UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

December 13, 2012

Via E-mail
Guy Macdonald
President and Chief Executive Officer
Tetraphase Pharmaceuticals, Inc.
480 Arsenal Street, Suite 110
Watertown, MA 02472

Re: Tetraphase Pharmaceuticals, Inc.
Confidential Draft Registration Statement on Form S-1
Submitted November 16, 2012
CIK No. 0001373707

Dear Mr. Macdonald:

We have reviewed your confidential draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended confidential draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended confidential draft registration statement or filed registration statement, we may have additional comments.

General

1. Please submit all exhibits as soon as practicable. We may have further comments upon examination of these exhibits.

2. Please provide us proofs of all graphic, visual or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

3. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications. Similarly, please supplementally provide us with any research reports about you that are published or

distributed in reliance upon Section 2(a)(3) of the Securities Act of 1933 added by Section 105(a) of the Jumpstart Our Business Startups Act by any broker or dealer that is participating or will participate in your offering.

4. We will deliver comments to your confidential treatment request under separate cover.

Prospectus Summary, page 1

5. We note your disclosure on page 2 that the U.S. government awarded you contracts for "potential funding of over $100 million" for the development of your antibiotic compounds. We also note your disclosure that you may receive up to $67 million in funding under the BARDA contract and $36 million under your NIAID contract. However, based upon your disclosures on page 100, it appears that you are only entitled to receive funding of approximately $39.8 million, $13.3 million and $980,000 pursuant to the BARDA contract, NIAID Grant, and NIAID Contract under the related CUBRC subcontracts. Please revise your disclosure here and throughout the prospectus as necessary to accurately state the actual potential funding available under your contacts instead of the overall amounts awarded.

Risk Factors, page 12

"Raising additional capital may cause dilution to our stockholders…," page 14

6. We note your disclosure that BARDA and NIAID are not obligated to provide continued funding beyond current-year amounts from Congressionally approved annual appropriations. Please revise your disclosure here and as applicable throughout the prospectus to identify the current-year amounts BARDA and NIAID are obligated to provide under your agreements.

"If we are sued for infringing intellectual property rights of third parties…," page 32

7. If you have received any notice of infringement from any third party please expand your disclosure to disclose the notice and the circumstances relating thereto.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Financial Overview
Research and Development Expenses, page 55

8. Please revise your tabular disclosure to include the research and development costs incurred during to date.

Stock-Based Compensation, page 58

9. We have reviewed your disclosure and have the following comments:

- Please tell us why the volatility used to value the common stock differs substantially from that used for stock-based compensation expense in 2011 and 2012. For instance the October 2011 common stock valuation used a 49% volatility whereas the volatility used to fair value stock options ranged from 63% to 67%
- Disclose the intrinsic value of the outstanding vested and unvested options based on the estimated IPO price and the options outstanding as of the most recent balance-sheet date presented in the registration statement.
- Please note that we may have additional comments related to the valuations when the price range for the offering becomes known. Once known, please provide quantitative and qualitative disclosures explaining the difference between the estimated offering price and the fair value of each equity issuance.

Business, page 74

Phase 1 clinical trials of intravenous formulation, page 82

10. You disclose on page 83 that "We have not conducted a head-to-head comparison of eravacycline and tigecycline in a clinical trial, but have compared the published data from Pfizer's Phase 1 clinical trials of tigecycline to the data from our Phase 1 clinical trials of eravacycline." Your disclosure then presents your conclusions based on this comparison. Please expand your disclosure to provide the data comparisons underlying your conclusions.

Eravacycline Phase 2 Trial Design, page 84

11. Please revise your narrative disclosure to account for the difference between the total patients enrolled (143) and the total patients randomized (139). Further, to the extent that these patients were excluded from the treatment groups analyzed, please describe why they were excluded and why they were not similarly excluded from the patient demographics analysis.

12. You disclose that the 1.5 mg/kg does group exhibited slightly higher APACHE scores than the other treatment groups. Please describe what effect, if any, that may have had on the results or a comparison of the results.

Future Clinical Plans, page 89

13. If known, please disclose where you intend to conduct your planned Phase 3 clinical program. If the location has not yet been determined, you may disclose the location generally, for example, in the United States.

Government Contracts, page 100
Eravacycline, page 100

14. Please expand you description of the BARDA five-year contract and your related subcontract relationship with CUBRC to more clearly describe the flow of funds from the development, manufacturing and clinical evaluation activities. Further, please indicate why your relationship with BARDA is structured in this manner in light of the fact that you will receive significantly less funding, $39.8 million as opposed to $67 million, by using this structure.

