

TETRAPHASE PHARMACEUTICALS INC

Form 424B5

July 27, 2017

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As Filed Pursuant to Rule 424(b)(5)

Registration No. 333-218816

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated July 27, 2017

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus Dated July 5, 2017)

\$60,000,000

Tetraphase Pharmaceuticals, Inc.

Common Stock

\$ Per Share

We are offering shares of our common stock having an aggregate offering price of \$60,000,000.

Our common stock trades on The NASDAQ Global Select Market under the symbol TTPH. On July 26, 2017, the last sale price of our common stock as reported on The NASDAQ Global Select Market was \$7.88 per share.

Investing in our common stock involves a high degree of risk. See **Risk Factors** beginning on page S-5.

	Per Share	Total
Public offering price	\$	\$
Underwriting discount (1)	\$	\$
Proceeds, before expenses, to Tetrphase Pharmaceuticals, Inc.	\$	\$

(1) We refer you to Underwriting beginning on page S-16 of this prospectus supplement for additional information regarding underwriter compensation.

The underwriters have the option to purchase up to an additional \$9,000,000 of shares of our common stock from us at the price to the public less the underwriting discount.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to the purchasers on or about _____, 2017.

Joint Book-Running Managers

Piper Jaffray

BMO Capital Markets
Lead Manager

Stifel

SunTrust Robinson Humphrey

Manager

H.C. Wainwright & Co.

Prospectus Supplement dated July _____, 2017.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreement, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not, and the underwriters have not, authorized anyone to provide you with information other than that which is contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. It is important for you to read and consider all information contained in this prospectus supplement and in the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled *Where You Can Find More Information* and *Incorporation by Reference* in this prospectus supplement and in the accompanying prospectus.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Unless the context otherwise indicates, all references in this prospectus supplement and the accompanying prospectus to we, us, our, Tetrphase, the Company and similar designations refer, collectively, to Tetrphase Pharmaceutic Inc., a Delaware corporation, and, where appropriate, its consolidated subsidiaries.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical facts, included in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, seek, target, goal, potential, will, would, could, words and terms of similar meaning are intended to help identify forward-looking statements, although not all forward-looking statements contain these identifying words. Forward-looking statements may also be identified by the fact that they do not relate strictly to historical or current facts. These forward-looking statements include, among other things, statements about:

the anticipated timing, costs and conduct of our ongoing development program for eravacycline for the treatment of complicated urinary tract infections, or cUTI, including our ongoing Phase 3 clinical trial of eravacycline for cUTI;

our expectations regarding the clinical effectiveness of eravacycline;

our anticipated timing for submitting applications for U.S. and foreign regulatory marketing approval for eravacycline;

our plans to commercialize eravacycline for complicated intra-abdominal infections, or cIAI, and cUTI;

our plans to develop and commercialize our other product candidates;

our commercialization, marketing and manufacturing capabilities and strategy;

our intellectual property position;

our competitive position;

our expectations related to the use of proceeds from this offering; and

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

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 prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, particularly the Risk Factors section of this prospectus supplement and in Part II, Item 1A of our most recent quarterly report on Form 10-Q that could cause actual results or events to differ materially from those indicated by these forward looking statements. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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*This summary highlights certain information about us, this offering and other selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information you should consider before investing in our common stock. You should carefully read this entire prospectus supplement, the accompanying prospectus and any free writing prospectus that we may authorize for use in connection with this offering, especially the risks described under *Risk Factors* contained in this prospectus supplement and in Part II, Item IA of our quarterly report on Form 10-Q filed with the SEC on May 8, 2017, which is incorporated by reference in this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus.*

Tetraphase Pharmaceuticals, Inc.**Overview**

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

Eravacycline IGNITE Phase 3 Clinical Program

We are conducting a global phase 3 clinical program for eravacycline called IGNITE (**I**nvestigating **G**ram-**N**egative **I**nfections **T**reated with **E**ravacycline). On July 25, 2017, we announced top-line data from our IGNITE4 trial, a global phase 3 randomized, double-blind, double-dummy, multicenter, prospective study assessing the efficacy, safety and pharmacokinetics of twice-daily IV eravacycline (1.0 mg/kg every 12 hours) compared with meropenem (1g every 8 hours) for the treatment of complicated intra-abdominal infections, or cIAI, that we conducted in 500 patients. In the trial, eravacycline met the primary endpoint of statistical non-inferiority of clinical response at the test-of-cure, or TOC, visit, under the guidance set by the United States Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA. Prior to IGNITE 4, we conducted IGNITE1, a phase 3 clinical trial of twice daily IV eravacycline (1.0 mg/kg every 12 hours) compared with ertapenem (1.0g IV every 24 hours) for the treatment of cIAI. In IGNITE1, eravacycline met the primary endpoint of statistical non-inferiority of clinical response.

We designed IGNITE4 as a non-inferiority study and to be responsive to guidance from both the FDA and the EMA. Under FDA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the microbiological intent-to-treat, or micro-ITT, population, which consisted of randomized patients in the trial who had baseline bacterial pathogens that cause cIAI and against which eravacycline has antibacterial activity. Under EMA guidance, the primary endpoint of the trial was clinical response at the TOC visit in the modified intent-to-treat, or MITT, population, which consisted of patients in the trial who received at least one dose of study drug, and in the clinically evaluable, or 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 eravacycline in the safety population and pharmacokinetic parameters after eravacycline administration.

Eravacycline achieved high clinical cure rates in patients with cIAI, comparable to cure rates in the patients in the meropenem group. 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 eravacycline (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 eravacycline (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 eravacycline (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.

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There were no treatment-related serious adverse events in the trial. Treatment-emergent adverse event rates were similar in both treatment groups. The most commonly reported drug-related adverse events for eravacycline were infusion site reactions, nausea and vomiting, each occurring at a rate of less than 5%. The safety profile for IV eravacycline in IGNITE4 was consistent with that seen in the previously completed phase 3 IGNITE1 and phase 2 clinical trials in cIAI. In addition, the spectrum of pathogens in this trial was similar to that seen in previously completed clinical trials of third party products in this patient population. The most common Gram-negative pathogens in the study included *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas* and *Bacteroides*.

Consistent with draft guidance issued by the FDA with respect to the development of antibiotics for cIAI and our discussions with the FDA, we believe that the positive results observed in both IGNITE1 and IGNITE4 are sufficient to support submission of a new drug application, or NDA, for eravacycline for the treatment of cIAI with the FDA. We anticipate submitting an NDA by the end of the first quarter of 2018. Consistent with discussions with the EMA, we are also planning to submit a marketing authorization application, or MAA, to the EMA for IV eravacycline for the treatment of cIAI in the third quarter of 2017 primarily based upon the results of IGNITE1.

