,334
Cost of revenue - intangible asset amortization	98	99	98	98
Research and development	6,737	8,166	5,348	2,534
Selling, general and administrative	13,314	15,113	11,350	9,266
Total expenses	20,313	23,685	17,678	13,232
Loss from operations	(19,040)	(22,612)	(14,338)	(11,542)
Other income and expenses				
Loss on extinguishment of debt	—		(1,568)	—
Other income	—	250	—	83
Interest income	507	416	252	87
Interest expense	(955)	(975)	(650)	—
Net loss	$ (19,488)	$ (22,921)	$ (16,304)	$ (11,372)
Net loss per share—basic and diluted	$ (7.25)	$ (8.45)	$ (6.00)	$ (2.75)

	Three Months Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(in thousands, except per share data) (unaudited)			
Revenue:				
Product revenue, net	$ —	$ —	$ —	$ 178
License and collaboration revenue	—	9,500	—	3,177
Government revenue	1,891	2,079	1,151	928
Total revenue	1,891	11,579	1,151	4,283
Expenses:				
Cost of revenue - product sales	—	—	—	130
Cost of revenue - intangible asset amortization	—	—	—	98
Research and development	18,127	14,370	11,665	10,717
Selling, general and administrative	5,705	7,165	9,481	14,727
Total expenses	23,832	21,535	21,146	25,672
Loss from operations	(21,941)	(9,956)	(19,995)	(21,389)
Interest income	365	413	437	532
Interest expense	—	—	—	(624)
Net loss	$ (21,576)	$ (9,543)	$ (19,558)	$ (21,481)
Net loss per share—basic and diluted	$ (8.36)	$ (3.68)	$ (7.39)	$ (8.00)

(16). Subsequent Events

On January 24, 2020, the Company completed a private placement with Armistice Capital, LLC, a healthcare-focused institutional investor priced at-the-market of (i) 1,270,000 shares of common stock and accompanying warrants to purchase an aggregate of 1,270,000 shares of common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 2,063,334 shares of common stock and accompanying warrants to purchase up to an aggregate of 2,063,334 shares of common stock. Each share of common stock and accompanying common stock warrant were sold together at a combined price of $3.00, and each pre-funded warrant and accompanying common stock warrant were sold together at a combined price of $2.999, for gross proceeds of approximately $10 million. Each pre-funded warrant had an exercise price of $0.001 per share, was exercisable immediately and was exercisable until all of the pre-funded warrants are exercised in full. Each common stock warrant had an exercise price of $2.87 per share, was exercisable immediately and will expire five years from the date of issuance.

Also on January 24, 2020, the Company completed a registered direct offering to certain healthcare-focused institutional investors priced at-the-market, of (i) 2,380,105 shares of common stock and accompanying warrants to purchase up to an aggregate of 2,380,105 shares of common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 120,000 shares of common stock and accompanying warrants to purchase up to an aggregate of 120,000 shares of common stock. Each share of common stock and accompanying common stock warrant were sold together at a combined price of $3.00, and each pre-funded warrant and accompanying common stock warrant were sold together at a combined price of $2.999, for gross proceeds of approximately $7.5 million. Each pre-funded warrant had an exercise price of $0.001 per share, was exercisable immediately and was exercisable until all of the pre-funded warrants are exercised in full. Each common stock warrant had an exercise price of $2.87 per share, was exercisable immediately and will expire five years from the date of issuance.

The net proceeds to the Company from the registered direct offering and the concurrent private placement, after deducting the placement agent's fees and other estimated offering expenses payable by the Company, were approximately $15.9 million.

On January 31, 2020, the Company amended its lease of office and laboratory space in Watertown, MA to reduce the square feet from approximately 37,438 square feet to approximately 21,539 square feet. This amendment is expected to reduce the Company’s lease and non-lease expense related to its office lease by approximately $1.3 million annually.

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 Senior Vice President, Finance, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. 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 Senior Vice President, Finance concluded that as of December 31, 2019, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our management including our principal executive officer and principal financial officer by others, particularly during the period in which this Annual Report on Form 10-K was prepared and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

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

Internal Control Over Financial Reporting

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

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our management, under the supervision and with the participation of our Chief Executive Officer and Senior Vice President of Finance, conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2019 based on the framework in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on the results of its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2019.

(b) Changes in Internal Control Over Financial Accounting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2019 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

Directors and Executive Officers

The following table sets forth for each director and executive officers of the Company and his or her position with the Company as of March 2, 2020.

Name	Title
Leonard Patrick Gage	Chairman of the Board
Larry Edwards	President, Chief Executive Officer and Director
Garen Bohlin	Director
Steven Boyd	Director
Jeffrey Chodakewitz	Director
John Freund	Director
Gerri Henwood	Director
Guy Macdonald	Director
Keith Maher	Director
Nancy Wysenski	Director
Maria Stahl	Chief Business Officer and General Counsel
Christopher Watt	Senior Vice President, Finance

Directors

Leonard Patrick Gage, Ph.D., age 77, has served as a member of our board of directors and as Chairman of our board of directors since December 2011. Since July 2002, Dr. Gage has served as a consultant to the biopharmaceutical industry. From 1998 to 2002, Dr. Gage served as President of Wyeth Research (now part of Pfizer, Inc.). Prior to joining Wyeth Research, he served in various positions at Genetics Institute, Inc., a publicly traded biotechnology company, from 1989 to 1998, first as head of Research and Development, then as Chief Operating Officer and eventually as President. From 1971 to 1989, Dr. Gage served in various positions in research management with Hoffmann-La Roche Inc., a pharmaceutical company, most recently serving as Vice President responsible for U.S. drug discovery. Dr. Gage has served on the board of directors of Cytokinetics, Incorporated, a publicly traded biopharmaceuticals company, since November 2009 and as Chairman of its board of directors since March 2010. Previously he served on the board of directors of PDL BioPharma, Inc., a publicly traded biotechnology company, from 2003 through 2008, as the Chairman of its board of directors in 2007, and as its Interim Chief Executive Officer from 2007 to 2008. Dr. Gage currently serves on the board of directors of Marine Biological Laboratories. Dr. Gage received an S.B. in physics from the Massachusetts Institute of Technology and a Ph.D. in biophysics from the University of Chicago. We believe that Dr. Gage's extensive industry and board experience as well as his independence allows him to serve as an effective Chairman of our board of directors and to be a key contributor to our board of directors.

Larry Edwards, age 48, has served as our President and Chief Executive Officer and a member of our board of directors since August 2019. Previously he served as our Chief Operating Officer from March 2018 to July 2019. From December 2016 to February 2018, Mr. Edwards served as our Senior Vice President, Chief Commercial Officer and from January 2016 to December 2016 as our Vice President, Commercial Operations. He also served as our Vice President, Marketing from July 2015 to January 2016. Prior to joining Tetraphase, from April 2014 to June 2015, Mr. Edwards served as Senior Director, Marketing at Cubist Pharmaceuticals, Inc., a publicly traded biopharmaceutical company acquired by Merck & Co. in January 2015. Mr. Edwards previously served in various roles at Merck & Co., a publicly traded pharmaceutical company, from 1999 to April 2014, most recently serving as Global Marketing Director, Clostridium Difficile and New Infectious Disease Products. Mr. Edwards received a B.S. from Ohio University. We believe Mr. Edwards extensive experience and knowledge of the antibiotic sector allows him to be a critical contributor to our board of directors.

Garen Bohlin, age 72, has served as a member of our board of directors since July 2010. Since May 2012, Mr. Bohlin has served on the boards of directors and as a consultant to multiple life sciences companies. From January 2010 until April 2012, he served as Executive Vice President of Constellation Pharmaceuticals, Inc., a biopharmaceutical company. Prior to joining Constellation, Mr. Bohlin served as Chief Operating Officer of Sirtris Pharmaceuticals, Inc., a biotechnology company, from 2006 to December 2009. Mr. Bohlin was the founding Chief Executive Officer of Syntonix Pharmaceuticals, Inc., a biopharmaceutical company, from 1999 through December 2005. Earlier in his career, he held multiple executive positions at Genetics Institute, Inc., a biotechnology company, and was a partner at Arthur Andersen & Co., a public accounting and consulting organization. Mr. Bohlin currently serves on the board of directors of Collegium Pharmaceutical, Inc. and Karyopharm Therapeutics, Inc., both publicly traded biotechnology companies. He also served on the board of directors for Acusphere, Inc., a specialty pharmaceutical company that was a publicly traded company, from 2005 to 2014; SpringLeaf Therapeutics, Inc., a private biotechnology company, from 2010 to 2013; Precision Dermatology, Inc., a private dermatology company from 2012 to 2014; and Proteon Therapeutics, Inc., a publicly traded biotechnology company from 2014 to January 2020. Mr. Bohlin received his B.S. in accounting and finance from The University of Illinois. We believe that Mr. Bohlin's industry and board experience, including his audit committee experience, with both publicly traded and privately held companies makes him a key contributor to our board of directors.

Steven Boyd, age 39, has served as a member of our board of directors since January 2020. Mr. Boyd has served since 2012 as the chief investment officer of Armistice Capital, LLC, a long-short equity hedge fund focused on the health care and consumer sectors. From 2005 to 2012, Mr. Boyd was a research analyst at Senator Investment Group, York Capital and SAB Capital Management, where he focused on health care. Mr. Boyd began his career as an analyst at McKinsey & Company. Mr. Boyd currently serves as a member of the boards of directors of Aytu BioScience, Inc., Cerecor Inc., EyeGate Pharmaceuticals, Inc. and Vaxart, Inc. Mr. Boyd received a B.S. in economics and a B.A. in political science from The Wharton School of the University of Pennsylvania. We believe Mr. Boyd's extensive investment experience allows him to be a key contributor to our board of directors.

Jeffrey A. Chodakewitz, M.D., age 64, has served as a member of our board of directors since June 2014. Dr. Chodakewitz currently serves as a senior advisor to Blackstone Life Sciences, a life sciences fund. From April 2018 to March 2019, Dr. Chodakewitz served as Executive Vice President, Clinical Medicine and External Innovation of Vertex Pharmaceuticals Incorporated, a publicly traded pharmaceutical company. From October 2014 to March 2018, Dr. Chodakewitz served as Executive Vice President, Global Medicines Development and Medical Affairs, and Chief Medical Officer of Vertex. From January 2014 to October 2014, Dr. Chodakewitz served as Senior Vice President and Chief Medical Officer of Vertex. Prior to joining Vertex, Dr. Chodakewitz spent more than 20 years at Merck & Co., Inc., where he held a variety of roles including Vice President of Clinical Research—Infectious Diseases & Vaccines, Vice President of Clinical Pharmacology/Early Stage Development, Senior Vice President of Late Stage Development, and Senior Vice President of Global Scientific Strategy (Infectious Diseases, Respiratory/Immunology). Prior to his tenure at Merck, he served as the Director of the HIV Outpatient Clinic at the Veterans Administration Medical Center in West Haven, Connecticut, and held various academic positions at Yale University and New York University Schools of Medicine. Dr. Chodakewitz serves on the board of directors of resTORbio, Inc., a publicly traded biopharmaceutical company focused on age-related diseases. Dr. Chodakewitz is a Diplomate of the National Board of Medical Examiners, the American Board of Internal Medicine (both Internal Medicine and Infectious Diseases). He received a B.S. in Biochemistry from Yale University, cum laude, and an M.D. from the Yale University School of Medicine. We believe that Dr. Chodakewitz's scientific, medical and business background allows him to be a key contributor to our board of directors.

