# TETRAPHASE PHARMACEUTICALS INC

## FORM 10-Q
(Quarterly Report)

Filed 08/02/17 for the Period Ending 06/30/17

| | |
|---|---|
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| SIC Code | 2834 - Pharmaceutical Preparations |
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| Fiscal Year | 12/31 |

# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, DC 20549**

# FORM 10-Q

**(Mark One)**

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

**For the quarterly period ended June 30, 2017**

**or**

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

**For the transition period from _____to _____**

**Commission File Number: 001-35837**

# TETRAPHASE PHARMACEUTICALS, INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **20-5276217** |
|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(I.R.S. Employer Identification No.)** |

**480 Arsenal Way**
**Watertown, MA**
**(Address of principal executive offices)**

**02472**
**(Zip Code)**

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

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

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

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

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☒ |
| Non-accelerated filer | ☐ (Do not check if a smaller reporting company) | Smaller reporting company | ☐ |
| | | Emerging growth company | ☐ |

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

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

As of August 2, 2017 there were 51,053,448 shares of the registrant's common stock, par value $0.001 per share, outstanding.

**TETRAPHASE PHARMACEUTICALS, INC.**

**FORM 10-Q**

**FOR THE QUARTER ENDED JUNE 30, 2017**

**TABLE OF CONTENTS**


| | | Page No. |
|---|---|---|
| **PART I. FINANCIAL INFORMATION** | | 3 |
| **Item 1.** | **Financial Statements (Unaudited)** | 3 |
| | Condensed Consolidated Balance Sheets as of June 30, 2017 and December 31, 2016 | 3 |
| | Condensed Consolidated Statements of Operations and Comprehensive Loss for the Three and Six Months Ended June 30, 2017 and 2016 | 4 |
| | Condensed Consolidated Statements of Cash Flows for the Six Months Ended June 30, 2017 and 2016 | 5 |
| | Notes to Condensed Consolidated Financial Statements | 6 |
| **Item 2.** | **Management's Discussion and Analysis of Financial Condition and Results of Operations** | 13 |
| **Item 3.** | **Quantitative and Qualitative Disclosures About Market Risk** | 22 |
| **Item 4.** | **Controls and Procedures** | 22 |
| **PART II. OTHER INFORMATION** | | 24 |
| **Item 1.** | **Legal Proceedings** | 24 |
| **Item 1A.** | **Risk Factors** | 24 |
| **Item 6.** | **Exhibits** | 52 |
| | **Signatures** | 51 |

## PART I — FINANCI AL INFORMATION

**Item 1. Financial Statements**

### TETRAPHASE PHARMACEUTICALS, INC.

**Condensed Consolidated Balance Sheets**
*(In thousands, except par value amounts)*
*(Unaudited)*

| | June 30, 2017 | December 31, 2016 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 118,214 | $ 142,086 |
| Accounts receivable | 2,682 | 1,789 |
| Prepaid expenses and other current assets | 5,117 | 6,582 |
| Total current assets | 126,013 | 150,457 |
| Property and equipment, net | 1,529 | 1,054 |
| Restricted cash | 199 | 199 |
| Other assets | — | - |
| Total assets | $ 127,741 | $ 151,710 |
| **Liabilities and stockholders' equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 6,918 | $ 2,555 |
| Accrued expenses | 12,124 | 7,685 |
| Deferred revenue | 1,548 | 1,255 |
| Total current liabilities | 20,590 | 11,495 |
| Other long term liabilities | 134 | 162 |
| Commitments and contingencies | | |
| Stockholders' equity: | | |
| Preferred stock, par value $0.001 per share; 5,000 shares authorized; no shares issued and outstanding | — | — |
| Common stock, par value $0.001 per share; 125,000 shares authorized; 40,012 and 36,942 shares issued and outstanding at June 30, 2017 and December 31, 2016, respectively | 40 | 37 |
| Additional paid-in capital | 515,378 | 487,148 |
| Accumulated deficit | (408,401) | (347,132) |
| Total stockholders' equity | 107,017 | 140,053 |
| Total liabilities and stockholders' equity | $ 127,741 | $ 151,710 |

*See accompanying notes to condensed consolidated financial statements*

**TETRAPHASE PHARMACEUTICALS, INC.**

**Condensed Consolidated Statements of Operations and Comprehensive Loss**
*(In thousands, except per share data)*
*(Unaudited)*

| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| **Revenues** | $ 1,586 | $ 1,243 | $ 3,071 | $ 3,205 |
| **Operating expenses** | | | | |
| Research and development | 28,513 | 13,746 | 54,460 | 27,269 |
| General and administrative | 5,065 | 4,759 | 10,198 | 10,012 |
| Total operating expenses | 33,578 | 18,505 | 64,658 | 37,281 |
| Loss from operations | (31,992) | (17,262) | (61,587) | (34,076) |
| **Other income (expense)** | | | | |
| Other income (expense), net | 181 | 94 | 318 | 167 |
| **Net loss** | $ (31,811) | $ (17,168) | $ (61,269) | $ (33,909) |
| **Net loss per share-basic and diluted** | $ (0.83) | $ (0.47) | $ (1.63) | $ (0.93) |
| **Weighted-average number of common shares used in net loss per share-basic and diluted** | 38,273 | 36,629 | 37,686 | 36,614 |
| **Comprehensive loss** | $ (31,811) | $ (17,168) | $ (61,269) | $ (33,909) |