We are also developing eravacycline for the treatment of cUTI. In January 2017, we initiated IGNITE3, a randomized, multi-center, double-blind, phase 3 clinical trial evaluating the efficacy and safety of once-daily IV eravacycline (1.5mg/kg every 24 hours) compared to ertapenem (1g every 24 hours), the control therapy in this trial, for the treatment of cUTI. IGNITE3 is expected to enroll approximately 1,000 adult patients, who will be randomized 1:1 to receive eravacycline or ertapenem for a minimum of five days, and will then be eligible to switch to an oral antibiotic. The co-primary endpoints of responder rate (a combination of clinical cure rate and microbiological success) in the micro-ITT population at the end-of-IV treatment visit and at the TOC visit (Day 14-17 after randomization) will be evaluated using a 10% non-inferiority margin. We expect to complete enrollment in IGNITE3 early in the fourth quarter of 2017. If IGNITE3 is successful, we plan to use the results from IGNITE3 to support submission of a supplemental new drug application, or sNDA, for IV eravacycline for the treatment of cUTI, assuming approval first of IV eravacycline for the treatment of cIAI.

In parallel with the clinical trials using IV eravacycline, we are continuing our development program for an oral formulation of eravacycline. We recently completed a phase 1 clinical trial in which the administration of oral eravacycline to patients in the fasted state resulted in increased drug exposure. Further clinical tests designed to evaluate other important variables are currently ongoing, with the goal of optimizing the oral eravacycline dosing regimen.

The FDA has granted Qualified Infectious Disease Product (QIDP) and Fast Track designations for IV and oral eravacycline for cIAI and cUTI.

Eravacycline Market Opportunity

We believe eravacycline's spectrum of coverage against a broad range of bacteria including Gram-negative, Gram-positive and anaerobic pathogens, as well as its potent activity against drug-resistant bacteria and its convenience of dose as well as favorable safety profile, could position it as an antibiotic of choice for use in high risk patients, including empiric treatment in high risk patients, patients with renal or hepatic impairment, patients who may require combination therapy, patients who have failed first-line treatment and patients with confirmed resistant infections.

cIAI. We plan to seek to initially commercialize eravacycline in patients with cIAI. Patients with cIAI are treated primarily with IV therapy because these patients are typically in the hospital recovering from a surgical procedure and need early, rapid treatment and broad spectrum coverage. Based on an analysis of industry sources, we believe that IV

therapy for cIAI represents approximately 88%, or 35 million, out of 40 million patient days of therapy for cIAI in hospitals in the United States and the European Union. Of these, approximately 10 million days of treatment are received by high risk patients. Approximately 90% of cIAI patients are treated empirically and 40% require second line treatment. We believe that eravacycline's broad spectrum of coverage, its activity against resistant pathogens and its convenient dosing regimen differentiate it from other antibiotics being developed or sold for cIAI. and support its potential as a treatment option for high risk cIAI patients.

cUTI. We also plan to seek to commercialize eravacycline in patients with cUTI. Patients with cUTI typically are treated initially with IV therapy in the hospital and when their symptoms improve, most patients are sent home and transitioned to oral therapy for the remainder of their treatment. Based on an analysis of industry sources, we believe that that IV therapy for cUTI represents a little more than half, or 34 million, of the 60 million patient days of therapy for cUTI in hospitals in the United States and the European Union. Of these, approximately 10 million days of treatment are received by high risk patients. Approximately 85% of cUTI patients are treated empirically and 20% require second line treatment. We believe that eravacycline's broad spectrum of coverage, its activity against resistant pathogens and its convenient dosing regimen differentiate it from other antibiotics being developed or sold for cUTI and support its potential as a treatment option for cUTI high risk patients.

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Pipeline Candidates

In June 2017, we announced positive results from a phase 1 single-ascending dose clinical trial of the IV formulation of TP-271, a fully-synthetic fluorocycline being developed for respiratory disease caused by bacterial biothreat pathogens, in healthy volunteers. In the study TP-271 was well tolerated at single doses that resulted in high plasma exposures. There were no clinically significant changes in lab values, ECG parameters, or physical exam findings. There were no serious or severe adverse events, or discontinuations due to an adverse event during the study. We plan to initiate a multiple-ascending dose trial for TP-271 in the third quarter of 2017. We are also conducting a single-ascending dose phase 1 study for the oral formulation of TP-271. In February 2017, we received Qualified Infectious Disease Product and Fast Track designations from the FDA.

In addition, we are developing TP-6076, a fully-synthetic fluorocycline derivative, as a lead candidate under our second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria. In June 2017 we announced positive results from a phase 1 randomized, placebo-controlled, double-blind, single-ascending dose study evaluating the safety, tolerability and pharmacokinetics of IV TP-6076. In the study TP-6076 was well tolerated, and there were no serious or severe adverse events, or discontinuations due to an adverse event. There were no clinically significant safety findings in any laboratory assessments, vital signs, ECGs or physical examinations. We also are conducting a multiple-ascending study in healthy volunteers of the IV formulation of TP-6076.

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

Recent Developments

On January 17, 2017, we entered into sales agreement with a sales agent in respect of an at-the-market offering program. On July 7, 2017, we entered into an amendment to the sales agreement to increase the maximum aggregate offering price of the shares of our common stock that we may issue and sell from time to time under the sales agreement from \$40,000,000 to \$80,000,000. As of July 26, 2017, we had sold 3,935,450 shares of our common stock under the sales agreement at an average price of \$7.78 per share for an aggregate offering price of \$30.6 million, before deducting sales commissions and offering expenses, which includes 611,865 shares sold on July 26, 2017 at an average price of \$7.79 per share for an aggregate offering price of approximately \$4.76 million, before deducting sales commissions and offering expenses.

Company Information

We were incorporated under the laws of the State of Delaware on July 7, 2006. Our principal executive offices are located at 480 Arsenal Way, Watertown, Massachusetts 02472, and our telephone number is (617) 715-3600. Our

website address is *www.tphase.com*. The information contained or accessible through our website is not incorporated by reference into, and is not considered a part of, this prospectus supplement. We have included our website address in this prospectus supplement and the accompanying prospectus solely as an inactive textual reference.

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The Offering

Common stock offered by us in this offering

shares.

Common stock to be outstanding after

this offering

shares.

Option to purchase additional shares

The underwriters have an option to purchase up to an additional \$9,000,000 of shares of our common stock from us. The underwriters can exercise this option at any time within 30 days from the date of this prospectus supplement.

Use of Proceeds

We estimate that the net proceeds to us from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$56.2 million, or approximately \$64.7 million if the underwriters exercise their option to purchase additional shares from us in full, in each case, based on an assumed public offering price of \$7.88 per share (the last reported sale price of our common stock on The NASDAQ Global Select Market on July 26, 2017). We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents, to fund our IGNITE3 clinical trial of eravacycline and further development of eravacycline, pre-commercialization and launch related activities for eravacycline, for further development of our other product candidates, and for working capital and other general corporate purposes. See **Use of Proceeds** on page S-8 of this prospectus supplement for more information.

Risk Factors

Investing in our common stock involves a high degree of risk. You should read the **Risk Factors** section in this prospectus supplement and in Part II, Item 1A of our quarterly report on Form 10-Q filed with the SEC on May 8, 2017, which is incorporated by reference in this prospectus supplement, for a discussion of factors to consider before deciding to purchase shares of our common stock.