John Freund, M.D., age 66, has served as a member of our board of directors since October 2012. Dr. Freund founded Skyline Ventures, a venture capital firm, in 1997 and has served as a managing director at Skyline since its founding. He is also co-founder, director and chief executive officer of Arixa Pharmaceuticals, Inc., a privately held antibiotic company. Prior to founding Skyline, Dr. Freund served as managing director in the private equity group of Chancellor Capital Management, a private capital investment firm. In 1995, he co-founded Intuitive Surgical, Inc. a medical device company, and served on its board of directors until 2000. From 1988 to 1994, Dr. Freund served in various positions at Acuson Corporation, a maker of ultrasound equipment that is now part of Siemens, most recently as Executive Vice President. Prior to joining Acuson, Dr. Freund was a general partner of Morgan Stanley Venture Partners from 1987 to 1988. From 1982 to 1988, Dr. Freund was at Morgan Stanley & Co., an investment banking company, where he co-founded the Healthcare Group in the Corporate Finance Department in 1983. He has served on the board of directors of Collegium Pharmaceutical, Inc., a publicly traded biotechnology company, since 2014; SI-BONE, Inc., a publicly traded medical device company, since 2012; and Sutro Biopharma, Inc., a publicly traded biotechnology company, since 2014. Dr. Freund also serves on the board of directors of six U.S. registered investment funds managed by Capital Research and Management. He also previously served on the board of directors of a number of publicly traded companies, including Proteon Therapeutics, Inc., a publicly traded biotechnology company; XenoPort, Inc., a biopharmaceutical company, where he served as chairman of the board; Map Pharmaceuticals, Inc. a biopharmaceutical company; Hansen Medical, Inc., a medical device company; Mako Surgical Corp., a medical device company; and Concert Pharmaceuticals, Inc., a biopharmaceutical company. Dr. Freund is a member of the Advisory Board for the Harvard Business School Healthcare Initiative. Dr. Freund received a B.A. in history from Harvard College, an M.D. from Harvard Medical School, and an M.B.A. from Harvard Business School. We believe that Dr. Freund's extensive investment experience, his experience as an executive and his service on the board of directors of numerous public and privately held companies allows him to be a key contributor to our board of directors.

Gerri Henwood, age 67, has served as a member of our board of directors since April 2015. Since 2008, Ms. Henwood has served as President and Chief Executive Officer and a director of Recro Pharma, Inc., a publicly traded contract development and manufacturing organization. Since 2019, Ms. Henwood has also served as President and Chief Executive Officer and a director of Baudax Bio, Inc., a publicly traded acute care specialty pharmaceutical company focusing on developing and commercializing innovative products for the acute care settings. Baudax Bio, Inc. was spun off from Recro Pharma, Inc. From 2006 to 2013, Ms. Henwood served as the President of Malvern Consulting Group, or MCG. She is the co-founder of Auxilium Pharmaceuticals, Inc. and served as its President, Chief Executive Officer and director from 1999 to 2006. Prior to founding Auxilium, in 1985, Ms. Henwood founded, and was President and Chief Executive Officer of, a publicly traded contract research organization, IBAH, Inc., which was acquired by Omnicare, Inc. Prior to founding IBAH, Inc., Ms. Henwood began her career with Smith Kline & French, now part of GlaxoSmithKline plc, in the pharmaceutical management program. She held many positions there, including the position of head of Regulatory and Medical Affairs for the U.S. business and the position of Group Director—Marketing in the International Pharmaceutical Division. Ms. Henwood holds a B.S. in Biology from Neumann University. We believe Ms. Henwood's expertise in product commercialization, clinical development and regulatory approval processes allows her to be a key contributor to our board of directors.

Guy Macdonald, age 61, has served as a member of our board of directors since January 2008 and served as our President and Chief Executive Officer from January 2008 until July 2019. 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 Scynexis, Inc., a publicly traded biotechnology company. Mr. Macdonald received an Honours Degree in biochemistry from Dundee University in Dundee, Scotland. We believe Mr. Macdonald's qualifications to serve on our board of directors include his extensive experience in the healthcare industry as well as his extensive knowledge of our company and our business through service as our President and Chief Executive Officer.

Keith Maher, M.D., age 51, has served as a managing director at Armistice Capital, LLC since 2019. From 2007 to 2018, Dr. Maher held senior roles at Schroder Investment Management, Omega Advisors and Gracie Capital. Dr. Maher joined Gracie from Valesco Healthcare Partners, a global healthcare fund he founded in partnership with Paramount Bio Capital. Prior to starting Valesco, Dr. Maher was a managing director at Weiss, Peck & Greer (WPG) Investments. He joined WPG from Lehman Brothers, where he worked as an equity research analyst covering medical device and technology companies. Dr. Maher currently serves on the boards of directors of EyeGate Pharmaceuticals, Inc. and Vaxart, Inc. Dr. Maher received a B.A. in biology from Boston University, an M.B.A. from Northwestern University's Kellogg Graduate School of Management and an M.D. from Albany Medical College. Dr. Maher completed his clinical training at the Mount Sinai Medical Center in the Department of Medicine. We believe Dr. Maher's extensive investment experience allows him to be a key contributor to our board of directors.

Nancy Wysenski, age 62, has served as a member our board of directors since March 2014. From December 2009 through June 2012, Ms. Wysenski served as the Executive Vice President and Chief Commercial Officer of Vertex Pharmaceuticals Incorporated, a publicly traded pharmaceutical company. Prior to joining Vertex, Ms. Wysenski held the position of Chief Operating Officer of Endo Pharmaceuticals, a 1,200-person specialty pharmaceutical company, where she led sales, marketing, commercial operations, supply chain management, human resources and various business development initiatives. Prior to her time at Endo, Ms. Wysenski participated in the establishment of EMD Pharmaceuticals, Inc., where she held various leadership positions, including the role of President and Chief Executive Officer from 2001 to 2006 and Vice President of Commercial from 1999 to 2001. From 1984 to 1998, Ms. Wysenski held several sales-focused roles at major pharmaceutical companies, including Vice President of Field Sales for Astra Merck, Inc. Ms. Wysenski serves as a director of Alkermes plc, a publicly traded biopharmaceutical company. She is a founder of the Research Triangle Park Chapter of the Healthcare Businesswomen's Association and served on the Nominating Committee and National Advisory Board of the Healthcare Businesswomen's Association. Ms. Wysenski received a B.S.N. in Nursing from Kent State University and an M.B.A. from Baldwin-Wallace College. We believe that Ms. Wysenski's experience, leadership skills and knowledge of the life sciences industry allow her to provide valuable insight to our board with respect to the launch and commercialization of pharmaceutical products.

Executive Officers (other than the Chief Executive Officer)

Maria Stahl, age 49, has served as our Chief Business Officer and General Counsel since June 2019 and served Senior Vice President and General Counsel from March 2015 to June 2019. Prior to joining Tetraphase, Ms. Stahl served as Senior Vice President, General Counsel of Idenix Pharmaceuticals, Inc., a publicly traded biotechnology company until its acquisition by Merck & Co., from October 2010 to August 2014. Ms. Stahl received a B.A. from Providence College and a J.D. from Yale Law School.

Christopher Watt, age 55, has served as our Senior Vice President, Finance since January 2017. He previously served as our Vice President, Finance from July 2015 to January 2017. Prior to joining Tetraphase, Mr. Watt spent ten years at Biogen, Inc., a publicly traded pharmaceutical company, most recently serving as Senior Director, Global Commercial Finance. From 2009 to 2011, Mr. Watt served as the Finance Director for Biogen's UK/Ireland affiliate and from 2006 to 2009 as Director of Business Planning, International. Prior to Biogen, Mr. Watt spent fifteen years in various financial roles at InterSystems Corporation, Putnam Investments, Procter and Gamble and Shawmut Bank. Mr. Watt received a B.A. from Colby College and an M.B.A. from the University of Michigan.

Audit Committee

We have established an Audit Committee consisting of the following individuals, each of whom qualifies as independent within the meaning of the applicable Listing Rules of the Nasdaq Stock Market LLC (the "Nasdaq Rules") and meets the criteria for independence set forth in Rule 10A-3(b)(1) under the Securities Exchange Act of 1934 ("Exchange Act"): Leonard Patrick Gage (Chairman), Garen Bohlin and John Freund. The Board of Directors has determined that Mr. Bohlin meets the qualifications of an "audit committee financial expert" under SEC Rules and the qualifications of "financial sophistication" under the applicable Nasdaq Rules.

Code of Business Conduct and Ethics

We have also adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is posted on the "Investors—Corporate Governance" section of our website, which is located at www.tphase.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a Current Report on Form 8-K to be filed with the Securities and Exchange Commission (the "SEC").

ITEM 11. Executive Compensation

This section explains our executive compensation program as it relates to our "named executive officers" whose compensation information is presented in the tables below in accordance with Securities and Exchange Commission rules for smaller reporting companies. It discusses the material elements of our executive compensation policies and decisions and the most important factors relevant to an analysis of these policies and decisions. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the tables below. Our named executive officers for 2019 are:

- Larry Edwards, our president and chief executive officer;
- Guy Macdonald, our former president and chief executive officer;
- Maria Stahl, our chief business officer and general counsel; and
- Christopher Watt, our senior vice president, finance.

We present our executive compensation program in the following sections:

- Overview of Our Executive Compensation Program;
- Compensation Governance: Our Executive Compensation Philosophy and Process;
- Key Elements of Our Compensation Program;
- Summary Compensation Table;
- 2019 Executive Compensation Decisions;
- Employment Agreements, Severance and Change in Control Arrangements;
- Other Compensation Agreements and Policies; and
- Outstanding Equity Awards at Fiscal Year-End.

Overview of Our Executive Compensation Program

We have designed our executive compensation program to motivate our management team to create long-term value for our stockholders through the achievement of strategic business objectives, while effectively managing the risks and challenges inherent in a biopharmaceutical company. Specifically, our executive compensation program is designed to promote the achievement of key strategic objectives by linking executives' short- and long-term cash and equity incentives to the achievement of measurable corporate and individual performance goals.

Our executive compensation programs are designed to be competitive with our peer group to enable us to attract, motivate, reward, and retain outstanding talent. Our compensation programs are based on the following key principles:

- Linkage of pay with performance and the achievement of our strategic goals.
- Alignment of our executives' interests with those of our stockholders through equity compensation.
- Overall compensation that is competitive in the industry in which we compete for executive talent. Compensation opportunities should be competitive with biotechnology companies of similar size and comparable stage of development, but also should be designed to be flexible enough to attract talent as needed from larger biopharmaceutical companies.
- Recognition of individual contributions, teamwork and corporate performance.

Compensation Governance: Our Executive Compensation Philosophy and Process

Role of the Compensation Committee

The compensation committee of our board of directors has primary responsibility for designing, implementing and maintaining our compensation program for our executive officers, including our named executive officers. The responsibilities of the compensation committee are set forth in detail in the compensation committee charter, which can be found on our website at www.tphase.com under the caption "Investors—Corporate Governance—Committee Charters." In particular, the compensation committee annually reviews the base salaries, cash incentives and equity compensation of our named executive officers and periodically reviews other elements of our compensation program.

Our General Practice

Compensation decisions are based primarily on the following:

- *Annual Performance Reviews*—Our chief executive officer conducts and presents an assessment of our corporate performance and the performance reviews of our other executive officers to the compensation committee after the end of each fiscal year. In reviewing and determining the compensation of each executive officer, the compensation committee also considers individual factors, such as potential for future contributions to our growth, industry experience and retention concerns.
- *Peer and Industry Data*—The compensation committee considers peer and industry data provided by its compensation consultant, W.T. Haigh & Company, as a reference in setting base salaries and target cash compensation, determining appropriate levels and mix of equity compensation and determining the type and portion of compensation tied to performance goals.
- *Chief Executive Officer Recommendations*—The compensation committee seeks input from our chief executive officer for setting the salary and target cash compensation levels for the other executive officers, and also for purposes of setting annual performance metrics and target incentive amounts for awards granted to the other executive officers.