*See accompanying notes to condensed consolidated financial statements*

**TETRAPHASE PHARMACEUTICALS, INC.**

**Condensed Consolidated Statements of Cash Flows**
*(In thousands)*
*(Unaudited)*

| | Six Months Ended June 30, | |
|---|---|---|
| | 2017 | 2016 |
| **Operating activities** | | |
| Net loss | $ (61,269) | $ (33,909) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation and amortization | 201 | 136 |
| Stock-based compensation expense | 6,236 | 6,985 |
| Changes in operating assets and liabilities: | | |
| Accounts receivable | (893) | 1,169 |
| Prepaid expenses and other assets | 1,465 | (1,543) |
| Accounts payable | 4,363 | (315) |
| Accrued expenses and other liabilities | 4,411 | (350) |
| Deferred revenue | 293 | 285 |
| Net cash used in operating activities | (45,193) | (27,542) |
| **Investing activities** | | |
| Purchases of property and equipment | (676) | (175) |
| Net cash used in investing activities | (676) | (175) |
| **Financing activities** | | |
| Proceeds from sale of common stock, net of issuance costs | 21,703 | — |
| Proceeds from issuance of stock under stock plans | 294 | 116 |
| Net cash provided by financing activities | 21,997 | 116 |
| Net decrease in cash and cash equivalents | $ (23,872) | $ (27,601) |
| Cash and cash equivalents at beginning of period | 142,086 | 205,912 |
| Cash and cash equivalents at end of period | $ 118,214 | $ 178,311 |

*See accompanying notes to condensed consolidated financial statements*

## 1. Organization and Operations

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

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

The Company has incurred annual net operating losses in every year since its inception. As of June 30, 2017, the Company had incurred losses since inception of $408.4 million. The Company has not generated any product revenues and has financed its operations primarily through public offerings and private placements of its equity securities, debt financings and funding from the United States government.

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

The Company believes that its existing cash and cash equivalents, together with net proceeds from its underwritten public offering, will enable it to fund its operating expenses and capital expenditure requirements into at least early 2019, which it believes would allow it to submit a new drug application ("NDA") and marketing authorization application ("MAA") for IV eravacycline for the treatment of complicated intra-abdominal infections ("cIAI"), obtain top-line complicated urinary tract infection ("cUTI") data from its IGNITE3 clinical study, to submit a supplemental new drug application ("sNDA") to the United States Food and Drug Administration ("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. The Company may never be profitable even if it is successful in launching eravacycline for one or more indications. Until such time as the Company is profitable, if ever, the Company will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

## 2. Summary of Significant Accounting Policies

### *Basis of Presentation*

The accompanying interim condensed consolidated financial statements are unaudited. These unaudited financial statements have been prepared in accordance with the rules and regulations of the United States Securities and Exchange Commission ("SEC") for interim financial information. Accordingly, they do not include all of the information and footnotes required by United States generally accepted accounting principles ("GAAP") for complete financial statements. These unaudited interim condensed consolidated financial statements should be read in conjunction with the audited consolidated financial statements and the accompanying notes for the year ended December 31, 2016 contained in the Company's annual report on Form 10-K filed with the SEC on March 13, 2017 (the "2016 Form 10-K"). The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and, in the opinion of management, reflect all adjustments (consisting of normal recurring adjustments) necessary to state fairly the Company's financial position as of June 30, 2017 and the results of operations and comprehensive loss and cash flows for the three and six months ended June 30, 2017 and 2016. Interim operating results for the three and sixth months ended June 30, 2017 are not necessarily indicative of the results that may be expected for future interim periods or for the fiscal year ending December 31, 2017.

The December 31, 2016 condensed consolidated balance sheet included herein was derived from audited consolidated financial statements, but does not include all disclosures including notes required by GAAP for complete financial statements.

***Use of Estimates***

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

***Principles of Consolidation***

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

***Going Concern Assessment***

Accounting Standards Update ("ASU") No. 2014-15, Presentation of Financial Statements - Going Concern, requires management to evaluate the company's ability to continue as a going concern one year beyond the filing date of the given financial statements. This evaluation requires management to perform two steps. First, management must evaluate whether there are conditions and events that raise substantial doubt about the entity's ability to continue as a going concern. Second, if management concludes that substantial doubt is raised, management is required to consider whether it has plans in place to alleviate that doubt. Disclosures in the notes to the financial statements are required if management concludes that substantial doubt exists or that its plans alleviate the substantial doubt that was raised. Based on a detailed cash forecast incorporating current development activities and related spending plans, the Company expects its cash to last more than one year beyond the date that the financial statements were issued. Based on this analysis, no additional disclosures are required.

***Recently Issued Accounting Pronouncements***

In May 2014, the Financial Accounting Standard Board ("FASB") issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* , which supersedes all existing revenue recognition requirements, including most industry-specific guidance. The new standard requires a company to recognize revenue when it transfers goods or services to customers in an amount that reflects the consideration that the company expects to receive for those goods or services. In August 2015, the FASB issued ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date* , which delayed the effective date of the new standard from January 1, 2017 to January 1, 2018. The FASB also agreed to allow entities to choose to adopt the standard as of the original effective date. The FASB has subsequently issued ASU 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net)* ; ASU 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing* ; ASU 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients* ; and ASU 2016-20, *Technical Corrections and Improvements to Topic 606, Revenue from Contracts with Customers* . The Company is currently evaluating the potential impact that these updates may have on its financial position, results of operations and cash flows, specifically the impact on its revenue produced via its contracts with the Biomedical Advanced Research and Development Authority ("BARDA"), the National Institute of Allergy and Infectious Diseases ("NIAID") and CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance. The Company is currently completing contract reviews and evaluating whether these contracts are subject to Topic 606. The Company expects these contract reviews to be completed in the third quarter. The Company plans to use the modified retrospective method of adoption, to be effective January 1, 2018.

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

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15") . This new standard provides guidance to ensure consistency in how transactions are reflected in the statement of cash flows. ASU 2016-15 will be effective for the Company for annual periods beginning after December 15, 2017. The Company is currently evaluating the potential impact that this standard may have on its statements of cash flows.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* ("ASU 2016-18") . ASU 20 16-18 clarifies how entities should present restricted cash and restricted cash equivalents in the statement of cash flows. The guidance will be applied retrospectively and will be effective for the Company for annual and interim periods beginning after De cember 15, 2017. The Company is currently evaluating the potential impact that this standard may have on its financial position, statements of operations and cash flows.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting* ("ASU 2017-09"). The new standard provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The new standard will be effective for the Company on January 1, 2018. The Company is currently evaluating the potential impact that this standard may have on its financial position, statements of operations and cash flows.