NASDAQ Global Select Market symbol

TTPH.

The number of shares of our common stock to be outstanding after this offering is based on 40,012,154 shares of our common stock issued and outstanding as of June 30, 2017 and excludes:

6,087,428 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2017, at a weighted-average exercise price of \$13.49 per share;

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165,616 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of June 30, 2017;

175,000 shares of our common stock issuable upon the vesting of performance stock units outstanding as of June 30, 2017;

1,103 shares of our common stock issuable upon the exercise of warrants outstanding as of June 30, 2017, at a weighted average exercise price of \$29.00 per share;

593,612 and 171,697 additional shares of our common stock available for future issuance, as of June 30, 2017, under our 2013 stock incentive plan and our 2014 employee stock purchase plan, respectively; and

7,284,458 shares of common stock available for sale as of June 30, 2017 under our sales agreement in respect of our at-the-market program, after giving effect to the amendment to the sales agreement dated as of July 7, 2017 (based on an aggregate of \$57.4 million of common stock available for sale under the sales agreement, as amended, and assuming sales at a price of \$7.88 per share, which was the closing price of our common stock on The NASDAQ Global Select Market on July 26, 2017).

Except as otherwise noted, we have presented the information in this prospectus supplement:

assumes no exercise of outstanding stock options or warrants described above; and

assumes no exercise by the underwriters of their option to purchase up to an additional \$9,000,000 of our common stock from us.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should carefully consider the risks and uncertainties described below and in Part II, Item IA Risk Factors of our most recent quarterly report on Form 10-Q filed with the SEC on May 8, 2017, together with the other information contained in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein and therein and any free writing prospectus we may authorize for use in connection with this offering. These updated Risk Factors will be incorporated by reference in this prospectus supplement. If any of these risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Ownership of Our Common Stock and this Offering

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

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. For example, our stock traded within a range of a high price of \$52.90 per share and a low price of \$3.11 per share for the period beginning on January 1, 2015 through July 26, 2017. 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:

results of clinical trials of eravacycline and any other product candidate;

the timing of clinical trials of eravacycline and any other product candidate;

regulatory actions by the FDA or equivalent authorities in foreign jurisdictions with respect to eravacycline and any other product candidate;

failure or discontinuation of any of our development programs;

the success of existing or new competitive products or technologies;

results of clinical trials of product candidates of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our product candidates or clinical development programs;

the results of our efforts to develop, in-license or acquire additional product candidates or products;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

announcement or expectation of additional financing efforts;

sales of our common stock by us, our insiders or other stockholders

variations in our financial results or those of companies that are perceived to be similar to us;

changes in estimates or recommendations by securities analysts, if any, that cover our stock;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this Risk Factors section and in Part II, Item 1A Risk Factors of our most recent quarterly report on Form 10-Q filed with the SEC on May 8, 2017.

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If you purchase shares of common stock in this offering, you will suffer immediate dilution in the book value of your investment.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. Based on an assumed public offering price of \$7.88 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on July 26, 2017, you will experience immediate dilution of \$4.02 per share, representing the difference between our net tangible book value per share after giving effect to this offering and the assumed public offering price. Furthermore, if the underwriters exercise their option to purchase additional shares or our previously issued options and warrants to acquire common stock at prices below the assumed public offering price are exercised, you will experience further dilution. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

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, you may not be able to sell your common stock at or above the public offering price or at the times that you 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.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

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

You may experience future dilution as a result of future or additional equity offerings.

In order to raise additional capital, we may at any time offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering. For example, we may, from time to time, issue and sell shares of our common stock having up to an aggregate offering price of \$80,000,000 under a sales agreement through an at the market offering program. We have agreed with the underwriters not to sell any securities, including under the sales agreement, for a period of up to 60 days following this offering. We may resume sales following the earlier of the expiration of, or release from, this lock-up period. As of July 26, 2017, we had sold 3,935,450 shares of our common stock under the sales agreement at an average price of \$7.78 per share for an aggregate offering price of \$30.6 million, before deducting sales commissions and offering expenses, which includes 611,865 shares sold on July 26, 2017 at an average price of \$7.79 per share for an aggregate offering price of approximately \$4.76 million, before deducting sales commissions and offering expenses.

A portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. After this offering, we will have 48,667,661 shares of common stock outstanding based on the 41,053,448 shares outstanding as of July 26, 2017 and assuming the issuance and sale of 7,614,213 shares of our common stock in this offering. Of these shares, 499,193 shares are subject to a contractual lock-up with the underwriters for this offering for a period of 60 days following this offering. These shares can be sold, subject to any applicable volume limitations under federal securities laws, after the earlier of the expiration of, or release from, the 60-day lock-up period. The balance of our outstanding shares of common stock may be freely sold in the public market at any time. Moreover, certain holders of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

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In addition, as of June 30, 2017, there were 6,428,044 shares subject to outstanding options, restricted stock units and performance stock units under our equity incentive plans, all of which we have registered under the Securities Act of 1933, as amended, which we refer to as the Securities Act, on a registration statement on Form S-8. These shares, once vested and, in the case of options, issued upon exercise, will be able to be freely sold in the public market, subject to volume limits applicable to affiliates and the lock-up agreements described above, to the extent applicable. Furthermore, as of June 30, 2017, there were 1,103 shares subject to outstanding warrants. These shares will become eligible for sale in the public market to the extent such warrants are exercised and to the extent permitted by Rule 144 under the Securities Act.

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USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately \$56.2 million, or approximately \$64.7 million if the underwriters exercise their option to purchase additional shares in full, in each case after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and based on an assumed public offering price of \$7.88 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on July 26, 2017.

We intend to use the net proceeds from this offering, together with our existing cash and cash equivalents of approximately \$118.2 million as of June 30, 2017, to fund our IGNITE3 clinical trial of eravacycline and further development of eravacycline, pre-commercialization and launch related activities for eravacycline, for development of our other product candidates, and for working capital and other general corporate purposes. The expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the status of and results from clinical trials of eravacycline and whether regulatory authorities require us to perform additional clinical trials of eravacycline in order to obtain marketing approvals. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering, and investors will be relying on our judgment regarding the application of the net proceeds of this offering. We may find it necessary or advisable to use the net proceeds from this offering for other purposes, and we will have broad discretion in the application of net proceeds.

We believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through at least 2018. We believe that our available funds following this offering will be sufficient to enable us to obtain top-line data from our ongoing Phase 3 clinical trial of eravacycline for the treatment of cUTI, to submit an NDA to the FDA and a marketing authorization application to the European Medicines Agency for eravacycline for the treatment of cIAI, to submit a supplemental NDA to the FDA for the treatment of cUTI if warranted, and to perform pre-commercialization activities and commercially launch eravacycline for the treatment of cIAI if approved. It is also possible that we will not achieve the progress that we expect with respect to eravacycline because the actual costs and timing of clinical development activities are difficult to predict and are subject to substantial risks and delays. We have no external sources of funds other than our subcontracts with, and subaward from, CUBRC, Inc., an independent, not-for-profit, research corporation that specializes in U.S. government-based contracts, with which we are collaborating under awards from the Biomedical Advanced Research and Development Authority, an agency of the U.S. Department of Health and Human Services, and the National Institute of Allergy and Infectious Diseases, a division of the National Institutes of Health. We expect that we will need to obtain additional funding in order to continue operations even after we commercially launch eravacycline.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and securities.