To achieve the objectives described herein, the compensation committee evaluates our compensation program with the goal of setting compensation at levels that are based on each executive's level of experience, performance and responsibility and that are aligned with our business objectives and competitive with those of other companies in our industry that compete with us for executive talent. The compensation committee seeks to ensure that our executive compensation program provides for an appropriate amount of compensation for each of our executive officers that is "at risk" and subject to the achievement of critical business objectives.

Role of the Compensation Consultant

To help set the appropriate levels of compensation with respect to each component of our compensation program, the compensation committee annually reviews the compensation level of our executive officers, including our named executive officers, against market information, including publicly available compensation levels of individuals in comparable positions of a peer group of companies. The compensation committee has the authority to retain compensation consultants and other outside advisors to assist in the evaluation of executive officer compensation. During 2019, the compensation committee again retained W.T. Haigh & Company, an independent executive compensation consulting firm, to provide assistance in evaluating and developing our executive compensation program. W.T. Haigh & Company provides consulting activities on behalf of the compensation committee and does not provide consulting or additional services for our management. The compensation committee has determined that no conflicts of interest exist with respect to W.T. Haigh & Company's work.

W.T. Haigh & Company provides the committee with compensation survey data for purposes of comparing each compensation component within our executive compensation program—namely base salary, cash performance incentives, equity awards and benefits. In gathering competitive market compensation data, W.T. Haigh & Company generally utilizes two primary sources: published compensation surveys for biotechnology and pharmaceutical companies and proxy information for a group of other publicly traded companies engaged in the discovery, development and commercialization of drug products, which are selected based primarily on the similarity of their stage of development, research and development spend, market capitalization, geography and headcount. W.T. Haigh & Company also provides the committee with the following:

- assistance interpreting various sets of compensation data;
- recommendations regarding our compensation policies in general, compensation packages for each of our executive officers and the competitiveness and effectiveness of our executive officer compensation levels; and
- assistance in the selection of our peer group companies.

In 2019, W.T. Haigh & Company utilized information from the Radford Global Life Sciences survey and comparable executive compensation information published in publicly available proxy statements for our peer group companies. In addition, W.T. Haigh & Company considered the overall economic environment and trends within the biopharmaceutical industry when making observations and recommendations. W.T. Haigh & Company presented its findings and observations in a written report to the compensation committee prior to the compensation committee making any determination regarding the 2019 compensation of our executive officers.

2019 Peer Group

Our compensation committee reviews and approves the list of peer group companies each year. At the time our 2019 peer group was selected in September 2019, our compensation committee considered biopharmaceutical companies that were of similar size to the Company in terms of market capitalization, stage of development and headcount. Our compensation committee also considered the geographic locations of the peer companies to the extent relevant when considering companies with which we compete for executive talent. Our 2019 peer group consists of:

Adamas Pharmaceuticals, Inc.

Aridis Pharmaceuticals, Inc.

Biocryst Pharmaceuticals, Inc.

Chimerix, Inc.

Cidara Therapeutics, Inc.

Concert Pharmaceuticals, Inc.

Iterum Therapeutics plc

Melinta Therapeutics, Inc.

Nabriva Therapeutics plc

Ocular Therapeutix, Inc.

Paratek Pharmaceuticals, Inc.

Seres Therapeutics, Inc.

SCYNEXIS, Inc.

Spero Therapeutics, Inc.

Trevena Inc.

Philosophy and Process Regarding Compensation Elements and Total Compensation

Our compensation committee reviews market practices and compensation data for our peer group companies' comparably situated executives when making decisions about compensating our executive officers. For 2019, the compensation committee established total compensation targets for our executive officers after considering information from the 2018 Radford Global Life Sciences Executive Compensation Survey (covering approximately 100 public companies with headcounts between 50 and 150 employees) and the proxy information of the 2019 peer group comprised of the 15 companies listed above.

The compensation committee regularly analyzes how changes in any element of each executive officer's compensation could impact other elements. Such analysis has become a key component in the compensation committee's review of an executive's compensation as the analysis allows the compensation committee to consider an executive's overall compensation rather than only one or two specific components of the executive's compensation.

When reviewing and analyzing the amount of each major component and the total compensation opportunity for each of our executive officers, our compensation committee reviews each component at the 25th, 50th and 75th percentiles of our peer companies' comparably situated executives for guidance. Our compensation committee reviews these pay levels as reference points in its overall decision making and as indicative of the level of compensation necessary to attract, retain and motivate our executive officers. Our compensation committee sets the actual amount of each element of compensation and the total compensation opportunity of each executive officer based in part on its review of peer group data and in part on the other factors discussed above and below.

The major components of our compensation program are salaries, cash performance incentive bonuses and long-term incentive plans. Determining appropriate base salaries is critical to the compensation program because other elements of our compensation are affected by changes in base salary. For example, payments under our annual cash performance incentive plan are targeted and paid out as a percentage of base salary. Adjustments to the base salary in any year are made based on comparisons to the peer group and survey data noted above and after evaluation of the executive's level of responsibility, experience and performance.

Our executive officers are eligible to participate in our annual cash performance incentive plan, which is an annual variable cash incentive plan offered to all our employees. The payout for our chief executive officer is based upon achievement of pre-determined corporate goals. Mr. Edwards does not have individual goals. The payout for our other executive officers is based upon achievement of both pre-determined corporate goals and individual goals. Our executive officers are also eligible to participate in long-term incentives through stock option grants, grants of time-based restricted stock units and grants of performance-based restricted stock units, which we believe helps to retain our executive officers and align their interests with those of our stockholders.

No executive officer, including our chief executive officer, recommends or determines any element or component of his or her own pay package or total compensation amount.

Process for Determining Annual Performance-Based Cash Incentive Compensation

In the beginning of each fiscal year, corporate goals for the year are prepared by the chief executive officer. These goals are weighted by the chief executive officer based on relative importance to our success and business strategy. The corporate goals are then presented to the compensation committee, which actively engages in the process of refining the objectives and their respective weightings for review and recommendation to the board of directors. The corporate goals and their respective weightings are finalized and approved by the board of directors. In addition, at the beginning of each fiscal year, the chief executive officer establishes individual goals for each other executive officer. Because the chief executive officer's cash incentive compensation is based solely on achievement of the corporate goals due to the unique nature of his position, individual goals are not established for the chief executive officer for purposes of the annual performance-based cash incentive compensation.

Following the end of each fiscal year, the extent to which corporate and individual goals (for officers other than the chief executive officer) are achieved in such fiscal year is used in determining annual cash incentive payments earned for that year and is also considered in determining equity awards for our executive officers. In the first quarter of each fiscal year, the compensation committee evaluates the company's actual performance for the prior year against the pre-determined corporate objectives to determine the amount of funding for the total cash incentive pool percentage for all employees, including our named executive officers.

Following completion of the fiscal year, the chief executive officer evaluates the performance of each executive officer (other than himself) and proposes a rating for each such officer based upon his or her achievement of the corporate and individual goals. The chief executive officer presents a summary recommendation to the compensation committee of the performance evaluations and ratings along with recommendations for annual cash incentive payouts for the other executive officers. The compensation committee reviews these recommended evaluations and ratings based on performance against the corporate goals and individual goals for each executive officer (other than the chief executive officer), as further described below, and decides whether to approve or adjust the

recommendations for individual executive officers made by the chief executive officer. In determining the actual success of the executive's performance in any year, including 2019, the compensation committee considers the difficulty of attaining the corporate and individual objectives, whether there were any extenuating circumstances or factors that needed to be considered and whether the stated objectives were actually met.

In addition, the compensation committee meets in executive session to discuss and review the compensation of the chief executive officer and his performance over the past year compared to the previously approved goals for the corresponding year and compares his compensation to third party compensation data prepared by W.T. Haigh & Company. For 2019, the board of directors also discussed, reviewed and approved Mr. Edwards' 2019 performance and his compensation for 2019.

Process for Determining Long-Term Time-Based and Performance-Based Equity Incentive Compensation

We believe that the grant of equity incentive awards provides our executive officers with a strong link to our long-term performance and creates an ownership culture that helps align the interests of our executive officers and stockholders. We grant time-based awards and performance-based awards. This vesting feature of our equity incentive grants (time-based and performance-based) furthers our goal of executive retention because this feature provides an incentive to our executive officers to remain in our employ during the vesting period. Equity incentive awards to our executive officers are typically granted annually in conjunction with the review of individual and corporate performance.

Beginning in 2017 and in response to feedback from our stockholders, the compensation committee established a long-term performance-based equity compensation program. The program was comprised of performance-based restricted stock units, that may be earned upon the achievement of certain milestones (clinical, regulatory, commercial or other) selected by the compensation committee, and only vest as to those shares that are earned on the third anniversary of the grant date, subject to the recipient's continued employment through the vesting date. The compensation committee determines whether a milestone has been achieved.

In December 2017, the compensation committee certified that three of the five milestones provided for in our 2017 RSU grants had been achieved. In December 2018, the compensation committee certified that the remaining two of the five milestones provided for in our 2017 RSU grants had been achieved.

With respect to the long-term performance-based equity compensation program established for 2018, in December 2018, the compensation committee certified that one of the five milestones provided for in our 2018 RSU grants had been achieved. That milestone related to the commercial launch of Xerava within eight weeks of receiving FDA approval. Three of the five milestones were not achieved.

With respect to the long-term performance-based equity compensation program established for 2019, none of the milestones have been achieved to date.

As a result of the 1-for-20 reverse stock split effected in September 2019, the number of shares available for grant under our equity compensation plan was severely reduced. As a result, there are not enough shares to grant equity award to all of our employees. For 2020, the compensation committee determined not to grant any employee a long-term performance-based equity award.

Key Elements of Our Compensation Program

We strive to recognize the efforts involved in managing our business by compensating our named executive officers for the demands and risks associated with our business through three elements that are designed to reward performance in a simple and straightforward manner—base salaries, annual performance-based cash incentives and long-term equity awards. The table below summarizes the purpose and key characteristics of each of our compensation elements.

Element	Purpose	Key Characteristics
Base Salaries	Provides a fixed level of compensation for performing the essential day-to-day elements of the job; gives executive officers a degree of certainty in light of having a majority of their compensation at risk.	Fixed compensation that is reviewed annually and adjusted if and when appropriate; reflects each named executive officer's performance, experience, skills, level of responsibility and the breadth, scope and complexity of the position as well as the competitive marketplace for executive talent specific to our industry.
Annual Cash Incentive Program	To motivate executive officers to achieve corporate and individual business goals annually, which we believe increase stockholder value, while providing flexibility to respond to opportunities and changing market conditions.	Annual cash incentive based on corporate and individual performance compared to pre-established goals. Our chief executive officer's incentive is based entirely on corporate goals. Corporate goals focus on overarching objectives for Tetraphase, while individual objectives represent key performance expectations at the departmental or individual level. Corporate goals are aligned with our business strategy and weighted by relative importance.
Long-Term Equity Incentives (Stock Options)	To motivate executive officers to achieve our business objectives by tying incentives to the appreciation of our common stock over the long term.	Stock options have an exercise price equal to or greater than the fair market value on the date of grant and vest over four years. The ultimate value realized, if any, depends on the appreciation of our common stock price and if our stock price does not appreciate, there is no value realized by our executive officers. In determining the aggregate size of equity grants in any given year, the compensation committee (or our board of directors in the case of our chief executive officer) generally considers the same factors described above under "Base Salaries" with respect to performance during the prior fiscal year, as well as the criticality of the executive to the long-term achievement of corporate goals. The compensation committee and the board also consider the impact of dilution by reviewing overall share utilization and usage.
Long-Term Equity Incentives (Time Based RSUs)	To motivate executive officers to achieve our corporate objectives by tying compensation to the performance of our common stock over the long term and/or the achievement of business and commercial goals over the long term; and to motivate our executive officers to remain with Tetraphase by mitigating swings in incentive values during periods when market volatility weighs on our stock price.	Restricted stock unit awards may vest based on continued service over a specified period of time; the ultimate value realized varies with our common stock price.