***Recently Adopted Accounting Standards***

In March 2016, the FASB issued ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, forfeiture rates, and classification on the statement of cash flows. The new guidance is effective for fiscal years beginning after December 15, 2016, including interim periods within those annual reporting periods. The Company adopted ASU No. 2016-09 as of January 1, 2017. As a result of adopting ASU No. 2016-09, the Company elected to recognize share-based award forfeitures only as they occur rather than by applying an estimated forfeiture rate as previously required. ASU No. 2016-09 requires that this change be applied using a modified-retrospective transition method by means of a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year in which the guidance is adopted. The Company did not make an adjustment to retained earnings as the amount was immaterial to the financial statements.

**3. Fair Value of Financial Instruments**

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

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

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

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

Financial instruments measured at fair value as of June 30, 2017 and December 31, 2016 are classified below based on the three fair value hierarchy tiers described above (in thousands):

| | | Fair Value Measurements at Reporting Date Using | | |
|---|---|---|---|---|
| | Balance | Level 1 | Level 2 | Level 3 |
| **June 30, 2017** | | | | |
| Cash and money market funds | $ 118,214 | $ 118,214 | $ — | $ — |
| **December 31, 2016** | | | | |
| Cash and money market funds | $ 142,086 | $ 142,086 | $ — | $ — |

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

**4. Net Loss per Common Share**

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of Common Stock outstanding for the period, without consideration for common stock equivalents. The Company's potentially dilutive shares, which include outstanding stock options, unvested restricted stock units and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The amounts in the table below were excluded from the calculation of net loss per share, due to their anti-dilutive effect:

| | June 30, | |
|---|---|---|
| | 2017 | 2016 |
| Warrants | 1,103 | 1,103 |
| Unvested restricted stock units | 340,616 | 475,100 |
| Outstanding stock options | 6,087,428 | 4,221,517 |
| Totals | 6,429,147 | 4,697,720 |

**5. Significant Agreements and Contracts**

***License Agreement***

In August 2006, the Company entered into a license agreement for certain intellectual property with Harvard University ("Harvard"). Under the license agreement, as of June 30, 2017, the Company has paid Harvard an aggregate of $4.4 million in upfront license fees and development milestone payments, and has issued 31,379 shares of common stock to Harvard. For each product covered by the license agreement, the Company is obligated to make certain payments totaling up to approximately $15.1 million upon achievement of certain development and regulatory milestones and to pay additional royalties on net sales of such product.

***Government Grant and Contracts***

*BARDA Contract for Eravacycline*

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

In connection with the BARDA Contract, in February 2012, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC Inc. ("CUBRC"), an independent, not for profit, research corporation that specializes in U.S. government-based contracts, which is also the direct recipient of the BARDA Contract. This subcontract, which currently expires in May 2018, granted the Company initial funding of up to $41.6 million, reflecting the portion of the BARDA Contract funding that may be paid to the Company for its activities. The total committed funding under the BARDA subcontract has increased since the initial award in 2012 due to BARDA's exercise of options to continue to fund specific work performed by the Company related to eravacycline.

Although the BARDA Contract and the Company's subcontract with CUBRC under the BARDA Contract have terms which currently expire in May 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to the Company. Committed funding from CUBRC under the Company's BARDA subcontract is for up to $41.6 million through May 10, 2018, the current contract end date, as a result of the exercise of several options by BARDA under the BARDA Contract. Total funds of $33.7 million had been received by the Company through June 30, 2017 under this contract. During the three months ended June 30, 2017 and 2016, the Company recognized revenue of $1.0 million and $0.5 million, respectively, from the Company's subcontract under the BARDA Contract. During the six months ended June 30, 2017 and 2016, the Company recognized revenue of $1.5 million and $1.6 million, respectively, from the Company's subcontract under the BARDA Contract.

*NIAID Grant and Contract for TP-271*

The Company has received funding for its phase 1 compound TP-271 under two awards from NIAID for the development, manufacturing and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia:

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

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

In connection with the NIAID Contract, in October 2011, the Company entered into a cost-plus-fixed-fee subcontract with CUBRC, the direct recipient of the NIAID Contract, which subcontract currently expires i n December 2018 under which the Company may receive funding of up to approximately $15.1 million, reflecting the portion of the NIAID Contract funding that may be paid to the Company for its activities. The total potential committed funding under the NIAID subcontract has increased since the initial award in 2011 due to NIAID's exercise of options to continue to fund specific work performed by the Company related to TP-271.

Although the NIAID Contract and the Company's subcontract with CUBRC under the NIAID Contract have terms which currently expire on December 31, 2018, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond the respective expiration dates. To the extent that NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to the Company. As of June 30, 2017, committed funding from CUBRC under the Company's subcontract with respect to the NIAID Contract is $15.1 million, of which $11.5 million had been received through June 30, 2017. In addition, the NIAID Grant and the company's subaward from CUBRC expired on May 31, 2017. Committed funding from CUBRC under the Company's subaward with respect to the NIAID Grant is $0.9 million, of which $0.9 million had been received through June 30, 2017.

During the three months ended June 30, 2017 and 2016, the Company recognized revenue of $0.2 million and $0.7 million, respectively, from the Company's subcontract under the NIAID Contract. During the three months ended June 30, 2017 and 2016, the Company recognized revenue of $3,000 and $43,000, respectively, from the Company's subaward under the NIAID Grant. During the six months ended June 30, 2017 and 2016, the Company recognized revenue of $1.2 million and $1.6 million, respectively, from the Company's subcontract under the NIAID Contract. During the six months ended June 30, 2017 and 2016, the Company recognized revenue of $9,000 and $63,000, respectively, from the Company's subaward under the NIAID Grant.