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The following table sets forth the high and low intraday sale prices per share of our common stock, as reported on The NASDAQ Global Select Market, for the quarterly periods indicated:

	High	Low
Year ended December 31, 2015		
First Quarter	\$ 44.55	\$ 32.40
Second Quarter	\$ 48.68	\$ 34.68
Third Quarter	\$ 52.90	\$ 7.24
Fourth Quarter	\$ 12.45	\$ 7.20
Year ended December 31, 2016		
First Quarter	\$ 9.98	\$ 3.48
Second Quarter	\$ 6.28	\$ 3.12
Third Quarter	\$ 4.65	\$ 3.62
Fourth Quarter	\$ 5.12	\$ 3.11
Year ended December 31, 2017		
First Quarter	\$ 9.93	\$ 3.57
Second Quarter	\$ 9.53	\$ 6.41
Third Quarter (through July 26, 2017)	\$ 8.75	\$ 6.77

On July 26, 2017, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$7.88 per share.

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DIVIDEND POLICY

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

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If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the public offering price per share you will pay in this offering and the as adjusted net tangible book value per share of our common stock after this offering. Our historical net tangible book value as of March 31, 2017 was \$119.0 million, or \$3.15 per share of common stock. Our net tangible book value per share set forth below represents our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding on March 31, 2017.

After giving effect to the assumed issuance and sale by us of 7,614,213 shares of our common stock in this offering at an assumed public offering price of \$7.88 per share (the last reported sale price of our common stock on The NASDAQ Global Select Market on July 26, 2017), and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, the as adjusted net tangible book value as of March 31, 2017 would have been \$175.2 million, or \$3.86 per share. This represents an immediate increase in net tangible book value to existing stockholders of \$0.71 per share. The public offering price per share significantly exceeds the as adjusted net tangible book value per share. Accordingly, new investors who purchase shares of common stock in this offering will suffer an immediate dilution of their investment of \$4.02 per share. The following table illustrates this per share dilution to the new investors purchasing shares of common stock in this offering without giving effect to the option to purchase additional shares granted to the underwriters:

Assumed public offering price per share		\$ 7.88
Net tangible book value per share as of March 31, 2017	\$ 3.15	
Increase per share attributable to sale of shares of common stock in this offering	0.71	
As adjusted net tangible book value per share after this offering		3.86
Dilution per share to new investors		\$ 4.02

A \$1.00 increase (decrease) in the assumed public offering price of \$7.88 per share, which was the last reported sale price of our common stock on The NASDAQ Global Select Market on July 26, 2017, would increase (decrease) dilution per share to new investors by approximately \$0.93 (or (\$0.91)), after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

If the underwriters exercise in full their option to purchase up to \$9,000,000 of additional shares from us at an assumed public offering price of \$7.88 per share, the as adjusted net tangible book value would increase to \$3.95 per share, representing an immediate increase to existing stockholders of \$0.80 per share and an immediate dilution of \$3.93 per share to new investors. If any shares are issued upon exercise of outstanding options or warrants or are issued and sold pursuant to our sales agreement in respect of our at-the-market program, in each case at prices below the assumed public offering price, you will experience further dilution.

The above discussion and table are based on 37,749,026 shares of our common stock issued and outstanding as of March 31, 2017 and excludes the following:

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5,912,563 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2017, at a weighted-average exercise price of \$13.73 per share;

166,353 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2017;

175,000 shares of our common stock issuable upon the vesting of performance stock units outstanding as of March 31, 2017;

1,103 shares of our common stock issuable upon the exercise of warrants outstanding as of March 31, 2017, at a weighted average exercise price of \$29.00 per share;

783,864 and 216,482 additional shares of our common stock available for future issuance, as of March 31, 2017, under our 2013 stock incentive plan and our 2014 employee stock purchase plan, respectively; and

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9,442,195 shares of common stock available for sale after March 31, 2017 under our sales agreement in respect of our at-the-market program, after to giving effect to the amendment to such sales agreement dated as of July 7, 2017 (based on \$74.4 million of common stock available for sale under the sales agreement, as amended, and assuming sales at a price of \$7.88 per share, which was the closing price of our common stock on The NASDAQ Global Select Market on July 26, 2017).

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MATERIAL U.S. FEDERAL TAX CONSIDERATIONS

The following is a general discussion of the material U.S. federal income and estate tax considerations applicable to non-U.S. holders with respect to their ownership and disposition of shares of our common stock. This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock who is not for U.S. federal income tax purposes:

an individual who is a citizen or resident of the United States;

a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;

an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

a trust if (1) a U.S. court is able to exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus supplement. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a capital asset, generally property held for investment.

This discussion does not address all aspects of U.S. federal income and estate taxation, including the Medicare contribution tax, that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

insurance companies;

tax-exempt organizations;

financial institutions;

brokers or dealers in securities;

regulated investment companies;

pension plans;

controlled foreign corporations;

passive foreign investment companies;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold our common stock through partnerships or other pass-through entities for U.S. federal income tax purposes.

A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling from the IRS with respect to the U.S. federal income or estate tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

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Distributions on Our Common Stock

Distributions on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in **Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock**. Any such distributions will also be subject to the discussion below under the section titled **Withholding and Information Reporting Requirements - FATCA**.

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to withhold any U.S. federal income tax on the distribution as permitted by U.S. Treasury Regulations. If we or another withholding agent withholds tax on such a distribution, a non-U.S. holder may be entitled to a refund of the tax withheld, which the non-U.S. holder may claim by timely filing the required information with the IRS.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is generally taxed at the same graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing the required information with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

In general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other taxable disposition of shares of our common stock unless:

the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally

will be taxed at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in *Distributions on Our Common Stock* also may apply;

the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the taxable disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the taxable disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any; or

we are, or have been, at any time during the five-year period preceding such taxable disposition (or the non-U.S. holder's holding period, if shorter) a U.S. real property holding corporation, unless our common stock is regularly traded on an established securities market and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the 5-year period ending on the date of the taxable disposition or the period that the non-U.S. holder held our common stock. If we are determined to be a U.S. real property holding corporation and the foregoing exception does not apply, then a purchaser may withhold 15% of the proceeds payable to a non-U.S. holder from a sale of our common stock and the non-U.S. holder generally will be taxed on its net gain derived from the disposition at the graduated U.S. federal income tax rates applicable to United States persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals

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or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

U.S. Federal Estate Tax

Shares of our common stock that are owned or treated as owned at the time of death by an individual who is not a citizen or resident of the United States, as specifically defined for U.S. federal estate tax purposes, are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Dividends paid to non-U.S. holders subject to the U.S. withholding tax, as described above in *Distributions on Our Common Stock*, generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Withholding and Information Reporting Requirements – FATCA

The Foreign Account Tax Compliance Act, or FATCA, will impose a U.S. federal withholding tax at a rate of 30% on payments of dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to certain foreign entities, unless (i) if the foreign entity is a foreign financial institution, such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a foreign financial institution, such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury Regulations, withholding under FATCA generally (1) applies to payments of dividends on our common stock and (2) will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. Under certain circumstances, a non-U.S. holder may

be eligible for refunds or credits of the tax. Certain intergovernmental agreements between the United States and other countries may modify these rules. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

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The underwriters named below have agreed to buy, subject to the terms of the underwriting agreement, the number of shares listed opposite their names below. The underwriters are committed to purchase and pay for all of the shares if any are purchased.