Benefits

We also maintain benefits that are provided to all employees, including health, dental and vision insurance, life and disability insurance and a 401(k) plan. All eligible and participating employees receive a 401(k) match of fifty percent (50%) on pre-tax contributions, up to the first six percent (6%) of eligible compensation. Executive officers are eligible to participate in all of our employee benefit plans, in each case on the same basis as other employees.

We also provide all employees, including executive officers, with a flexible spending account plan, the right to purchase common stock under an employee stock purchase plan and paid time off benefits, including vacation, sick time and holidays. We do not offer or provide any additional perquisites (other than those noted here) to the chief executive officer or any other executive officer of the company.

Summary Compensation Table

The following table sets forth information regarding compensation earned by our named executive officers for the years ended December 31, 2019 and 2018.

Name and Principal Position	Year	Salary ($)[1]	Bonus ($)	Stock Awards ($)[2]	Option Awards ($)[2]	Non-Equity Incentive Plan Compensation ($)[3]	All Other Compensation ($)[4]	Total ($)
Larry Edwards,	2019	$ 455,154	$ —	$ 345,170	$ —	$ —	$ 9,210	$ 809,534
President and Chief Executive Officer	2018	360,500	—	321,280	544,364	137,600	8,910	1,372,654
Guy Macdonald,	2019	339,077	—	556,000	—	—	249,972	1,145,049
Former President and Chief Executive Officer	2018	560,000	—	786,000	1,443,120	264,800	10,422	3,064,342
Maria Stahl,	2019	399,180	—	277,995	—	—	9,210	686,385
Chief Business Officer and General Counsel	2018	365,601	—	321,280	544,364	125,285	9,060	1,365,590
Christopher Watt,	2019	313,497	—	111,200	—	—	60,722	485,420
Senior Vice President, Finance	2018	313,497	—	91,200	236,680	78,304	59,492	779,174

(1) Mr. Edwards was promoted to president and chief executive officer effective August 2019 and his base salary was increased to $500,000 per annum. Mr. Macdonald ceased to serve as our president and chief executive officer effective on July 31, 2019 and was paid severance based upon his employment arrangement through regular payroll. Ms. Stahl was promoted to chief business officer and general counsel in June 2019 and her base salary was increased to $415,000 per annum. The amounts reflected in this column for Messrs. Edwards and Macdonald and Ms. Stahl represent actual base salary (and severance in the case of Mr. Macdonald) paid during 2019.

(2) The assumptions we used in valuing equity awards are described in Note 7, “Stock-based Compensation,” to our audited financial statements included in this Annual Report on Form 10-K. With respect to stock awards, amounts reported reflect the grant date fair value which was determined to be equal to the fair market value of the underlying shares on the date of grant. With respect to option awards, amounts reported reflect the aggregate grant date fair value as calculated in accordance with ASC 718 for the indicated year in connection with options we granted in the indicated year, adjusted to disregard the effects of any estimate of forfeitures related to service-based vesting.

(3) This amount consists of cash bonuses paid to our named executive officers under our annual performance-based incentive plan for performance in the year indicated. As of the filing of this Annual Report on Form 10-K cash bonuses for 2019 had not yet been determined.

(4) Represents the value of perquisites and other personal benefits which include company-paid premiums for group term life insurance, long term disability and a company match to executive officers’ 401(k) contributions. The severance and consulting fees paid to Mr. Macdonald during 2019 are also included in this column as well as the personal benefits during the severance period. Mr. Watt received a special cash bonus in each of 2018 and 2019 of $50,000.

2019 Executive Compensation Decisions

Base Salary

With respect to base salaries for 2019, in January 2019 the compensation committee (and the board of directors with respect to Mr. Macdonald, our former president and chief executive officer) determined that base salaries for our named executive officers would be increased as a result of individual performance (corporate performance in the case of Mr. Macdonald’s base salary) and data provided by W.T. Haigh & Company (including benchmark data from the Radford Global Life Sciences survey and from the 2019 peer companies) regarding the annual base salaries of similarly positioned officers as follows: 2019 base salaries were paid to Mr. Macdonald and Mr. Edwards (our current president and chief executive officer who was then serving as our chief operating officer) at a rate of $580,000 and $420,000 per annum, respectively. In June 2019, Ms. Stahl was promoted to chief business officer and general counsel at an increased base salary of $415,000 per annum. In August 2019, Mr. Edwards was promoted to president and chief executive officer at an increased base salary of $500,000 per annum. For 2020, the base salaries for Mr. Edwards, Ms. Stahl and Mr. Watt will not be increased

Cash Incentive Performance for 2019

In the first quarter of 2019, upon recommendation by our chief executive officer and the compensation committee, the board established the corporate goals for evaluating corporate performance during the 2019 fiscal year that were used for purposes of determining annual cash incentive awards for 2019 and the equity incentive awards granted in March 2020. For 2019, the compensation committee evaluated in December 2019 and March 2020, each corporate performance goal adopted for 2019, established a percentage rating for each goal based on the extent to which the goal was achieved and then determined an overall corporate rating based on the cumulative weightings of the ratings for all the goals. These goals fell into several categories as described below. The determination of the corporate rating, while based primarily on the numerical rating for each goal and the relative weight assigned to each goal, also reflected the compensation committee's qualitative assessment of performance. As of the date of the filing of this Form 10-K, the overall corporate rating for 2019 had not yet been determined.

For 2019, the corporate performance objectives fell into several categories, including the following: (1) regulatory approvals for manufacturing sites in the United States; (2) goals associated with the commercial launch of Xerava in the United States (3) certain clinical goals associated with our pipeline prior to our June 2019 restructuring; and (4) certain operational and financial goals. In evaluating management's performance in 2019 against the 2019 goals and objectives, our compensation committee assigned an achievement level that was then used to determine each named executive officer's bonus.

Each named executive officer has a target cash performance bonus amount based on a percentage of his or her salary. This target is determined by the compensation committee annually based upon a review of the peer and industry data provided by W.T. Haigh & Company to the compensation committee. Mr. Edwards was eligible for a performance bonus for 2019 of up to 55% of his base salary. Ms. Stahl was eligible for a performance bonus for 2019 of up to 40% of her base salary. Mr. Watt was eligible for a performance bonus for 2019 of up to 30% of his base salary. Mr. Macdonald, who ceased serving as our president and chief executive officer in August 2019, was not eligible for a bonus. In reviewing current bonus targets for the named executive officers compared to data provided, the compensation committee determined that bonus targets did not need to increase based on the data and therefore would remain the same for 2020 as 2019 for all the named executive officers.

Equity Incentive Grants in 2019

In January 2019, as part of its annual compensation review, the compensation committee (and the board of directors in the case of Mr. Macdonald) awarded the following time-based RSUs to our named executive officers based on achievement of 2018 corporate and individual goals and market data: Mr. Macdonald, 15,000 time-based RSUs; Mr. Edwards, 7,500 time-based RSUs; Ms. Stahl, 7,000 time-based RSUs, and Mr. Watt, 4,000 time based RSUs. Each RSU represents a contingent right to receive one share of our common stock. Each of these RSU awards vests in three annual installments beginning on January 17, 2020.

In January 2019, the compensation committee (and the board of directors in the case of Mr. Macdonald) also adopted the January 2019 long-term performance-based RSU program and granted the following performance-based RSUs to our named executive officers: Mr. Macdonald, 5,000 RSUs; Mr. Edwards, 2,250 RSUs; and Ms. Stahl, 2,000 RSUs. Mr. Watt was not granted any performance-based RSUs. The RSUs represent a contingent right to receive one share of our common stock. Under our January 2019 long-term performance-based RSU program, performance-based RSUs may be earned upon the achievement of various commercial and other milestones, and if earned, will vest no earlier than March 1, 2020 and no later than March 1, 2022 subject to continued employment through that date.

In August 2019, following Mr. Edwards' and Ms. Stahl's respective promotions, the compensation committee approved long-term performance RSUs and time-based RSUs to both of them. Each of Mr. Edwards and Ms. Stahl was granted 2,500 performance-based RSUs and 7,500 time-based RSUs. Under this August 2019 long-term performance-based RSU program, performance-based RSUs may be earned upon the achievement of various commercial and financial milestones, and if earned, will vest no earlier than August 1, 2020 and no later than August 1, 2021, subject to the recipient's continued employment through the respective vesting date.

Equity Incentive Grants in 2020

Due to pricing pressures, slow commercial uptake for new antibiotics and general investor sentiment, antibiotic companies are presently experiencing significant volatility in their stock prices. Our own stock price decreased significantly in 2019 in spite of two regulatory approvals and the commercial launch of Xerava in 2018. There is a level of uncertainty in the long-term viability of almost every antibiotic company, including us, due to current market conditions. For these market reasons, in March 2020 the board of directors determined that it would grant time-based restricted stock units instead of time-based stock options to employees, including our named executive officers. In this manner, the board of directors intended to more directly tie our employees' compensation to the performance of our common stock over the next two to three year period. In making this decision, the board of directors recognized the challenges currently facing our business and was not setting a precedent for future equity grants. The restricted stock units represent a contingent right to receive one share of our common stock. For 2020, no equity grants will be made to our named executive officers.

Employment Agreements, Severance and Change in Control Arrangements

We have entered into employment offer letters with each of Mr. Edwards, Ms. Stahl and Mr. Watt, pursuant to which such executive officer is employed "at will," meaning he or we may terminate the employment arrangement at any time. Such offer letters confirm the named executive officers' titles, compensation arrangements, eligibility for benefits made available to employees generally and also provide for certain benefits upon termination of employment under specified conditions.

Benefits Provided Upon Termination Without Cause

Under the terms of the offer letters we have entered into with each of Mr. Edwards and Ms. Stahl, if such executive's employment is terminated by us without cause, subject to the executive's signing a separation agreement that will include a general release of potential claims against us, he or she will be entitled to continue to receive his or her monthly base salary for a period of 12 months and we will continue to provide medical, dental and vision benefits (to the extent that he was receiving them at the time of termination) for 12 months.

Under the terms of the offer letter we have entered into with Mr. Watt, if such executive's employment is terminated by us without cause, subject to the executive's signing a separation agreement that will include a general release of potential claims against us, he will be entitled to continue to receive his monthly base salary for a period of 6 months and we will continue to provide medical, dental and vision benefits (to the extent that he was receiving them at the time of termination) for 6 months.

Under the terms of the offer letter we entered into with Mr. Macdonald, because Mr. Macdonald signed a separation agreement that included a general release of potential claims against us, which entitled him to receive the severance benefits applicable to terminations without cause under his employment agreement, he was entitled to continue to receive his monthly base salary for a period of 12 months beginning in August 2019 and we will continue to provide medical, dental and vision benefits (to the extent that he was receiving them at the time of termination) for 12 months until August 2020.