*CARB-X Award for TP-6076*

In March 2017, CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance, selected the Company to receive up to $4.0 million in research funding over eighteen months for TP-6076. In connection with this funding, the Company entered into a cost reimbursement Sub-Award Agreement (the "Sub-award Agreement") with the Trustees of Boston University, the administrator of the program. The Company began recognizing revenue from the Sub-Award Agreement in April 2017. During the three months ended June 30, 2017, the Company recognized revenue of $0.4 million under this Sub-Award Agreement. This Sub-Award Agreement will fund certain activities through the end of 2018. This Sub-Award Agreement can be terminated for convenience at any time, subject to 30 days written notice.

**6. Accrued Expenses**

Accrued expenses at June 30, 2017 and December 31, 2016 consisted of the following (in thousands):

| | June 30, 2017 | December 31, 2016 |
|---|---|---|
| Clinical trial related | $ 5,941 | $ 1,129 |
| Drug supply and development | 2,412 | 2,698 |
| Salaries and benefits | 1,986 | 2,498 |
| Professional fees | 1,104 | 965 |
| Preclinical | 216 | 163 |
| Other | 465 | 232 |
| Total | $ 12,124 | $ 7,685 |

**7. Stock-Based Compensation**

In January 2017, the number of shares available for issuance under the Tetraphase Pharmaceuticals, Inc. Stock Incentive Plan (the "2006 Plan") and the amended 2013 Stock Incentive Plan ("2013 Plan") was increased by approximately 1.5 million shares as a result of the automatic increase provision of the 2013 Plan. As of June 30, 2017, the total number of shares of common stock available for issuance under the 2013 Plan was approximately 0.6 million.

***Stock-Based Compensation Expense***

During the three and six months ended June 30, 2017, and 2016, the Company recognized the following stock-based compensation expense (in thousands):

| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| Research and development | $ 1,596 | $ 1,089 | $ 3,174 | $ 3,480 |
| General and administrative | 1,564 | 1,720 | 3,062 | 3,505 |
| Total | $ 3,160 | $ 2,809 | $ 6,236 | $ 6,985 |

| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| Stock options | $ 2,946 | $ 2,482 | $ 5,815 | $ 5,887 |
| Restricted stock units | 185 | 285 | 368 | 991 |
| Employee stock purchase plan | 29 | 42 | 53 | 107 |
| Total | $ 3,160 | $ 2,809 | $ 6,236 | $ 6,985 |

***Stock Options***

The following table summarizes the stock option activity for the six months ended June 30, 2017 :

| | Shares | Weighted-Average Exercise Price |
|---|---|---|
| Outstanding at December 31, 2016 | 4,066,411 | $ 18.42 |
| Granted | 2,172,750 | $ 4.18 |
| Exercised | (46,502) | $ 3.03 |
| Forfeited | (105,231) | $ 16.34 |
| Outstanding at June 30, 2017 | 6,087,428 | $ 13.49 |
| Exercisable at June 30, 2017 | 2,584,305 | $ 16.80 |

As of June 30, 2017, there was $21.8 million of total unrecognized stock-based compensation cost related to employee unvested stock options granted under the 2006 Plan and the 2013 Plan. The Company expects to recognize that cost over a remaining weighted-average period of 2.7 years.

***Restricted Stock Units***

In January 2016, the Company granted additional restricted stock units to employees. These restricted stock units vest in annual increments over three years, subject to continued employment with the Company and had a grant date fair value of $8.47 per share, which was the closing price of the Company's common stock on the date of grant.

In January 2017, the Company issued 175,000 restricted stock units with service and performance conditions to certain employees, none of which vested during the six months ended June 30, 2017. Vesting of these awards is contingent on the occurrence of certain milestone events and fulfillment of any remaining service condition. As a result, the related compensation cost is recognized as an expense when achievement of the milestone is considered probable.

The following table summarizes the restricted stock activity for the six months ended June 30, 2017:

| | Shares | Weighted-Average Grant Date Fair Value |
|---|---|---|
| Unvested at December 31, 2016 | 254,378 | $ 8.47 |
| Granted | 175,000 | $ 3.83 |
| Forfeited | (3,990) | $ 8.47 |
| Vested/Released | (84,772) | $ 8.47 |
| Unvested at June 30, 2017 | 340,616 | $ 6.09 |

As of June 30, 2017, there was $1.7 million of total unrecognized stock-based compensation expense related to restricted stock units granted under the 2013 Plan. The expense is expected to be recognized over a weighted-average period of 2.1 years.

***Employee stock purchase plan***

Under the Company's 2014 ESPP, an aggregate of 300,000 shares of common stock have been reserved for issuance pursuant to purchase rights granted to the Company's employees. As of June 30, 2017, 171,697 shares remained available for issuance. During the six months ended June 30, 2017 and 2016, 44,785 shares and 21,178 shares of common stock were issued under the 2014 ESPP, respectively.

**8. Equity**

On January 17, 2017, the Company entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement"), with Cantor Fitzgerald & Co. as sales agent ("Cantor"). On July 7, 2017, the Company entered into an amendment to the Sales Agreement to increase the maximum aggregate offering price of the shares of common stock that it may issue and sell from time to time under the Sales Agreement from $40,000,000 to $80,000,000.

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

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

As of June 30, 2017, the Company had sold an aggregate of 2,894,156 shares of common stock under the Sales Agreement, at an average selling price of approximately $7.81 per share for aggregate gross proceeds of $22.6 million and net proceeds of $21.7 million after deducting the sales commissions and offering expenses. As of August 1, 2017, an additional 1,041,294 shares were sold under the original and amended Sales Agreements subsequent to June 30, 2017, for aggregate gross proceeds of $8.0 million and net proceeds of $7.8 million after deducting sales commissions and offering expenses, which will be recognized during the third quarter of 2017. As of August 1, 2017, $49.4 million of common stock remained available to be sold under the amended Sales Agreement, subject to certain conditions specified therein.