Underwriter	Number of Shares
Piper Jaffray & Co.	
BMO Capital Markets Corp.	
Stifel, Nicolaus & Company, Incorporated	
SunTrust Robinson Humphrey, Inc.	
H.C. Wainwright & Co., LLC	
Total	

The underwriters have advised us that they propose to offer the shares to the public at \$ _____ per share. The underwriters propose to offer the shares to certain dealers at the same price less a concession of not more than \$ _____ per share. The underwriters may allow and the dealers may reallow a concession of not more than \$ _____ per share on sales to certain other brokers and dealers. After the offering, these figures may be changed by the underwriters.

We have granted to the underwriters an option to purchase up to an additional _____ shares of common stock from us at the same price to the public, and with the same underwriting discount, as set forth in the table above. The underwriters may exercise this option any time during the 30-day period after the date of this prospectus. To the extent the underwriters exercise the option, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares as it was obligated to purchase under the underwriting agreement.

The following table shows the underwriting fees to be paid to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the option to purchase additional shares.

	No Exercise	Full Exercise
Per share	\$	\$
Total	\$	\$

The expenses of this offering that are payable by us are estimated to be approximately \$200,000 (excluding underwriting discounts and commissions). We have also agreed to reimburse the underwriters for certain of their expenses, in an amount of up to \$30,000, incurred in connection with review by the Financial Industry Regulatory Authority, Inc. of the terms of this offering, as set forth in the underwriting agreement. Additionally, we have agreed to reimburse Piper Jaffray & Co. for certain of its expenses in an amount not to exceed \$100,000.

We have agreed to indemnify the underwriters against certain liabilities, including civil liabilities under the Securities Act, or to contribute to payments that the underwriters may be required to make in respect of those liabilities.

We and all of our directors and executive officers have agreed that, for a period of 60 days after the date of this prospectus supplement, subject to certain limited exceptions, we and they will not directly or indirectly, without the prior written consent of Piper Jaffray & Co. and BMO Capital Markets Corp., (1) offer for sale, sell, pledge, or otherwise dispose of (or enter into any transaction or device that is designed to, or could be expected to, result in the disposition by any person at any time in the future of) any shares of common stock (including, without limitation, shares of common stock that may be deemed to be beneficially owned by them in accordance with the rules and regulations of the SEC and shares of common stock that may be issued upon exercise of any options or warrants) or securities convertible into or exercisable or exchangeable for common stock, (2) enter into any swap or other derivatives transaction that transfers to another, in whole or in part, any of the economic benefits or risks of ownership of shares of common stock, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or other securities, in cash or otherwise, (3) make any demand for or exercise any right or file or cause to be filed a registration statement, including any amendments thereto, with respect to the registration of any shares of common stock or securities convertible into or exercisable or exchangeable for common stock or any of our other securities, or (4) publicly disclose the intention to do any of the foregoing.

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Piper Jaffray & Co. and BMO Capital Markets Corp., in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release common stock and other securities from lock-up agreements, Piper Jaffray & Co. and BMO Capital Markets Corp. will consider, among other factors, the holder's reasons for requesting the release, the number of shares of common stock and other securities for which the release is being requested and market conditions at the time.

To facilitate the offering, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock during and after the offering. Specifically, the underwriters may over-allot or otherwise create a short position in the common stock for their own account by selling more shares of common stock than have been sold to them by us. The underwriters may elect to cover any such short position by purchasing shares of common stock in the open market or by exercising the option granted to the underwriters to purchase additional shares. In addition, the underwriters may stabilize or maintain the price of the common stock by bidding for or purchasing shares of common stock in the open market and may impose penalty bids. If penalty bids are imposed, selling concessions allowed to syndicate members or other broker-dealers participating in the offering are reclaimed if shares of common stock previously distributed in the offering are repurchased, whether in connection with stabilization transactions or otherwise. The effect of these transactions may be to stabilize or maintain the market price of the common stock at a level above that which might otherwise prevail in the open market. The imposition of a penalty bid may also effect the price of the common stock to the extent that it discourages resales of the common stock. The magnitude or effect of any stabilization or other transactions is uncertain. These transactions may be effected on The Nasdaq Global Select Market or otherwise and, if commenced, may be discontinued at any time.

In connection with this offering, some underwriters (and selling group members) may also engage in passive market making transactions in the common stock on the Nasdaq Global Select Market. Passive market making consists of displaying bids on the Nasdaq Global Select Market limited by the prices of independent market makers and effecting purchases limited by those prices in response to order flow. Rule 103 of Regulation M promulgated by the SEC limits the amount of net purchases that each passive market maker may make and the displayed size of each bid. Passive market making may stabilize the market price of the common stock at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

Listing on The NASDAQ Global Select Market

Our common stock is listed on The NASDAQ Global Select Market under the symbol TTPH.

Stamp Taxes

If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for the issuer and its affiliates, for which they received or may in the future receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments of the issuer or its affiliates. If the underwriters or their affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of securities described in this prospectus may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

in any other circumstances that do not require the publication of a prospectus pursuant to Article 3 of the Prospectus Directive,

provided that no such offer of securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive. For purposes of this provision, the expression an offer of securities to the public in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive) and includes any relevant implementing measure in each relevant member state, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the securities as contemplated in this prospectus. Accordingly, no purchaser of the securities, other than the underwriters, is authorized to make any further offer of the securities on behalf of us or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive (Qualified Investors) that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (ii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Notice to Prospective Investors in Canada

This prospectus supplement constitutes an exempt offering document as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar regulatory authority in Canada in connection with the offer and sale of the common stock. No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this prospectus supplement or on the merits of the common stock and any representation to the contrary is an offence.

Canadian investors are advised that this prospectus supplement has been prepared in reliance on section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105). Pursuant to section 3A.3 of NI 33-105, this prospectus supplement is exempt from the requirement that the Company and the underwriter(s) provide investors with certain conflicts of interest disclosure pertaining to connected issuer and/or related issuer relationships that may exist between the Company and the underwriter(s) as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.

Resale Restrictions

The offer and sale of the common stock in Canada is being made on a private placement basis only and is exempt from the requirement that the Company prepares and files a prospectus under applicable Canadian securities laws. Any resale of the common stock acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which

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may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, pursuant to a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the common stock outside of Canada.