Benefits Provided Upon a Change in Control

We have designed our change-in-control policies to provide income continuity after a change-in-control of the company that results in the executive being separated from the company. Our policy in the case of change-in-control benefits has been to structure these as "double trigger" benefits. In other words, the change-in-control does not itself trigger benefits; rather, benefits are paid only if the employment of the executive is terminated or the executive terminates his or her employment for good reason during a specified period after the change-in-control. We believe a "double trigger" benefit maximizes shareholder value because it prevents an unintended windfall to executives in the event of a friendly change-in-control, while still providing them appropriate incentives to cooperate in negotiating any change-in-control in which they believe they may lose their jobs. Under the terms of their respective employment arrangements, if, within one year following a change in control, each of our executive officer's employment is terminated by us or the succeeding company, as applicable, without cause or he or she terminates his or her employment for good reason (as defined in the applicable offer letter), subject to the executive's signing a separation agreement that will include a general release of potential claims against us:

- in the case of Mr. Edwards, (1) he will be entitled to continue to receive his monthly base salary for a period of 18 months, (2) he will be entitled to receive a lump-sum payment equal to 100% of his target bonus at the time he ceases to be employed by the company or the succeeding company, as applicable, and (3) the company or the succeeding company, as applicable, will continue to provide medical and dental benefits (to the extent that he was receiving them at the time he ceased to be employed by the company) for eighteen months;
- in the case of each of Ms. Stahl and Mr. Watt, (1) she or he will be entitled to continue to receive her or his monthly base salary for a period of 12 months, (2) she or he will be entitled to receive a lump-sum payment equal to 100% of her or his target bonus at the time she or he ceases to be employed by the company or the succeeding company, as applicable, and (3) the company or the succeeding company, as applicable, will continue to provide medical and dental benefits (to the extent that she or he was receiving them at the time she or he ceased to be employed by the company) for 12 months; and
- in the case of all executive officers, immediate vesting and exercisability of all stock option awards (but no acceleration of vesting of any RSU awards, unless approved by our board of directors).

Other Compensation Agreements and Policies

Other Agreements

We have also entered into non-competition, non-solicitation and non-disclosure agreements with each of our executive officers. Under the non-competition, non-solicitation and non-disclosure agreements, each executive officer has agreed (i) not to compete with us during his or her employment and for a period of one year after the termination of his or her employment, (ii) not to solicit our employees during his or her employment and for a period of one year after the termination of his or her employment, (iii) to protect our confidential and proprietary information, and (iv) to assign to us related intellectual property developed during the course of his or her employment.

Insider Trading Policy Prohibitions and Hedging Policy

Our company maintains an Insider Trading Policy that prohibits our officers, directors and employees from, among other things, engaging in speculative transactions in our securities, including by way of the purchase or sale of “put” or “call” options or other derivative securities directly linked to our equity; short sales of our equity; the use of our equity as a pledge or as collateral in a margin account; and trading in straddles, equity swaps, or other hedging transactions directly linked to our equity, even if such persons do not possess material, non-public information.

Compliance with Internal Revenue Code Section 162(m)

Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code, generally disallows a tax deduction to public companies for compensation in excess of $1 million paid in any one year to each of certain of the company’s current and former executive officers. Historically, compensation that qualified under Section 162(m) as performance-based compensation was exempt from the deduction limitation. However, subject to certain transition rules, tax legislation signed into law on December 31, 2017 eliminated the performance-based compensation exception. As a result, for taxable years beginning after December 31, 2017, all compensation in excess of $1 million paid in any one year to each of the specified officers that is not covered by the transition rules will not be deductible by us. The Compensation Committee has and will continue to review on a periodic basis the potential effect of Section 162(m) periodically and may use its judgment to authorize compensation payments that may be subject to the limit when the Compensation Committee believes such payments are appropriate, after taking into consideration changing business conditions and the performance of our employees.

Outstanding Equity Awards at Fiscal Year-End

The following table shows information regarding unexercised stock options and other equity awards held by our named executive officers as of December 31, 2019. Mr. Macdonald ceased to serve as our president and chief executive officer effective July 31, 2019. Mr. Macdonald did not hold any stock options or other equity awards as of December 31, 2019.

	Option Awards				Stock Awards			
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock that Have Not Vested (#)	Market Value of Shares or Units of Stock that Have Not Vested ($)(1)	Equity Incentive Plan Awards: Number of Unearned Shares or Other Rights that Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares or Other Rights that Have Not Vested ($)
Larry Edwards	2,875(2)	2,875	$ 124.80	1/6/2028	1,000(6)	$ 2,810	1,600(9)	$ 4,496
	3,438(3)	1,562	$ 163.40	4/12/2027	7,500(7)	$ 21,075	2,250(10)	$ 6,323
	3,188(4)	1,062	$ 73.80	1/29/2027	7,500(8)	$ 21,075	2,500(11)	$ 7,025
	2,000(5)	—	$ 169.40	1/5/2026				
	3,000(5)	—	$ 957.60	6/30/2025				
Maria Stahl	2,875(2)	2,875	$ 124.80	1/6/2028	1,000(6)	$ 2,810	1,250(12)	$ 3,513
	4,312(4)	1,438	$ 73.80	1/29/2027	7,000(7)	$ 19,670	1,600(9)	$ 4,496
	4,000(5)	—	$ 169.40	1/5/2026	7,500(8)	$ 21,075	2,000(10)	$ 5,620
	6,250(5)	—	$ 770.00	3/3/2025			2,500(11)	$ 7,025
Christopher Watt	1,250(2)	1,250	$ 124.80	1/6/2028	4,000(7)	$ 11,240	750(12)	$ 2,108
	2,250(4)	750	$ 73.80	1/29/2027				
	1,250(5)	—	$ 169.40	1/5/2026				
	2,500(5)	—	$ 1,009.80	7/14/2025				

(1) Based on the closing price of the stock on December 31, 2019 of $2.81.

(2) This option vested as to 6.25% of the shares on April 17, 2018 and is scheduled to vest as to 6.25% of the shares at the end of each successive three-month period thereafter until January 17, 2022.

(3) This option vested as to 6.25% of the shares on July 13, 2017 and is scheduled to vest as to 6.25% of the shares at the end of each successive three-month period thereafter until April 13, 2021.

(4) This option vested as to 6.25% of the shares on April 30, 2017 and is scheduled to vest as to 6.25% of the shares at the end of each successive three-month period thereafter until January 30, 2021.

(5) This option is fully vested as of December 31, 2019.

(6) These RSUs are scheduled to vest in April 2020.

(7) These RSUs are scheduled to vest in equal installments in January 2020, January 2021 and January 2022.

(8) These RSUs are scheduled to vest in equal installments in August 2020, August 2021 and August 2022.

(9) These performance-based RSUs vest in January 2021 but only if specific regulatory and commercial milestones are achieved, subject to the named executive officer’s continued employment. The compensation committee has certified as of December 2018 that all the regulatory and commercial milestones associated with these units have been achieved.

(10) These performance-based RSUs vest no earlier than March 1, 2020 and no later than March 1, 2022 but only if specific commercial milestones are achieved, subject to the named executive officer’s continued employment.

(11) These performance-based RSUs vest no earlier than August 1, 2020 and no later than August 1, 2021 but only if specific financial and operational milestones are achieved, subject to the named executive officer’s continued employment.

(12) These performance-based RSUs vest in January 2022 but only if specific commercial and clinical milestones are achieved, subject to the named executive officer’s continued employment.

Director Compensation

Under our director compensation program, we pay our non-employee directors both cash and equity retainers. We do not pay any compensation to our president and chief executive officer in connection with his service on our board of directors. The compensation that we pay to our president and chief executive officer is discussed elsewhere in this Annual Report on Form 10-K.

Each non-employee director receives a cash retainer for service on the board of directors and for service on each committee of which the director is a member. The chairmen of the board and of each committee receive higher retainers for such service. These fees are payable quarterly in arrears. The fees paid in 2019 to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member were as follows:

	Member Annual Fee	Chairman Annual Fee
Board of Directors	$ 40,000	$ 70,000
Audit Committee	10,000	20,000
Compensation Committee	7,500	15,000
Nominating and Corporate Governance Committee	5,000	10,000

For 2020, no changes were made to the fees paid for service on our board of directors or any committee thereof.

In addition, under our director compensation program, upon their initial election to the board of directors, each non-employee director receives an option to purchase 1,750 shares of our common stock, which option vests in equal quarterly installments over a three-year period measured from the date of grant, subject to the non-employee director's continued service as a director, and becomes exercisable in full upon a change in control of our company. Further, on the date of the first board meeting held after each annual meeting of stockholders, each non-employee director that has served on our board of directors for at least six months receives an option to purchase 825 shares of our common stock. Each of these options vests in equal quarterly installments over a one-year period measured from the date of grant, subject to the non-employee director's continued service as a director, and becomes exercisable in full upon a change in control of our company. The exercise price of these options equals the fair market value of our common stock on the date of grant.

This program is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Mr. Boyd and Dr. Maher joined our board of directors in January 2020. Neither Mr. Boyd nor Dr. Maher will receive any compensation for their respective service on our board of directors or any committee thereof. Mr. Macdonald did not receive any compensation for his board service during 2019. We entered into a consulting agreement with Mr. Macdonald pursuant to which he received $26,250 for consulting services provided to us and the vesting of 21,000 shares of our common stock were accelerated upon the termination of the consulting agreement. Mr. Macdonald held no options as of December 31, 2019.

We reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings. The following table sets forth information regarding compensation earned by our non-employee directors during the year ended December 31, 2019.

Director Compensation for 2019

Name	Fees Earned or Paid in Cash ($)	Stock Option Awards($)(1)(2)	Total ($)
Leonard Patrick Gage, Ph.D.(3)	$ 90,000	$ 9,950	$ 99,950
Garen Bohlin(4)	60,000	9,950	69,950
Jeffrey Chodakewitz, M.D.(5)	47,500	9,950	57,450
John Freund, M.D.(6)	55,000	9,950	64,950
Gerri Henwood(7)	47,500	9,950	57,450
Nancy Wysenski(8)	55,000	9,950	64,950

(1) The amounts in the Stock Option Awards column reflect the grant date fair value of stock option awards granted during 2019 under our stock incentive plans, in accordance with Financial Accounting Standards Codification Topic 718, Compensation-Stock Compensation, or FASB ASC Topic 718. There can be no assurance that FASB ASC Topic 718 amounts will reflect actual amounts realized. Refer to Note 7, "Stock-Based Compensation", in the Notes to Consolidated Financial Statements included in this Annual Report on Form 10-K for the relevant assumptions used to determine the valuation of our option awards.

(2) The number of shares underlying stock option awards granted to our non-employee directors in 2019 and the grant date fair value of such stock options as determined in accordance with FASB ASC Topic 718 are:

Director	Grant Date	Number of Shares Underlying Stock Option Grants in 2019	Grant Date Fair Value of Stock Option Grants in 2019 ($)
Dr. Gage	6/10/2019	825	$ 9,950
Mr. Bohlin	6/10/2019	825	9,950
Dr. Chodakewitz	6/10/2019	825	9,950
Dr. Freund	6/10/2019	825	9,950
Ms. Henwood	6/10/2019	825	9,950
Ms. Wysenski	6/10/2019	825	9,950

(3) At December 31, 2019, Dr. Gage held stock options to purchase 5,552 shares of our common stock.

(4) At December 31, 2019, Mr. Bohlin held stock options to purchase 6,203 shares of our common stock.

(5) At December 31, 2019, Dr. Chodakewitz held stock options to purchase 4,075 shares of our common stock.

(6) At December 31, 2019, Dr. Freund held stock options to purchase 4,575 shares of our common stock.

(7) At December 31, 2019, Ms. Henwood held stock options to purchase 3,575 shares of our common stock.

(8) At December 31, 2019, Ms. Wysenski held stock options to purchase 4,075 shares of our common stock.