**9. Subsequent Events**

On August 2, 2017, the Company sold 10,000,000 shares of common stock in an underwritten public offering at an offering price to the public of $6.50 per share, resulting in net proceeds to the Company of $60.9 million after deducting underwriting discounts and commissions of $3.9 million and offering costs of $0.2 million. In connection with the offering, the Company granted the underwriters an option to purchase 1,500,000 additional shares on the same terms and conditions as the offering.

**Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations**

*The interim financial statements included in this quarterly report on Form 10-Q and this Management's Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the financial statements and notes thereto for the year ended December 31, 2016, and the related Management's Discussion and Analysis of Financial Condition and Results of Operations, contained in our annual report on Form 10-K filed with the United States Securities and Exchange Commission, or the SEC, on March 13, 2017, which we refer to as our annual report. In addition to historical information, this discussion and analysis contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements are subject to risks and uncertainties, including those set forth in Part II — Other Information, Item 1A. Risk Factors below and elsewhere in this report that could cause actual results to differ materially from historical results or anticipated results.*

**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.

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.

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 authorizat ion 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 complicated urinary tract infections, or 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 approxi mately 1,000 adult patients, who will be randomized 1:1 to receive eravacycline or ertapenem for a minim um 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.

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 commenced business operations in July 2006. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our proprietary chemistry technology, identifying potential product candidates and undertaking preclinical studies and clinical trials of our product candidates. To date, we have not generated any product revenue and have primarily financed our operations through public offerings and private placements of our equity securities, debt financings and funding from the United States government. As of June 30, 2017, we had received an aggregate of $482.2 million in net proceeds from the issuance of equity securities and borrowings under debt facilities and an aggregate of $46.1 million from government grants and contracts. As of June 30, 2017, our principal source of liquidity was cash and cash equivalents, which totaled $118.2 million.

As of June 30, 2017, we had an accumulated deficit of $408.4 million. Our net losses were $31.8 million and $17.2 million for the three months ended June 30, 2017 and 2016, respectively. Our net losses were $61.3 million and $33.9 million for the six months ended June 30, 2017 and 2016, respectively. We expect that our expenses will increase as we continue development of eravacycline, seek marketing approval for eravacycline, conduct pre-commercialization activities for eravacycline , pursue development of eravacycline for additional indications, manufacture drug product for our clinical and pre-clinical trials, conduct our phase 1 clinical trial of TP-271 in healthy volunteers, and our phase 1 clinical trial of TP-6076 in healthy vol unteers and satisfy our obligations under our license agreement with Harvard University, or Harvard. If we obtain marketing approval of eravacycline, we also expect to incur significant sales, marketing, distribution and manufacturing expenses. Furthermore , we expect to incur ongoing research and development expenses relating to our product candidates other than eravacycline and that our general and administrative costs will increase as we grow and continue to operate as a public company, and comply with in creased disclosure requirements since we are no longer an emerging growth company.

On August 2, 2017, the Company sold 10,000,000 shares of common stock in an underwritten public offering at an offering price to the public of $6.50 per share, resulting in net proceeds to the Company of $60.9 million after deducting underwriting discounts and commissions of $3.9 million and offering costs of $0.2 million. In connection with the offering, the Company granted the underwriters an option to purchase 1,500,000 additional shares on the same terms and conditions as the offering.

We believe that our cash and cash equivalents, together with the net proceeds from our underwritten public offering, will enable us to fund our operating expenses and capital expenditure requirements at least into at least early 2019, which we believe will allow us to obtain top-line data from IGNITE3 and submit the NDA and MAA for IV eravacycline for the treatment of cIAI, to submit an sNDA 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 will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. Moreover, we will need to generate significant revenue to achieve profitability, and we may never do so.

**Financial overview**

***Contract and Grant Revenue***

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

- We have received funding for our lead product candidate, eravacycline, under an award from the Biomedical Advanced Research and Development Authority, or BARDA, an agency of the U.S. Department of Health and Human Services. In January 2012, BARDA awarded CUBRC an initial five-year contract, which has been extended, that provides for up to a total of $67.3 million in funding for the development, manufacturing and clinical evaluation of eravacycline for the treatment of disease caused by bacterial biothreat pathogens. We refer to this contract as the BARDA Contract. The funding under the BARDA Contract is also being used for the development, manufacturing and clinical evaluation of eravacycline to treat certain infections caused by life-threatening multidrug-resistant bacteria. We refer to this contract as the BARDA Contract.
- We have received funding for our phase 1 compound TP-271 under two awards from the National Institute of Allergy and Infectious Diseases, or NIAID, a division of National Institutes of Health, for the development, manufacturing and clinical evaluation of TP-271 for respiratory diseases caused by biothreat and antibiotic-resistant public health pathogens, as well as bacterial pathogens associated with community-acquired bacterial pneumonia:
    - a grant awarded to CUBRC in July 2011 that provided up to a total of approximately $2.9 million through May 31, 2017, which we refer to as the NIAID Grant; and
    - a contract awarded to CUBRC in September 2011 that provides up to a total of approximately $35.8 million in funding through December 31, 2018, which we refer to as the NIAID Contract.

We are collaborating with CUBRC on these grants and contracts, because when we initially decided to seek government funding, we recognized that we did not have any expertise in bidding for, administrating or managing government-funded contracts. CUBRC serves as the prime contractor under the BARDA Contract, the NIAID Grant and the NIAID Contract, primarily carrying out

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

- In connection with the BARDA Contract, in February 2012, we entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on May 10, 2018 under which we may receive funding of up to approximately $41.6 million, reflecting the portion of the BARDA Contract funding that may be paid to us for our activities.
- In connection with the NIAID Contract, in October 2011, we entered into a cost-plus-fixed-fee subcontract with CUBRC which currently expires on December 31, 2018 under which we may receive funding of up to approximately $15.1 million, reflecting the portion of the NIAID Contract funding that may be paid to us for our activities.
- In connection with the NIAID Grant, in November 2011, CUBRC awarded us an initial 55-month, no-fee subaward which was extended and expired on May 31, 2017 under which we received funding of up to approximately $0.9 million, reflecting the portion of the NIAID Grant funding that was paid to us for our activities.