Representations of Purchasers

Each Canadian investor who purchases the common stock will be deemed to have represented to the Company and the underwriter(s) that the investor (i) is purchasing the common stock as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an accredited investor as such term is defined in section 1.1 of National Instrument 45-106 Prospectus Exemptions (NI 45-106) or, in Ontario, as such term is defined in section 73.3(1) of the Securities Act (Ontario); and (iii) is a permitted client as such term is defined in section 1.1 of National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations.

Taxation and Eligibility for Investment

Any discussion of taxation and related matters contained in this prospectus supplement does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the common stock and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the common stock or with respect to the eligibility of the common stock for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

Rights of Action for Damages or Rescission

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum (such as this prospectus supplement), including where the distribution involves an eligible foreign security as such term is defined in Ontario Securities Commission Rule 45-501 Ontario Prospectus and Registration Exemptions and in Multilateral Instrument 45-107 Listing Representation and Statutory Rights of Action Disclosure Exemptions, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a misrepresentation as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies, must be exercised or delivered, as the case may be, by the purchaser within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. Par la réception de ce document, chaque investisseur Canadien confirme par les présentes qu'il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d'achat ou tout avis) soient rédigés en anglais seulement.

Notice to Prospective Investors in France

This prospectus has not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Règlement Général of the Autorité des marchés financiers (the AMF) and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. Neither this prospectus nor any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription on sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

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Notice to Residents of Germany

Each person who is in possession of this prospectus is aware of the fact that no German securities prospectus (wertpapierprospekt) within the meaning of the securities prospectus act (wertpapier-prospektgesetz, or the Act) of the Federal Republic of Germany has been or will be published with respect to the shares of our common stock. In particular, each underwriter has represented that it has not engaged and has agreed that it will not engage in a public offering in the Federal Republic of Germany (öffentliches angebot) within the meaning of the Act with respect to any of the shares of our common stock otherwise than in accordance with the act and all other applicable legal and regulatory requirements.

Notice to Residents of Switzerland

The securities which are the subject of the offering contemplated by this prospectus may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. None of this prospectus or any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

None of this prospectus or any other offering or marketing material relating to the offering, us or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of the securities.

Notice to Residents of the Netherlands

The offering of the shares of our common stock is not a public offering in The Netherlands. The shares of our common stock may not be offered or sold to individuals or legal entities in The Netherlands unless (i) a prospectus relating to the offer is available to the public, which has been approved by the Dutch Authority for the Financial Markets (Autoriteit Financiële Markten) or by the competent supervisory authority of another state that is a member of the European Union or party to the Agreement on the European Economic Area, as amended or (ii) an exception or exemption applies to the offer pursuant to Article 5:3 of The Netherlands Financial Supervision Act (Wet op het financieel toezicht) or Article 53 paragraph 2 or 3 of the Exemption Regulation of the Financial Supervision Act, for instance due to the offer targeting exclusively qualified investors (gekwalificeerde beleggers) within the meaning of Article 1:1 of The Netherlands Financial Supervision Act.

Notice to Residents of Japan

The underwriters will not offer or sell any of the shares of our common stock directly or indirectly in Japan or to, or for the benefit of any Japanese person or to others, for re-offering or re-sale directly or indirectly in Japan or to any Japanese person, except in each case pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law of Japan and any other applicable laws and regulations of Japan. For purposes of this paragraph, Japanese person means any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Residents of Hong Kong

The underwriters and each of their affiliates have not (1) offered or sold, and will not offer or sell, in Hong Kong, by means of any document, any shares of our common stock other than (a) to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance; and (2) issued or had in its possession for the purposes of issue, and will not issue or have in its possession for the purposes of issue, whether in Hong Kong or elsewhere any advertisement, invitation or document relating to the shares of our common stock which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance and any rules made under that Ordinance. The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

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Notice to Residents of Singapore

This document has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this document and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares of our common stock may not be circulated or distributed, nor may shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the Securities and Futures Act), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the Securities and Futures Act or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the Securities and Futures Act.

Where shares of our common stock are subscribed or purchased under Section 275 by a relevant person which is:

- (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares of our common stock under Section 275 except:
 - (1) to an institutional investor or to a relevant person, or to any person pursuant to an offer that is made on terms that such rights or interest are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets;
 - (2) where no consideration is given for the transfer; or
 - (3) by operation of law.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Certain legal matters related to this offering will be passed upon for the underwriters by Latham & Watkins LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at www.tphase.com. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement. You may also read and copy any document we file at the SEC's Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus supplement is part of a registration statement that we filed with the SEC. This prospectus supplement and the accompanying prospectus omit some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our subsidiaries and the securities we are offering. Statements in this prospectus supplement and the accompanying prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's website.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement and the accompanying prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus are continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-35837) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive Proxy Statement on Schedule 14A filed in connection with our 2017 annual meeting of stockholders;

our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2017;

our Current Reports on Form 8-K filed with the SEC on each of January 17, 2017, February 3, 2017, April 3, 2017, June 2, 2017 June 20, 2017, July 7, 2017 and July 25, 2017; and

the description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on March 15, 2013, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or phone number:

Tetraphase Pharmaceuticals, Inc.

480 Arsenal Way

Watertown, MA 02472

Attn: Investor Relations

(617) 715-3600

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PROSPECTUS

\$100,000,000

TETRAPHASE PHARMACEUTICALS, INC.

Debt Securities

Common Stock

Preferred Stock

Warrants

We may offer and sell securities from time to time in one or more offerings of up to \$100,000,000 in aggregate offering price. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The NASDAQ Global Select Market under the symbol TTPH.

Investing in these securities involves certain risks. See Risk Factors included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 5, 2017

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a shelf registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate initial offering price of up to \$100,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading **Where You Can Find More Information** beginning on page 1 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to **we**, **our** and **us** refer, collectively, to Tetraphase Pharmaceuticals, Inc., a Delaware corporation, and its consolidated subsidiaries.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described in this prospectus and any accompanying prospectus supplement, including the risk factors set forth in our filings with the SEC that are incorporated by reference herein, including the risk factors in our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2017, before making an investment decision pursuant to this prospectus and any accompanying prospectus supplement relating to a specific offering.

Our business, financial condition and results of operations could be materially and adversely affected by any or all of these risks or by additional risks and uncertainties not presently known to us or that we currently deem immaterial that may adversely affect us in the future.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at www.tphase.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus. You may also read and copy any document we file at the SEC's Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or the SEC's website.

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INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded.

This prospectus incorporates by reference the documents listed below (File No. 000-35837) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

Our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive Proxy Statement on Schedule 14A filed in connection with our 2016 annual meeting of stockholders;

Our Quarterly Reports on Form 10-Q for the fiscal quarter ended March 31, 2017;

Our Current Report on Form 8-K filed with the SEC on each of January 17, 2017, February 3, 2017, April 3, 2017 and June 2, 2017;

The description of our common stock contained in our Registration Statement on Form 8-A filed with the SEC on March 15, 2013, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or phone number:

Tetraphase Pharmaceuticals, Inc.