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

Unless otherwise provided below, the following table sets forth information regarding beneficial ownership of our common stock as of March 1, 2020 by:

- each person, or group of affiliated persons, known to us to be the beneficial owner of 5% or more of the outstanding shares of our common stock;
- each of our current directors;
- each of named executive officers; and
- all of our directors and executive officers as a group.

Beneficial ownership is determined in accordance with SEC rules. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities and include shares of common stock issuable upon the exercise of stock options, warrants or other rights that are immediately exercisable or exercisable or that will vest, as applicable, within 60 days after March 1, 2020. Except as otherwise indicated, all of the shares reflected in the table are shares of common stock and all persons listed below have sole voting and investment power with respect to the shares beneficially owned by them, subject to applicable community property laws. The information is not necessarily indicative of beneficial ownership for any other purpose.

The column entitled "Percentage of Shares Beneficially Owned" is based on a total of 7,259,236 shares of our common stock outstanding as of March 1, 2020. Except as otherwise indicated in the footnotes below, the address of the beneficial owner is c/o Tetraphase Pharmaceuticals, Inc., 480 Arsenal Way, Watertown, MA 02472.

Name of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Stockholders		
Armistice Capital, LLC(1)	1,419,507	19.6%
CVI Investments, Inc.(2)	666,666	9.2%
Intracoastal Capital LLC(3)	725,197	9.9%
Sabby Volatility Warrant Master Fund Limited(4)	666,667	9.2%
Named Executive Officers and Directors		
Larry Edwards(5)	21,490	*
Leonard Patrick Gage, Ph.D.(6)	7,481	*
Garen Bohlin(7)	5,997	*
Steven Boyd(1)(8)	1,419,507	19.6%
Jeffrey Chodakewitz (9)	3,869	*
John Freund, M.D. (10)	4,369	*
Gerri Henwood(11)	3,369	*
Guy Macdonald	21,000	*
Keith Maher, M.D. (1)(12)	1 419,507	19.6%
Nancy Wysenski(9)	3,869	*
Maria Stahl(13)	22,526	*
Christopher Watt(14)	11,110	*
All current executive officers and directors as a group (12 persons)(15)	1,524,587	21.0%

* Represents beneficial ownership of less than 1% of our outstanding common stock.

(1) Consists of 1,419,507 shares of common stock held by Armistice Capital Master Fund Ltd. ("Armistice"). As a result of the application of a beneficial ownership cap in the warrants issued to Armistice in our January 2020 private placement (the "January 2020 Warrants)", the table above under the heading "Shares of Common Stock Beneficially Owned" does not include 5,396,668 shares of common stock issuable upon exercise of warrants to purchase common stock held by Armistice. While such shares are being registered under the registration statement of which this prospectus forms a part, Armistice is not permitted to exercise the January 2020 Warrants to the extent that such exercise would result in Armistice and its affiliates beneficially owning more than 19.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of the January 2020 Warrants. As a result of the application of a beneficial ownership cap in the warrants issued to Armistice in our November 2019 registered direct offering (the "November 2019 Warrants"), the table above under the heading "Shares of Common Stock Beneficially Owned" does not include 3,560,986 shares of common stock issuable upon exercise of warrants to purchase common stock held by Armistice. Armistice is not permitted to exercise the November 2019 Warrants to the extent that such exercise would result in Armistice and its affiliates beneficially owning more than 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of the November 2019 Warrants. Armistice has the right to increase this beneficial ownership limitation in its discretion on 61 days' prior written notice to us, provided that in no event is Armistice permitted to exercise the November 2019 Warrants to the extent that such exercise would result in Armistice and its affiliates beneficially owning in the aggregate more than 9.99% of the number of shares of our common stock outstanding or the combined voting power of our securities outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of the November 2019 Warrants. Armistice Capital LLC ("Armistice Capital") has shared voting power of 1,419,507 shares of common stock with Armistice, a Cayman Islands corporation, and Steven Boyd. Mr. Boyd is the managing member of Armistice Capital, a director of Armistice and a member of our board of directors. Keith Maher, a member of our board of directors, is a managing director of Armistice Capital. Armistice's address is 510 Madison Avenue, 7th Floor, New York, NY 10022.This information is based, in part, on a Schedule 13D filed by Armistice with the SEC on January 23, 2020.

(2) Consists of 666,666 shares of common stock held by CVI Investments, Inc. (“CVI”). As a result of the application of a beneficial ownership cap in the warrants issued to CVI, the table above under the heading “Shares of Common Stock Beneficially Owned” does not include 666,666 shares of common stock issuable upon exercise of warrants to purchase common stock held by CVI. CVI is not permitted to exercise such warrants to purchase common stock to the extent that such exercise would result in CVI and its affiliates beneficially owning more than 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants to purchase common stock. CVI has shared voting and dispositive power with Heights Capital Management, Inc., the investment manager of CVI. CVI’s address is Ugland House, South Church Street, George Town, Grand Cayman Islands. This information is based, in part, on a Schedule 13G filed by CVI with the SEC on January 31, 2020.

(3) Consists of 725,197 shares of common stock held by Intracoastal Capital LLC (“Intracoastal”). As a result of the application of a beneficial ownership cap in the warrants issued to Intercoastal, the table above under the heading “Shares of Common Stock Beneficially Owned” does not include 460 shares of common stock issuable upon exercise of warrants to purchase common stock held by Intracoastal. Intracoastal is not permitted to exercise such warrants to purchase common stock to the extent that such exercise would result in Intracoastal and its affiliates beneficially owning more than 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants to purchase common stock. Intracoastal has shared voting power with Mitchell Kopin and Daniel Asher. Intracoastal’s address is 245 Palm Trail, Delray Beach, FL 33483. This information is based, in part, on a Schedule 13G filed by Intracoastal with the SEC on January 31, 2020.

(4) Consists of 666,667 shares of common stock held by Sabby Volatility Warrant Master Fund, Ltd. (“Sabby”). As a result of the application of a beneficial ownership cap in the warrants issued to Sabby, the table above under the heading “Shares of Common Stock Beneficially Owned” does not include 666,667 shares of common stock issuable upon exercise of warrants to purchase common stock held by Sabby. Sabby is not permitted to exercise such warrants to purchase common stock to the extent that such exercise would result in Sabby and its affiliates beneficially owning more than 4.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants to purchase common stock. Sabby has shared voting and dispositive power with Sabby Management, LLC and Hal Mintz. Sabby’s address is 10 Mountainview Road, Suite 205, Upper Saddle River, NJ 07458. This information is based, in part, on a Schedule 13G filed by Sabby with the SEC on January 28, 2020.

(5) Includes 15,438 shares of common stock issuable upon the exercise of options exercisable and 1,000 restricted stock units that will vest within 60 days after March 1, 2020.

(6) Consists of 1,944 shares of common stock held directly by Dr. Gage, 191 shares of common stock held by Dr. Gage’s spouse and 5,346 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 1, 2020.

(7) Consists of 5,997 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 1, 2020.

(8) Mr. Boyd is the managing member of Armistice Capital and a director of Armistice.

(9) Consists of 3,869 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 1, 2020.

(10) Consists of 4,369 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 1, 2020.

(11) Consists of 3,369 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 1, 2020.

(12) Dr. Maher is a managing director of Armistice Capital.

(13) Includes 18,156 shares of common stock issuable upon the exercise of options exercisable and 1,000 restricted stock units that will vest within 60 days after March 1, 2020.

(14) Includes 7,594 shares of common stock issuable upon the exercise of options exercisable that will vest within 60 days after March 1, 2020.

(15) Includes 68,007 shares of common stock issuable upon the exercise of options exercisable within 60 days after March 1, 2020 or restricted stock units that will vest within 60 days of March 1, 2020.

Equity Compensation Plan Information

The following table contains information about our equity compensation plans as of December 31, 2019. In addition, from time to time, we grant "inducement grants" pursuant to Nasdaq Listing Rule 5635(c)(4).

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights		Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
	(a)		(b)	(c)
Equity compensation plans approved by security holders	252,451	(1)	$ 136.64	217,548 (2)
Equity compensation plans not approved by security holders	3,598,902	(3)	2.40	—
Total	3,851,353		$ 11.20	217,548

(1) Consists of (i) 3,391 shares of our common stock issuable under our 2006 stock incentive plan, (ii) 157,079 shares of our common stock issuable under our 2013 stock incentive plan and (iii) 91,981 restricted stock units issuable under our 2013 stock incentive plan.

(2) Consists of (i) 215,042 shares of our common stock available for future issuance under our 2013 stock incentive plan; and (ii) 2,506 shares of our common stock available for future issuance under our 2014 employee stock purchase plan.

(3) Consists of (i) 2,151,111 shares of warrants, (ii) 1,430,493 shares of pre-funded warrants and (ii) 17,298 shares of our common stock under stock options issued as inducement grants as of December 31, 2019. These stock options are generally subject to the same terms and conditions as those awarded pursuant to the plans approved by our stockholders.

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

Certain Relationships and Related Party Transactions

We have not been a party to any transactions since January 1, 2018 in which any of our directors, executive officers or beneficial owners of more than 5% of our voting securities, or affiliates or immediate family members of any of our directors, executive officers or beneficial owners of more than 5% of our voting securities, had or will have a direct or indirect material interest, other than Mr. Boyd and Dr. Maher who are principals of Armistice Capital Master Fund, Ltd. ("Armistice").

On November 1, 2019, Armistice purchased, in a registered direct offering priced at-the-market, (i) 300,000 shares of common stock and accompanying warrants to purchase an aggregate of 300,000 shares of common stock (the "November Common Stock Warrants"), and (ii) pre-funded warrants to purchase up to an aggregate of 1,830,493 shares of common stock (the "November Pre-Funded Warrant") and accompanying November Common Stock Warrants to purchase an aggregate of 1,830,493 shares of common stock. Each share of common stock and accompanying November Common Stock Warrant was sold together at a combined price of $3.755, and each November Pre-Funded Warrant and accompanying November Common Stock Warrant was sold together at a combined price of $3.745.

On January 24, 2020, Armistice purchased, in a private placement priced at-the-market under Nasdaq rules, (i) 1,270,000 shares of common stock (the "Unregistered Shares") and accompanying warrants (the "Unregistered Common Warrants") to purchase an aggregate of 1,270,000 shares of common stock, for a combined price of $3.00, and (ii) pre-funded warrants to purchase 2,063,334 shares of common stock (the "Unregistered Pre-Funded Warrants") and accompanying Unregistered Common Warrants to purchase 2,063,334 shares of common stock, for a combined price of $2.999 (the "Private Placement"). As a result of the Private Placement the size of the Company's Board of Directors was increased from eight (8) to ten (10), and two directors designated by Armistice (Mr. Boyd and Dr. Maher) were elected to serve as Class III directors. As of March 1, 2020, Armistice beneficially owned approximately 19.6% of our common stock on an outstanding basis.

Determination of Independence

Rule 5605 of the Nasdaq Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent, that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and that compensation committee members also satisfy independence criteria set forth in Rule 10C-1 under the Exchange Act.

Under Rule 5605(a)(2) of the Nasdaq Listing Rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 of the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In addition, in affirmatively determining the independence of any director who will serve on a company's compensation committee, Rule 10C-1 under the Exchange Act requires that a company's board of directors consider all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (i) the source of compensation of the director, including any consulting, advisory or other compensatory fee paid by such company to the director; and (ii) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Mr. Macdonald, is an "independent director" as defined under Rule 5605(a)(2) of the Nasdaq Listing Rules. Our board of directors also determined that Garen Bohlin, John Freund and Leonard Patrick Gage, who comprise our audit committee, Jeffrey Chodakewitz, Gerri Henwood and Nancy Wysenski, who comprise our compensation committee, and John Freund and Leonard Patrick Gage, who comprise our nominating and corporate governance committee, satisfy the independence standards for such committees established by the SEC and the Nasdaq Listing Rules, as applicable. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

ITEM 14. Principal Accounting Fees and Services

Principal Accountant Fees and Services

Ernst & Young LLP audited our financial statements for the year ended December 31, 2019. The board of directors has appointed Ernst & Young LLP to serve as our independent registered public accounting firm for the fiscal year ending December 31, 2020.