Although the BARDA Contract and our subcontract with CUBRC under the BARDA Contract have terms which currently expire on May 10, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is up to $41.6 million from the initial contract date through May 10, 2018, of which $33.7 million had been received through June 30, 2017.

Similarly, although the NIAID Contract and our subcontract with CUBRC under the NIAID Contract have terms which currently expire on December 31, 2018, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond December 31, 2018. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subcontract with respect to the NIAID Contract is for up to $15.1 million, from the initial contract date through December 31, 2018, of which $11.5 million had been received through June 30, 2017.

In March 2017, CARB-X, an international public-private partnership focused on advancing new antimicrobial products to address the threat of antibiotic resistance, selected us to receive up to $4.0 million in research funding over 18 months for TP-6076. In connection with this funding, the Company entered into a cost reimbursement Sub-Award Agreement with the Trustees of Boston University, the administrator of the program. The Company began recognizing revenue from the Sub-Award Agreement in April 2017. Of the $4.0 million in committed funding none had been received through June 30, 2017. Although the Sub-Award Agreement has a term which currently expires on December 31, 2018, the project can be terminated for convenience at any time.

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

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

***Research and Development Expenses***

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

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

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

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

We track external development expenses and personnel expense on a program-by-program basis and allocate common expenses, such as scientific consultants and laboratory supplies, to each program based on the personnel resources allocated to such program. Expenses related to facilities, consulting, travel, conferences, stock-based compensation and depreciation are not allocated to a program and are separately classified as other research and development expenses. The following table summarizes our research and development expenses on a program-specific basis for the three and six months ended June 30, 2017 and 2016:

| | Three Months Ended June 30, | | Six Months Ended June 30, | |
|---|---|---|---|---|
| | 2017 | 2016 | 2017 | 2016 |
| | (in thousands) | | | |
| Eravacycline | $ 22,361 | $ 6,970 | $ 42,792 | $ 12,860 |
| TP-6076 | 920 | 1,967 | 1,650 | 3,121 |
| BARDA Contract | 925 | 653 | 1,344 | 1,321 |
| CARB-X Award | 398 | - | 398 | - |
| NIAID Contract and NIAID Grant | 58 | 197 | 959 | 1,202 |
| Other development programs | 706 | 489 | 981 | 1,100 |
| Other research and development | 3,145 | 3,470 | 6,336 | 7,665 |
| Total research and development expenses | $ 28,513 | $ 13,746 | $ 54,460 | $ 27,269 |

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

As of June 30, 2017, we had incurred an aggregate of $223.6 million in research and development expenses related to the development of eravacycline, and $32.4 million in research and development expenses related to the development of eravacycline that were funded under the BARDA Contract. We expect that our research and development expenses will increase in 2017 compared to 2016 as we conduct IGNITE3 and complete IGNITE4 , incur nonclinical, regulatory and drug manufacturing costs in support of NDA-related activities, pursue development of eravacycline for additional indications, advance our other product candidates and satisfy our obligations under our license agreement with Harvard.

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

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

***General and Administrative Expense s***

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

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

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

***Interest Income***

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

**Critical Accounting Policies and Significant Judgments and Estimates**

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to revenue recognition, accrued clinical expenses, and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that we and our management believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

There have been no significant changes to our critical accounting policies since the beginning of this fiscal year. Our critical accounting policies are described under *Management's Discussion and Analysis of Financial Condition and Results of Operations* in our annual report, filed on form 10-K with the SEC on March 13, 2017 for the year ended December 31, 2016.

**Results of Operations**

***Comparison of the Three Months Ended June 30, 2017 and 2016***

The following table summarizes the results of our operations for the three months ended June 30, 2017 and 2016, together with the changes in those items in dollars and as a percentage:

| | Three Months Ended June 30, | | Increase/ | |
|---|---|---|---|---|
| | 2017 | 2016 | (decrease) | % |
| | (in thousands) | | | |
| Revenues | $ 1,586 | $ 1,243 | $ 343 | 28% |
| Operating expenses: | | | | |
| Research and development | 28,513 | 13,746 | 14,767 | 107% |
| General and administrative | 5,065 | 4,759 | 306 | 6% |
| Total operating expenses | 33,578 | 18,505 | 15,073 | 81% |
| Loss from operations | (31,992) | (17,262) | (14,730) | 85% |
| Other income | 181 | 94 | 87 | 93% |
| Net loss | $ (31,811) | $ (17,168) | $ (14,643) | 85% |

*Revenue from U.S. Government Contracts and Grants*

The following table sets forth our contract and grant revenue for the three months ended June 30, 2017 and 2016:

| | Three Months Ended June 30, | | Increase/ | |
|---|---|---|---|---|
| | 2017 | 2016 | (decrease) | % |
| | (in thousands) | | | |
| Revenues | | | | |
| BARDA Contract | $ 988 | $ 483 | $ 505 | 105% |
| NIAID Contract | 178 | 718 | (540) | (75)% |
| CARB-X Award | 417 | — | 417 | n/a |
| NIAID Grant | 3 | 42 | (39) | (93)% |
| | $ 1,586 | $ 1,243 | $ 343 | 28% |

Contract and grant revenue was $1.6 million for the three months ended June 30, 2017 compared to $1.2 million for the three months ended June 30, 2016, an increase of $0.3 million, or 28%. This increase was due to the scope and timing of activities conducted under our subcontract with respect to the BARDA Contract and the start of activities under the CARB-X Award, offset in part by a decrease in clinical development activities with respect to TP-271 under our subcontract with respect to the NIAID Contract.

*Research and Development Expenses*

Research and development expenses for the three months ended June 30, 2017 were $28.5 million compared to $13.7 million for the three months ended June 30, 2016, an increase of $14.8 million, or 107%. This increase was primarily due to costs associated with conducting IGNITE3 and IGNITE4 during the three months ended June 30, 2017.