480 Arsenal Way

Watertown, MA 02472

Attn: Investor Relations

(617) 715-3600

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FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Such forward-looking statements include statements about our plans and strategy for our business, the possible achievement of discovery and development goals and milestones, our future discovery and development efforts, our collaborations, our future operating results and financial position, and other objectives for future operations. We often use words such as anticipate, believe, estimate, expect, intend, may, plan, predict, project, seek, target, goal, potential, will, would, and other words and terms of similar meaning to help 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 actual results or events to differ materially from those indicated by forward-looking statements. These risks and uncertainties include those inherent in pharmaceutical research and development, such as adverse results in our drug discovery and clinical development activities, decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our product candidates, our ability to obtain, maintain and enforce intellectual property rights for our drug candidates, competition, our ability to obtain any necessary financing to conduct our planned activities, and other risk factors that are referenced in the section of any accompanying prospectus supplement entitled Risk Factors. You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. We undertake no obligation to revise or update any forward-looking statements except to the extent required by law.

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TETRAPHASE PHARMACEUTICALS, INC.

Our Business

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

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

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

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

In parallel with the clinical trials of the intravenous formulation of eravacycline, we are continuing our development program for an oral formulation of eravacycline. We recently completed phase 1 clinical testing in which the administration of oral eravacycline to patients in the fasted state resulted in increased drug exposure. Further clinical tests designed to evaluate other important variables are currently ongoing, with the goal of optimizing the oral eravacycline dosing regimen.

The FDA has granted Qualified Infectious Disease Product (QIDP) and Fast Track designations for IV and oral eravacycline for cIAI and cUTI.

In January 2016, we initiated a phase 1 clinical trial of the IV formulation of TP-271, a fully-synthetic fluorocycline being developed for respiratory disease caused by bacterial biothreat pathogens, in healthy volunteers. In February 2017, we received Qualified Infectious Disease Product and Fast Track designations from the FDA and initiated a single-ascending dose phase 1 study for the oral formulation of TP-271. In addition to eravacycline and TP-271, we

are pursuing development of TP-6076, a fully-synthetic fluorocycline derivative, as a lead candidate under our second-generation program to target unmet medical needs, including multidrug-resistant Gram-negative bacteria. In July 2016, we initiated a phase 1 clinical trial using single doses of the IV formulation of TP-6076 in healthy volunteers and have recently initiated a study using multiple doses of the IV formulation of TP-6076. Furthermore, in March 2017, we were selected to receive \$4.0 million in research funding to be received over eighteen months for TP-6076 from the 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.

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

Our principal executive offices are located at 480 Arsenal Way, Watertown, Massachusetts 02472 and our telephone number is (617) 715-3600.

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The following table sets forth, for each of the periods presented, our ratio of earnings to fixed charges and the related coverage deficiency. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus.

(In thousands)	Three Months Ended March 31,		Years Ended December 31,			
	2017	2016	2015	2014	2013	2012
Net loss	\$ (29,458)	\$ (77,480)	\$ (83,189)	\$ (66,742)	\$ (29,636)	\$ (15,087)
Ratio of earnings to fixed charges(1), (2)	N/A	N/A	N/A	N/A	N/A	N/A
Coverage deficiency	\$ (29,458)	\$ (77,480)	\$ (83,189)	\$ (66,742)	\$ (29,636)	\$ (15,087)

- (1) For purposes of calculating the ratio of earnings to fixed charges, earnings consist of net income (loss) from continuing operations before income taxes, plus fixed charges. Fixed charges include interest expense and the estimated interest component of rental expense.
- (2) We did not record earnings for the three months ended March 31, 2017 or for the years ended December 31, 2016, 2015, 2014, 2013 and 2012. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include working capital and capital expenditures, research and development expenses, including clinical trial costs, general and administrative expenses, potential acquisition of, or investment in, companies, technologies, products or assets that complement our business, and repayment and refinancing of debt. We may temporarily invest the net proceeds in investment-grade, interest-bearing securities until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to the Company, we, our, and us in this section, we mean Tetraphase Pharmaceuticals, Inc., excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

None of the indentures will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsubordinated general obligations and will rank pari passu with our other unsubordinated obligations. The subordinated debt securities will constitute our subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading **Certain Terms of the Subordinated Debt Securities Subordination**. The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiaries unless such subsidiaries expressly guarantee such debt securities.

The debt securities will be our unsecured obligations unless otherwise specified in the applicable prospectus supplement. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and/or free writing prospectus will include any additional or different terms of the debt securities being offered, including the following terms:

the title and type of the debt securities;

whether the debt securities will be senior or subordinated debt securities, and, with respect to debt securities issued under the subordinated indenture the terms on which they are subordinated;

the aggregate principal amount of the debt securities;

the price or prices at which we will sell the debt securities;

the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;

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the rate or rates, if any, per year, at which the debt securities will bear interest, or the method of determining such rate or rates;

the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates and the related record dates;

the right, if any, to extend the interest payment periods and the duration of that extension;

the manner of paying principal and interest and the place or places where principal and interest will be payable;

provisions for a sinking fund, purchase fund or other analogous fund, if any;

any redemption dates, prices, obligations and restrictions on the debt securities;

the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;

any conversion or exchange features of the debt securities;

whether and upon what terms the debt securities may be defeased;

any events of default or covenants in addition to or in lieu of those set forth in the indenture;

whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;

whether the debt securities will be guaranteed as to payment or performance;

whether the debt securities will be secured by any collateral and, if so, a general description of the collateral and the terms and provisions of such collateral, security, pledge or other related agreements;

any material tax implications of the debt securities; and

any other material terms of the debt securities.

When we refer to principal in this section with reference to the debt securities, we are also referring to premium, if any.

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement.

We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

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Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust (subject to certain exceptions provided for in the senior indenture);

the successor entity assumes our obligations on the senior debt securities and under the senior indenture;

immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and

certain other conditions are met.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture for any series of senior debt securities:

failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 90 days (or such other period as may be specified for such series);

failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);

default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90

days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;

certain events of bankruptcy or insolvency, whether or not voluntary; and

any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs with respect to us and is continuing, the entire principal amount of and accrued interest, if any, on each series of senior debt securities then outstanding shall become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

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Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive an existing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

the holder gives the trustee written notice of a continuing event of default;

the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;

the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;

the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and

during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security to receive payment of the principal of and interest, if any, on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

we pay or cause to be paid, as and when due and payable, the principal of and any interest on all senior debt securities of such series outstanding under the senior indenture; or

all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year) and we deposit in trust a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and discharge and covenant defeasance will apply to any series of debt securities issued under the indentures.

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Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series (called "legal defeasance") if certain conditions are met, including the following:

We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.