The following table summarizes the fees of Ernst & Young LLP billed or expected to be billed to us for each of the last two fiscal years.

Fee Category	2019	2018
Audit Fees(1)	$ 615,000	$ 817,000
Audit-Related Fees(2)	187,080	107,000
Tax Fees(3)	40,000	134,500
Total Fees	$ 842,080	$ 1,058,500

(1) "Audit Fees" consist of fees for the audit of our annual financial statements, the review of our interim financial statements included in our quarterly reports on Form 10-Q, and consultations on miscellaneous SEC filings and other professional services provided in connection with regulatory filings or engagements.

(2) "Audit-Related Fees" consists of fees billed by an independent registered public accounting firm for assurance and related services that are reasonably related to the performance of the audit or review of our consolidated financial statements.

(3) "Tax Fees" consist of fees for tax compliance, advice and tax services, including fees for tax preparation.

(4) "All Other Fees" consists of fees billed for products and services, other than those described above under Audit Fees and Tax fees.

All such accountant services and fees were pre-approved by our audit committee in accordance with the "Audit Committee Pre-Approval Policies and Procedures" described below.

Audit Committee Pre-Approval Policies and Procedures

Our audit committee has adopted procedures requiring the pre-approval of all audit and non-audit (including tax) services that are to be performed by our independent registered public accounting firm in order to assure that these services do not impair the auditor's independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is to be reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the audit committee for each engagement of the independent registered public accounting firm to perform any other audit or non-audit services. The audit committee does not delegate its responsibility to approve services performed by the independent registered public accounting firm to any member of management.

The standard applied by the audit committee in determining whether to grant approval of any type of non-audit service, or of any specific engagement to perform a non-audit service, is whether the services to be performed, the compensation to be paid therefor and other related factors are consistent with the independent registered public accounting firm's independence under guidelines of the SEC and applicable professional standards. Relevant considerations include whether the work product is likely to be subject to, or implicated in, audit procedures during the audit of our financial statements, whether the independent registered public accounting firm would be functioning in the role of management or in an advocacy role, whether the independent registered public accounting firm's performance of the service would enhance our ability to manage or control risk or improve audit quality, whether such performance would increase efficiency because of the independent registered public accounting firm's familiarity with our business, personnel, culture, systems, risk profile and other factors, and whether the amount of fees involved, or the non-audit services portion of the total fees payable to the independent registered public accounting firm in the period would tend to reduce the independent registered public accounting firm's ability to exercise independent judgment in performing the audit.

All of the services rendered by Ernst & Young LLP with respect to the 2019 and 2018 fiscal years were pre-approved by the audit committee in accordance with this policy.

PART IV

ITEM 15. Exhibits and Financial Statement Schedules

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

(1) Financial Statements

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets

Consolidated Statements of Operations and Comprehensive Loss

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

Consolidated Statements of Cash Flows

Notes to Consolidated Financial Statements

(2) Schedules

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

(3) Exhibits

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

ITEM 16. Form 10-K Summary

None.

EXHIBIT INDEX

Exhibit Number	Description	Registrant's Form	Incorporated by Reference from File No.	Date Filed with the SEC	Exhibit Number
3.1	Restated Certificate of Incorporation of the Registrant, as amended	10-Q	001-35837	11/12/2019	3.1
3.2	Amended and Restated Bylaws of the Registrant	10-Q	001-35837	5/13/2013	3.2
4.1	Specimen certificate evidencing shares of common stock	S-1/A	333-186574	3/5/2013	4.1
4.2	Form of Warrant to Purchase Stock entered into in connection with the Loan and Security Agreement, dated as of November 2, 2018	8-K	001-35837	11/5/2018	4.1
4.3	Form of Pre-Funded Warrant	8-K	001-35837	10/30/2019	4.1
4.4	Form of Common Stock Warrant	8-K	001-35837	10/30/2019	4.2
4.5	Form of Unregistered Pre-Funded Warrant	8-K	001-35837	1/23/2020	4.1
4.6	Form of Unregistered Common Warrant	8-K	001-35837	1/23/2020	4.2
4.7	Form of Registered Pre-Funded Warrant	8-K	001-35837	1/23/2020	4.3
4.8	Form of Registered Common Warrant	8-K	001-35837	1/23/2020	4.4
4.10*	Description of Registrant's Securities				
10.1#	2006 Stock Incentive Plan, as amended	S-1	333-186574	2/11/2013	10.5
10.2#	Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan	S-1	333-186574	2/11/2013	10.6
10.3#	Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan	S-1	333-186574	2/11/2013	10.7
10.4#	2013 Stock Incentive Plan	S-1/A	333-186574	3/5/2013	10.8
10.5#	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-186574	3/5/2013	10.9
10.6#	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-186574	3/5/2013	10.10
10.7#	Form of Restricted Stock Agreement under 2013 Incentive Plan	10-K	001-35837	3/13/2017	10.7
10.8#	2014 Employee Stock Purchase Plan	10-Q	001-35837	8/12/2014	10.1
10.9#	Amendment No. 1 to the Registrant 2014 Employee Stock Purchase Plan, dated March 13, 2019	10-Q	001-35837	5/8/2019	10.1
10.10#	Form of Nonstatutory Option Agreement for Inducement Grants	10-Q	001-35837	5/7/2015	10.3
10.11#	Separation agreement, dated as of July 31, 2019, by and between the Registrant and Guy Macdonald	10-Q	001-35837	8/8/2019	10.3
10.12#	Consulting agreement, dated as of July 31, 2019, by and between the Registrant and Guy Macdonald	10-Q	001-35837	8/8/2019	10.4
10.13#	Offer letter, dated as of February 16, 2015, by and between the Registrant and Maria Stahl	10-Q	001-35837	5/7/2015	10.2
10.14#	Form of Indemnification Agreement entered into between the Registrant and each of its directors and executive officers	S-1/A	333-186574	3/5/2013	10.27

Exhibit Number	Description	Registrant's Form	Incorporated by Reference from File No.	Date Filed with the SEC	Exhibit Number
10.15	Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended on September 9, 2011, March 15, 2012, September 18, 2012, November 20, 2013, March 24, 2015 and June 18, 2015	10-Q	001-35837	8/6/2015	10.1
10.16	Amendment, dated September 4, 2014, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended	10-Q	001-35837	11/10/2014	10.1
10.17	Amendment, dated March 24, 2015, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended	10-Q	001-35837	5/7/2015	10.1
10.18	Amendment, dated June 18, 2015, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended	10-Q	001-35837	8/6/2015	10.1
10.19	Amendment, dated November 29, 2018, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended	10-K	001-35837	3/15/2019	10.21
10.20*	Amendment, dated January 31, 2020, to Lease Agreement, dated as of November 16, 2006, by and between the Registrant and ARE-480 Arsenal Street, LLC, as amended				
10.21†	License Agreement, dated as of August 3, 2006, by and between the Registrant and the President and Fellows of Harvard College, as amended	S-1	333-186574	2/11/2013	10.20
10.22†	Amendment, dated as of December 5, 2017, by and between the Registrant and the President and Fellows of Harvard College, as amended	10-K	001-35837	3/6/2018	10.22
10.23†	Subcontract Agreement, dated as of February 1, 2012, by and between the Registrant and CUBRC, Inc.	S-1	333-186574	2/11/2013	10.21
10.24†	Subcontract Agreement, dated as of September 30, 2011, by and between the Registrant and CUBRC, Inc.	S-1	333-186574	2/11/2013	10.22
10.25#	Offer letter, dated as of June 20, 2015, by and between the Registrant and Christopher Watt	10-K	001-35837	2/25/2016	10.17
10.26†	Master Manufacturing Services Agreement, dated June 14, 2017, by and between the Registrant and Patheon UK Limited	10-Q	001-35837	8/2/2017	10.1
10.27†	Commercial Supply Agreement, dated October 16, 2017, by and between the Registrant and Finorga SAS	10-Q	001-35837	11/1/2017	10.1
10.28†	License Agreement, dated February 20, 2018, by and between the Registrant and Everest Medicines Limited	10-K	001-35837	3/6/2018	10.28
10.29#	Amendment No.1, dated July 29, 2019, to the License Agreement between Everest Medicines Limited and the Registrant	10-Q	001-35837	8/8/2019	10.1
10.30#	Offer letter, dated as of July 31, 2019, by and between the Registrant and Larry Edwards	10-Q	001-35837	8/8/2019	10.2

Exhibit Number	Description	Registrant's Form	Incorporated by Reference from File No.	Date Filed with the SEC	Exhibit Number
10.31	Payoff Letter, entered into as of August 30, 2019, by and among the Registrant, Solar Capital Ltd., as collateral agent and lender, and the other lenders named therein	8-K	001-35837	8/30/2019	10.1
10.32	First Amendment to Loan and Security Agreement, dated as of March 14, 2019, by and between the registrant and Solar Capital Ltd., in its capacity as collateral agent	10-Q	001-35837	5/8/2019	10.2
10.33	Form of Securities Purchase Agreement, dated October 29, 2019, between the Registrant and the Purchaser	8-K	001-35837	10/30/2019	10.1
10.34	Form of PIPE Securities Purchase Agreement, dated January 22, 2020, by and among the Registrant and the other persons party thereto	8-K	001-35837	1/23/2020	10.1
10.35	Form of Registration Rights Agreement, dated January 22, 2020, by and among the Registrant and the other persons party thereto	8-K	001-35837	1/23/2020	10.2
10.36	Form of RD Securities Purchase Agreement, dated January 22, 2020, by and among the Registrant and the other persons party thereto	8-K	001-35837	1/23/2020	10.3
21.1*	Subsidiaries of the Registrant				
23.1*	Consent of Ernst & Young LLP				
31.1*	Chief Executive Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
31.2*	Principal Financial Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				
32.1*	Chief Executive Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
32.2*	Principal Financial Officer—Certification pursuant to Rule 13a-14(a) of the Securities Exchange Act of 1934 and 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				
101.INS*	XBRL Instance Document				
101.SCH*	XBRL Taxonomy Extension Schema Document				
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document				
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document				

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

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 11, 2020

By: /s/ Larry Edwards
Larry Edwards
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/ Larry Edwards **Larry Edwards**	Director, President and Chief Executive Officer *(Principal Executive Officer)*	March 11, 2020
/s/ Christopher Watt **Christopher Watt**	Senior Vice President, Finance *(Principal Financial and Accounting Officer)*	March 11, 2020
/s/ L. Patrick Gage **L. Patrick Gage, Ph.D.**	Chairman	March 11, 2020
/s/ Garen Bohlin **Garen Bohlin**	Director	March 11, 2020
/s/ Steven Boyd **Steven Boyd**	Director	March 11, 2020
/s/ Jeffrey A. Chodakewitz **Jeffrey A. Chodakewitz**	Director	March 11, 2020
/s/ John G. Freund **John G. Freund**	Director	March 11, 2020
/s/ Geraldine Henwood **Geraldine Henwood**	Director	March 11, 2020
/s/ Guy Macdonald **Guy Macdonald**	Director	March 11, 2020
/s/ Keith Maher **Keith Maher**	Director	March 11, 2020
/s/ Nancy Wysenski **Nancy Wysenski**	Director	March 11, 2020

EXHIBIT 4.10

DESCRIPTION OF SECURITIES REGISTERED UNDER SECTION 12 OF THE EXCHANGE ACT

General

The following description of the capital stock of Tetraphase Pharmaceuticals, Inc. (the "Company") is intended as a summary only and therefore is not a complete description of the Company's capital stock. This description is based upon, and is qualified by reference to, the Company's restated certificate of incorporation, as amended (the "Certificate of Incorporation"), and its amended and restated bylaws (the "Bylaws"), which are filed as exhibits to the Annual Report on Form 10-K, of which this Exhibit 4.10 is a part.