*General and Administrative Expenses*

General and administrative expenses for the three months ended June 30, 2017 were $5.1 million compared to $4.8 million for the three months ended June 30, 2016, an increase of $0.3 million, or 6%. This increase was primarily due to an increase in legal and patent costs offset in part by a decrease in stock-based compensation expense.

*Other Income*

The increase in other income was driven by implementation of a new cash sweep account and improved overall yields on our money market funds for the three months ended June 30, 2017 as compared to the same period in 2016.

***Comparison of the Six Months Ended June 30, 2017 and 2016***

The following table summarizes the results of our operations for the six months ended June 30, 2017 and 2016, together with the changes in those items in dollars and as a percentage:

| | Six Months Ended June 30, | | Increase/ | |
|---|---|---|---|---|
| | 2017 | 2016 | (decrease) | % |
| | (in thousands) | | | |
| Revenues | $ 3,071 | $ 3,205 | $ (134) | (4)% |
| Operating expenses: | | | | |
| Research and development | 54,460 | 27,269 | 27,191 | 100% |
| General and administrative | 10,198 | 10,012 | 186 | 2% |
| Total operating expenses | 64,658 | 37,281 | 27,377 | 73% |
| Loss from operations | (61,587) | (34,076) | (27,511) | 81% |
| Other income | 318 | 167 | 151 | 90% |
| Net loss | $ (61,269) | $ (33,909) | $ (27,360) | 81% |

*Revenue from U.S. Government Contracts and Grants*

The following table sets forth our contract and grant revenue for the six months ended June 30, 2017 and 2016:

| | Six Months Ended June 30, | | Increase/ | |
|---|---|---|---|---|
| | 2017 | 2016 | (decrease) | % |
| | (in thousands) | | | |
| Revenues | | | | |
| BARDA Contract | $ 1,452 | $ 1,574 | $ (122) | (8)% |
| NIAID Contract | 1,193 | 1,568 | (375) | (24)% |
| CARB-X Award | 417 | — | 417 | n/a |
| NIAID Grant | 9 | 63 | (54) | (86)% |
| | $ 3,071 | $ 3,205 | $ (134) | (4)% |

Contract and grant revenue was $3.1 million for the six months ended June 30, 2017 compared to $3.2 million for the six months ended June 30, 2016, a decrease of $0.1 million, or 4%. This decrease was primarily due to the scope and timing of activities conducted under our subcontracts with respect to the BARDA and NIAID offset by an increase in activities related to our award with CARB-X during the six months ended June 30, 2017 as compared to the six months ended June 30, 2016.

*Research and Development Expenses*

Research and development expenses for the six months ended June 30, 2017 were $54.5 million compared to $27.3 million for the six months ended June 30, 2016, an increase of $27.2 million, or 100%. This increase was primarily due to costs associated with conducting IGNITE3 and IGNITE4 during the six months ended June 30, 2017.

*General and Administrative Expenses*

General and administrative expenses for the six months ended June 30, 2017 were $10.2 million compared to $10.0 million for the six months ended June 30, 2016, an increase of $0.2 million, or 2%. This increase was primarily due to an increase in legal and patent costs offset in part by a decrease in stock-based compensation expense.

*Other Income*

The increase in other income was driven by implementation of a new cash sweep account and improved overall yields on our money market funds for the six months ended June 30, 2017 as compared to the same period in 2016.

**Liquidity and Capital Resources**

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

Since our inception, we have funded our operations principally through the receipt of funds from public offerings and private placements of equity securities, debt financings and contract research funding and research grants from the United States government.

As of June 30, 2017, we had cash and cash equivalents of approximately $118.2 million. We invest cash in excess of immediate requirements in accordance with our investment policy, primarily with a view to liquidity and capital preservation. As of June 30, 2017, our funds were held in cash and money market funds.

On January 17, 2017, we entered into a Controlled Equity Offering Sales Agreement, or sales agreement, with Cantor Fitzgerald & Co., as sales agent, or Cantor. On July 7, 2017, we entered into an amendment to the sales agreement, or the amended sales agreement. In accordance with the terms of the sale agreement, we may offer and sell through Cantor, from time to time, shares of our common stock up to an aggregate offering price of $80,000,000 through an "at-the-market" offering program. As of June 30, 2017, we had sold 2,894,156 shares under the Agreement at an average price of $7.81 per share and we had received aggregate cash proceeds of $21.7 million, after deducting the sales commissions and offering expenses.

As of August 1, 2017, an additional 1,041,294 shares were sold under the original and amended Sales Agreements subsequent to June 30, 2017, for aggregate gross proceeds of $8.0 million and net proceeds of $7.8 million after deducting sales commissions and offering expenses, which will be recognized during the third quarter of 2017.

On August 2 , 2017, we sold 10,000,000 shares of common stock in a n underwritten public offering at a n offering price to the public of $6.50 per share, resulting in net proceeds to the Company of $60.9 million after deducting underwriting discounts and commissions of $3.9 million and offering costs of $0.2 million. In connection with the offering, we granted the underwriters an option to purch ase 1,500,000 additional shares on the same terms and conditions as the offering.

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

| | Six Months Ended June 30, | |
|---|---|---|
| | 2017 | 2016 |
| **Cash Flows from Operations:** | | |
| Net cash used in operating activities | $ (45,193) | $ (27,542) |
| Net cash used in investing activities | (676) | (175) |
| Net cash provided by financing activities | 21,997 | 116 |
| Net (decrease) increase in cash and cash equivalents | $ (23,872) | $ (27,601) |

*Cash Flows from Operating Activities* . The $17.7 million increase in cash used in operating activities for the six months ended June 30, 2017, compared to the six months ended June 30, 2016, was primarily due to increased spending on IGNITE 3 and IGNITE 4 clinical trials offset in part by changes in working capital.