We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change of current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called "covenant defeasance"). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities without the consent of any holder:

to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;

to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;

to comply with the requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;

to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;

to provide for or add guarantors with respect to the senior debt securities of any series;

to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;

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to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;

to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms, purposes of issue, authentication and delivery of any series of senior debt securities;

to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or

to make any change that does not adversely affect the rights of any holder in any material respect. Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of all series affected by the amendment or modification (voting together as a single class); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

extends the final maturity of any senior debt securities of such series;

reduces the principal amount of any senior debt securities of such series;

reduces the rate or extends the time of payment of interest on any senior debt securities of such series;

reduces the amount payable upon the redemption of any senior debt securities of such series;

changes the currency of payment of principal of or interest on any senior debt securities of such series;

reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;

waives an uncured default in the payment of principal of or interest on the senior debt securities (except in the case of a rescission of acceleration as described above);

changes the provisions relating to the waiver of past defaults or changes or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;

modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification; or

reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies, amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

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The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such principal, premium or interest became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal of or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term *senior indebtedness* of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

all of the indebtedness of that person for money borrowed;

all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;

all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;

all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and

all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated debt indenture.

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DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, our bylaws and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and bylaws, which are filed as exhibits to the registration statement, of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 125,000,000 shares of common stock, par value \$0.001 per share, and 5,000,000 shares of preferred stock, par value \$0.001 per share, all of which preferred stock is undesignated. The following description of our capital stock and provisions of our restated certificate of incorporation and bylaws are summaries and are qualified by reference to our certificate of incorporation and bylaws. Copies of these documents are filed with the SEC as exhibits to our Quarterly Report on Form 10-Q filed with the SEC on May 13, 2013.

Common Stock

As of June 12, 2017, we had outstanding 38,722,519 shares of common stock, held of record by 8 stockholders. We believe that the number of beneficial owners of our common stock at that date was substantially greater.

Holders of our 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 our 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 Anti-Takeover Effects of Delaware Law and Our Charter and Bylaws, (3) in the future to the extent that we have 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 our stockholders at any meeting, shall be decided by the affirmative vote of our 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 our board of directors, subject to any preferential dividend rights of our outstanding preferred stock.

In the event of our 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 our outstanding preferred stock.

Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Listing on The NASDAQ Global Market

Our common stock is listed on The NASDAQ Global Market under the symbol TTPH.

Authorized but Unissued Shares

The authorized but unissued shares of common stock are available for future issuance without stockholder approval, subject to any limitations imposed by the NASDAQ Listing Rules. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued

and unreserved common stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Preferred Stock

Under the terms of our certificate of incorporation, our 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. Our 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.

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If we decide to issue any preferred stock pursuant to this prospectus, we will describe in a prospectus supplement the specific terms of the preferred stock, including, if applicable, the following:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date, and method of calculation for dividends;

whether dividends will be cumulative and, if cumulative, the date from which dividends will accumulate;

the relative ranking and preference of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs

the procedures for any auction and remarketing;

the provisions for a sinking fund;

the provisions for redemption or repurchase and any restrictions on our ability to exercise those redemption and repurchase rights;

the listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock and, if convertible, the conversion price, or how it will be calculated, and the conversion period;

whether the preferred stock will be exchangeable into debt securities and, if exchangeable, the exchange price, or how it will be calculated, and the exchange period;

voting rights of the preferred stock;

preemptive rights;

restrictions on transfer, sale or other assignment;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

The preferred stock could have other rights, including economic rights that are senior to our common stock that could adversely affect the market value of our common stock. The issuance of the preferred stock may also have the effect of delaying, deferring or preventing a change in control of us without any action by the shareholders.

Anti-Takeover Effects of Delaware Law and Our Charter and Bylaws

Delaware law, our certificate of incorporation and our bylaws contain provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. 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 us to first negotiate with our board of directors.

Staggered Board; Removal of Directors

Our certificate of incorporation and bylaws divide our 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 our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. The classification of our 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 our company.

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Stockholder Action by Written Consent; Special Meetings

Our certificate of incorporation provides that any action required or permitted to be taken by our 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. Our certificate of incorporation and bylaws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our chief executive officer or our board of directors.

Advance Notice Requirements for Stockholder Proposals

Our 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 our 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 our 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 our 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 our outstanding voting securities. These provisions could also discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our 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, which we refer to as the DGCL, is applicable to us. 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 our 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 our 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 our outstanding voting stock, or

the interested stockholder owns at least 85% of our outstanding voting stock as a result of a transaction in which such stockholder acquired 15% or more of our 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. Our bylaws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders of at least 75% of the votes that all of our 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 of our 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 our certificate of incorporation described above under Staggered Board; Removal of Directors and Stockholder Action by Written Consent; Special Meetings.

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DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock or debt securities, or any combination of those securities, as described in the applicable prospectus supplement. The applicable prospectus supplement will also describe the following terms of any warrants:

the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;

whether the warrants are to be sold separately or with other securities;

whether the warrants will be issued in definitive or global form or in any combination of these forms;

any applicable material U.S. federal income tax consequences;

the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;

the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;

the designation and terms of any equity securities purchasable upon exercise of the warrants;

the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the preferred stock with which the warrants are issued and, the number of warrants issued with each security;

the number of shares of common stock or preferred stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;

any redemption or call provisions; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

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FORMS OF SECURITIES

Each debt security and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depository or its nominee as the owner of the debt securities or warrants represented by these global securities. The depository maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities and warrants in the form of one or more fully registered global securities that will be deposited with a depository or its nominee identified in the applicable prospectus supplement and registered in the name of that depository or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depository for the global security, the nominees of the depository or any successors of the depository or those nominees.

If not described below, any specific terms of the depository arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depository arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depository or persons that may hold interests through participants. Upon the issuance of a global security, the depository will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depository, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depository, or its nominee, is the registered owner of a global security, that depository or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture or warrant agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depository for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of

a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture or warrant agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants, represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent or any other agent of ours, or any agent of any trustee or warrant agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

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We expect that the depository for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depository. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in street name, and will be the responsibility of those participants.

If the depository for any of the securities represented by a global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act, and a successor depository registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depository. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depository gives to the relevant trustee, warrant agent or other relevant agent of ours or theirs. It is expected that the depository's instructions will be based upon directions received by the depository from participants with respect to ownership of beneficial interests in the global security that had been held by the depository.

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PLAN OF DISTRIBUTION

We may sell securities:

to or through underwriters;

to or through brokers or dealers;

through agents;

directly to one or more purchasers in negotiated sales or competitively bid transactions; or

through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or

through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from time to time in one or more transactions:

at a fixed price, or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

the name of the agent or any underwriters;

the public offering or purchase price and the proceeds we will receive from the sale of the securities;

any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;

all other items constituting underwriting compensation;

any discounts and commissions to be allowed or re-allowed or paid to dealers; and

any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

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Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in three business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than three scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, to the extent applicable, the aggregate maximum discount, commission or agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

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LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

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\$60,000,000

Tetraphase Pharmaceuticals, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

Piper Jaffray

BMO Capital Markets

Stifel

SunTrust Robinson Humphrey

H.C. Wainwright & Co.

July , 2017