The Company's authorized capital stock consists of 125,000,000 shares of common stock, par value $0.001 per share (the "Common Stock"), and 5,000,000 shares of preferred stock, par value $0.001 per share (the "Preferred Stock"), all of which Preferred Stock is undesignated.

Common Stock

Holders of Common Stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by the Company's stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. In general, except (1) for the election of directors, (2) as described below under "—Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions", (3) in the future to the extent that the Company has two or more classes or series of stock outstanding with separate voting rights and (4) as otherwise required by law, any matter to be voted on by the Company's stockholders at any meeting, shall be decided by the affirmative vote of the Company's stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter.

Holders of Common Stock are entitled to receive proportionately any dividends as may be declared by the Company's board of directors, subject to any preferential dividend rights of outstanding Preferred Stock.

In the event of the Company's liquidation or dissolution, the holders of Common Stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of the Company's outstanding Preferred Stock.

Holders of Common Stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of Common Stock are subject to and may be adversely affected by the rights of the holders of shares of any series of Preferred Stock that may be designated and issued in the future.

Preferred Stock

Under the terms of the Certificate of Incorporation, the Company's board of directors is authorized to issue 5,000,000 shares of Preferred Stock, par value $0.001 per share, in one or more series without stockholder approval. The board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of Preferred Stock.

The Preferred Stock could have other rights, including economic rights that are senior to the Common Stock that could adversely affect the market value of the Common Stock. The issuance of the Preferred Stock may also have the effect of delaying, deferring or preventing a change in control of the Company without any action by the shareholders.

Delaware Anti-Takeover Law and Certain Charter and Bylaw Provisions

Delaware law, the Certificate of Incorporation and the Bylaws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of the Company. These provisions, which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of the Company to first negotiate with the Company's board of directors.

Staggered Board; Removal of Directors

The Certificate of Incorporation and Bylaws divide the Company's board of directors into three classes with staggered three-year terms. In addition, a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of the Company's stockholders would be entitled to cast in an annual election of directors. Any vacancy on the Company's board of directors, including a vacancy resulting from an enlargement of the Company's board of directors, may be filled only by vote of a majority of the directors then in office. The classification of the Company's board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of the Company.

Stockholder Action by Written Consent; Special Meetings

The Certificate of Incorporation provides that any action required or permitted to be taken by the stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. The Certificate of Incorporation and Bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by the chairman of the board, the chief executive officer or the board of directors.

Advance Notice Requirements for Stockholder Proposals

The Bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to the Company's secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of the outstanding voting securities. These provisions could also discourage a third party from making a tender offer for the Common Stock, because even if the third party acquired a majority of the Company's outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Delaware Business Combination Statute

Section 203 of the General Corporation Law of the State of Delaware, or the DGCL, is applicable to the Company. Section 203 of the DGCL restricts some types of transactions and business combinations between a corporation and a 15% stockholder. A 15% stockholder is generally considered by Section 203 to be a person owning 15% or more of the corporation's outstanding voting stock. Section 203 refers to a 15% stockholder as an "interested stockholder." Section 203 restricts these transactions for a period of three years from the date the stockholder acquires 15% or more of the Company's outstanding voting stock. With some exceptions, unless the transaction is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock of the corporation, Section 203 prohibits significant business transactions such as:

- a merger with, disposition of significant assets to or receipt of disproportionate financial benefits by the interested stockholder, and
- any other transaction that would increase the interested stockholder's proportionate ownership of any class or series of the Company's capital stock.

The shares held by the interested stockholder are not counted as outstanding when calculating the two-thirds of the outstanding voting stock needed for approval.

The prohibition against these transactions does not apply if:

- prior to the time that any stockholder became an interested stockholder, the board of directors approved either the business combination or the transaction in which such stockholder acquired 15% or more of the Company's outstanding voting stock, or

- the interested stockholder owns at least 85% of the Company's outstanding voting stock as a result of a transaction in which such stockholder acquired 15% or more of the Company's outstanding voting stock. Shares held by persons who are both directors and officers or by some types of employee stock plans are not counted as outstanding when making this calculation.

Amendment of Certificate of Incorporation and Bylaws

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. The Bylaws may be amended or repealed by a majority vote of the board of directors or by the affirmative vote of the holders of at least 75% of the votes that all stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of the Certificate of Incorporation described above under "—Staggered Board; Removal of Directors" and "—Stockholder Action by Written Consent; Special Meetings".

NINTH AMENDMENT TO LEASE

THIS NINTH AMENDMENT TO LEASE (this "**Ninth Amendment**") is made as of January 31, 2020 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 further amended by that certain Second Amendment to Lease dated as of March 15, 2012, as further amended by that certain Third Amendment to Lease dated as of September 18, 2012, as further amended by that certain Fourth Amendment to Lease dated as of November 20, 2013, as further amended by that certain Fifth Amendment to Lease dated as of September 4, 2014, as further amended by that certain Sixth Amendment to Lease dated as of March 24, 2015, as further amended by that certain Seventh Amendment to Lease dated as of June 18, 2015, and as further amended by that certain Eighth Amendment to Lease dated as of November 29, 2018 (as amended, the "**Lease**") Pursuant to the Lease, Tenant leases certain premises containing approximately 37,438 rentable square feet (the "**Premises**") in a building located at 480 Arsenal Street, Watertown, Massachusetts ("**Building**") The Premises are more particularly described In the Lease. 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 cond1t1ons set forth below, to, among other things, reflect the surrender of a portion of the Premises consisting of approximately 15,899 rentable square feet of the Project, as more particularly shown on **Exhibit A** attached hereto (the "**Surrender Premises**") as of 11:59 p.m. on January 31, 2020 (the "**Surrender Date**").

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. **Surrender of Surrender Premises** The Lease with respect to the Surrender Premises shall terminate as provided for In the Lease on the Surrender Date Tenant shall voluntarily surrender the Surrender Premises on such date m accordance with all surrender requirements contained in the Lease and in the condition in which Tenant is required to surrender the Premises as of the expiration of the Lease From and after the Surrender Date, Tenant shall have no further rights of any kind with respect to the Surrender Premises. Notwithstanding the foregoing, those provisions of the Lease which, by their terms, survive the termination of the Lease shall survive the surrender of the Surrender Premises and termination of the Lease with respect to the Surrender Premises as provided for herein. Nothing herein shall excuse Tenant from Its obligations under the Lease with respect to the Surrender Premises prior to the Surrender Date.

2. **Definition of Premises.** Commencing February 1, 2020, the defined terms "**Premises**" and "**Rentable Area of Premises**" on Page 1 of the Lease, respectively, are deleted in their entirety and replaced with the following

"**Premises:** That certain portion of the Building, containing approximately 21,539 rentable square feet, consisting of: (i) approximately 13,711 rentable square feet (the "**Second Expansion Premises**"), and (ii) approximately 7,828 rentable square feet (the "**Third Expansion Premises**"), all as shown on **Exhibit A**."

"**Rentable Area of Premises**: 21,539 sq ft."

Commencing on February 1, 2020, **Exhibit A** of the Lease shall be amended to delete the Surrender Premises.

3. **Base Rent** Tenant shall continue to pay Base Rent for the entire Premises (including the Surrender Premises) as provided for in the Lease through the Surrender Date Commencing on February 1, 2020, Tenant shall continue to pay Base Rent with respect to the remaining Premises (but not the Surrender Premises) through the Eighth Amendment Expiration Date.

4. **Tenant's Share of Operating Expenses** Commencing February 1, 2020, the defined term "Tenant's Share of Operating Expenses" on Page 1 of the Lease 1s deleted in its entirety and replaced with the following

"**Tenant's Share of Operating Expenses**: 15.30%"

5. **OFAC**. Tenant and, to the best of Tenant's knowledge, ail 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 US person is prohibited from conducting business under the OFAC Rules.

6. **Miscellaneous**.

a. This Ninth Amendment 1s 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 Ninth Amendment may be amended only by an agreement in writing, signed by the parties hereto.

b. 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 Ninth Amendment and that no Broker brought about this transaction Landlord and Tenant each hereby agree to indemnify and hold the other harmless from and against any claims by any Broker 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.

c. This Ninth Amendment is binding upon and shall inure to the benefit of the parties hereto, and their respective successors and assigns.

d. This Ninth Amendment may be executed in 2 or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument Counterparts may be delivered via facsimile, electronic mall (including pdf or any electronic signature process complying with the U.S. federal ESIGN Act of 2000) or other transmission method and any counterpart so delivered shall be deemed to have been duly and validly delivered and be valid and effective for all purposes Electronic signatures shall be deemed original signatures for purposes of this Ninth Amendment and all matters related thereto, with such electronic signatures having the same legal effect as original signatures.

e. Except as amended and/or modified by this Ninth 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 Ninth Amendment in the event of any conflict between the provisions of this Ninth Amendment and the provisions of the Lease, the prov1s1ons of this Ninth Amendment shall prevail whether or not specifically amended by this Ninth 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 Ninth Amendment.

[Signatures are on the next page]

IN WITNESS WHEREOF, the parties hereto have executed this Ninth 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/ Cary Dean*
Its Senior Vice President RE Legal Affairs

TENANT:

TETRAPHASE PHARMACEUTICALS, INC.
a Delaware corporation

By: */s/ Maria Stahl*
Its CBO and General Counsel

Exhibit 21.1

SUBSIDIARIES OF THE REGISTRANT

Name	Jurisdiction of Organization	Percentage Ownership
Tetraphase Pharma Securities, Inc.	Massachusetts	100%
Tetraphase Ireland Limited	Republic of Ireland	100%
Tetraphase UK Limited	United Kingdom	100%

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Forms S-8 No. 333-232161 and 333-198098) pertaining to the 2014 Employee Stock Purchase Plan of Tetraphase Pharmaceuticals, Inc., as amended,
(2) Registration Statements (Forms S-8 No. 333-230364 and 333-209991) pertaining to the 2013 Stock Incentive Plan and Inducement Stock Option Awards of Tetraphase Pharmaceuticals, Inc.,
(3) Registration Statements (Forms S-8 No. 333-223985, 333-216742, 333-202576, and 333-194125) pertaining to the 2013 Stock Incentive Plan of Tetraphase Pharmaceuticals, Inc.,
(4) 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., and
(5) Registration Statements (Forms S-3 No. 333-222699, 333-218816, 333-214500, 333-202613, and No. 333-195631) of Tetraphase Pharmaceuticals, Inc.

of our report dated March 11, 2020, with respect to the consolidated financial statements of Tetraphase Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Tetraphase Pharmaceuticals, Inc. for the year ended December 31, 2019.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 11, 2020

Exhibit 31.1

CERTIFICATION

I, Larry Edwards, 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 11, 2020

/s/ Larry Edwards
Larry Edwards
Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Christopher Watt, 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 11, 2020

/s/ Christopher Watt
Christopher Watt
Senior Vice President, Finance

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, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Larry Edwards, 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 11, 2020

/s/ Larry Edwards
Larry Edwards
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, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Christopher Watt, Senior Vice President, Finance 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 11, 2020

/s/ Christopher Watt
Christopher Watt
Senior Vice President, Finance