15. Please expand your disclosure to further describe the division of responsibilities and activities between you and CUBRC pursuant to the collaboration subcontract.

16. Please expand your disclosure to include any material performance, development or reporting obligations associated with the BARDA contract or CUBRC subcontract.

TP-271, page 100

17. Please expand your disclosure to include any material performance, development or reporting obligations associated with the NIAID Grant, NIAID Contract or CUBRC subcontract.

Recent Changes in the Regulatory Landscape, page 102

18. Please revise your disclosure to indicate how the FDA's published draft guidance in February and September 2012 and the potential revision of the FDA suggested primary efficacy endpoints for cIAI and cUTI trials compare with the primary endpoint used for your eravacycline Phase 2 trial. As applicable, disclose whether the FDA's draft guidance will affect your ability to rely on the data from the Phase 2 trial. Please also discuss whether finalization of the FDA guidance will delay or affect in any way your planned Phase 3 clinical program.

U.S. Government Regulation, page 102
Marketing Approval, page 104

19. We note that you have conducted certain of your eravacycline trials in India. Please expand your discussion of the FDA approval process to include a discussion of regulations governing reliance on data from clinical trials conducted outside the United States submitted as the basis for an NDA.

Employees, page 110

20. Please expand your disclosure to indicate whether your employees are dedicated to a particular development program – BARDA, NIAID or eravacycline, and, if so, disclose the number of employees dedicated to each development program.

Management, page 111

21. We note your disclosure on page 99 regarding a consulting agreement with your scientific founder, Dr. Andrew Myers. Disclose the material terms of this agreement and file a copy of this agreement as an exhibit to the registration statement. Alternatively, please provide us with your analysis as to why this consulting agreement is not required to be filed.

Director Compensation, page 118

22. We note your disclosure that Dr. Gage and Mr. Bohlin received annual cash retainers and options to purchase common stock in return for their service as directors in 2011. Please revise your prospectus to include tabular disclosure highlighting all compensation provided to directors in the last completed fiscal year.

Description of Capital Stock, page 132

23. Please expand your disclosure to indicate the voting threshold for matters besides election of directors that may be voted on by stockholders.

Shares Eligible for Future Sale, page 136

24. Once available, please file copies of each of the lock-up agreements.

Index to Consolidated Financial Statements
Notes to Consolidated Financial Statements
Note 2. Summary of Significant Accounting Policies
Revenue Recognition, page F-12

25. Please revise your revenue recognition policy to further clarify how revenue is recognized in accordance with ASC 912-605-25. Further please clarify for us and to the extent necessary your disclosure, how your model accounts for the provision in the contract indicating that the parties are not obligated to provide funding beyond the initial periods or current year amounts.

Note 8. Stockholders' Equity
Conversion, page F-21

26. Please disclose the "certain dilutive events" that change the conversion rate of the preferred stock issuances.

Note 9. Stock-Based Compensation, page F-22

27. You disclose that the volatility is 63% for 2010, and a range of 63% - 67% for 2011. Please address the following:
    - Please explicitly disclose whether you used implied volatility, historical volatility, or a combination of both. Refer to Question Five of ASC 718-10-S99.
    - For periods where you have provided a range of volatilities, please tell us why you do not disclose the weighted-average expected volatility. Refer to ASC 718-10-50-2-f-2ii.

General

If you intend to respond to these comments with an amended draft registration statement, please submit it and any associated correspondence in accordance with the guidance we provide in the Division's October 11, 2012 announcement on the SEC website at http://www.sec.gov/divisions/corpfin/cfannouncements/drsfilingprocedures101512.htm.

Please keep in mind that we may publicly post filing review correspondence in accordance with our December 1, 2011 policy (http://www.sec.gov/divisions/corpfin/cfannouncements/edgarcorrespondence.htm). If you intend to use Rule 83 (17 CFR 200.83) to request confidential treatment of information in the correspondence you submit on EDGAR, please properly mark that information in each of your confidential submissions to us so we do not repeat or refer to that information in our comment letters to you.

You may contact Tabatha Akins, Staff Accountant, at (202) 551-3658 or Joel Parker, Accounting Branch Chief, at (202) 551-3651if you have questions regarding comments on the financial statements and related matters. Please contact Karen Ubell, Staff Attorney, at (202) 551-3873, Bryan Pitko, Staff Attorney, at (202) 551-3203 or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ Bryan J. Pitko

Jeffrey P. Riedler
Assistant Director

cc: Via E-mail
Stuart M. Falber, Esq.
Wilmer Cutler Pickering Hale and Dorr LLP