*Cash Flows from Investing Activities.* The $0.5 million increase in cash used in investing activities for the six months ended June 30, 2017, compared to the six months ended June 30, 2016, was due to purchases of property and equipment to facilitate our increased research and development activities.

*Cash Flows from Financing Activities.* The $21.9 million increase in cash provided by financing activities for the six months ended June 30, 2017, compared to the six months ended June 30, 2016 was primarily due to sales of common stock under our amended sales agreement with Cantor Fitzgerald.

***Operating Capital Requirements***

We expect to incur operating losses for at least the next several years as we continue development of eravacycline, seek marketing approval for eravacycline, manufacture drug product for our clinical and pre-clinical trials, conduct pre-commercialization activities for eravacycline, conduct our phase 1 clinical trials of TP-271 in healthy volunteers, and our phase 1 clinical trials of TP-6076 in healthy volunteers and satisfy our obligations under our license agreement with Harvard. We may not be able to complete the development and initiate commercialization of eravacycline or our other product candidates if, among other things, our preclinical research and clinical trials are not successful, our manufacturing efforts are not successful, the FDA or the EMA does not approve eravacycline or our other product candidates when we expect, or at all, or funding under the NIAID Contract or the BARDA Contract is discontinued.

The Company believes that its existing cash and cash equivalents, together with net proceeds from its underwritten public offering, will enable it to fund its operating expenses and capital expenditure requirements into at least early 2019, which we believe will allow us to obtain top-line date from IGNITE3 and submit the NDA and MAA for IV eravacycline for the treatment of cIAI, to submit an sNDA 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. We may never be profitable even if we are successful in launching eravacycline for one or more indications. Until such time as we become profitable, if ever, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

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

- the timing and costs of our clinical development program for eravacycline;
- manufacturing costs related to regulatory filings and anticipated commercial launch;
- the initiation, progress, timing, costs and results of preclinical studies and clinical trials for our other product candidates and potential product candidates;
- the amount of funding that we receive under our subcontracts under the BARDA and NIAID Contracts, and the activities funded under the BARDA Contract, the NIAID Contract and our agreement with CARB-X;

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

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

**Off-Balance Sheet Arrangements**

We do not have any off-balance sheet arrangements.

**Contractual Obligations**

During the six months ended June 30, 2017, there were no material changes to our contractual obligations and commitments outside the ordinary course of business from those disclosed in our annual report, filed on form 10-K with the SEC on March 13, 2017 for the year ended December 31, 2016.

***Recent Accounting Pronouncements***

Refer to Note 2, *Summary of Significant Accounting Policies* , in the accompanying notes to the condensed consolidated financial statements.

**Item 3. Quantitati ve and Qualitative Disclosures about Market Risk**

There have not been any material changes to our exposure to market risk during the six months ended June 30, 2017. For additional information regarding market risk, refer to the *Qualitative and Quantitative Disclosures About Market Risk* section of our annual report.

**Item 4. Controls and Procedures**

**Evaluation of Disclosure Controls and Procedures**

The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, refers to controls and procedures that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and

communicated to the company's management, including its principal executive and principal financial officers, or per sons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achiev ing their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Senior Vice President of Finance (Principal Financial Officer), has evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2017, the end of the period covered by this quarterly report on Form 10-Q. Based upon such evaluation, our Chief Executive Officer and Principal Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

**Changes in Internal Control over Financial Reporting**

There was no change in our internal control over financial reporting that occurred during the period covered by this quarterly report on Form 10-Q that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

## PART II – OTHE R INFORMATION

### Item 1. Legal Proceedings

In January 2016 and March 2016, two securities class action lawsuits were filed against us, our chief executive officer, our former chief operating officer and our former chief financial officer, in the United States District Court for the District of Massachusetts. In May 2016, the court consolidated the two lawsuits and appointed lead plaintiffs and lead counsel. The lead plaintiffs filed a consolidated amended complaint in July 2016 and filed a second consolidated amended complaint in August 2016. The second amended complaint is brought on behalf of an alleged class of those who purchased our common stock between March 5, 2015 and September 8, 2015, and alleges claims arising under Sections 10 and 20 of the Exchange Act of 1934, as amended. The complaint generally alleges that the defendants violated the federal securities laws by, among other things, mak ing material misstatements or omissions concerning IGNITE2. The complaint seeks, among other relief, unspecified compensatory damages, attorneys' fees, and costs. In October 2016, we filed a motion to dismiss the second amended complaint in its entirety, which plaintiffs have opposed. Our motion to dismiss was granted by the United States District Court for the District of Massachusetts in May 2017. In July 2017 plaintiffs appealed this decision to the United States Court of Appeals for the First Circuit. We believe we have valid defenses against these claims, and will engage in a vigorous defense of such litigation.

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

### Item 1A. RISK FACTORS

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

#### Risks Relating to Our Financial Position and Need for Additional Capital

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

We have incurred annual net operating losses in every year since our inception. Our net loss was $61.3 million for the six months ended June 30, 2017, $77.5 for the year ended December 31, 2016 and $83.2 million for the year ended December 31, 2015. As of June 30, 2017, we had an accumulated deficit of $408.4 million. We have not generated any product revenues and have financed our operations primarily through the public offering and private placements of our equity securities, debt financings and revenue from U.S. government grants and contract awards. We have not completed development of any product candidate and have devoted substantially all of our financial resources and efforts to research and development, including preclinical and clinical development.

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

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

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

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

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

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

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

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

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

We believe that our existing cash and cash equivalents, together with net proceeds from our underwritten public offering, will enable us to fund our operating expenses and capital expenditure requirements into at least early 2019, which we believe will allow us to obtain top-line data from IGNITE3 and to submit an NDA and MAA for IV eravacycline for the treatment of cIAI, to submit an sNDA 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. As a result, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

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

Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

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

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

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

Currently, our only external source of funds is funding under subcontracts awarded to us by CUBRC pursuant to government contracts from BARDA and NIAID, and an award from CARB-X. Although the BARDA contract and our subcontract with CUBRC under the BARDA contract have terms which currently expire on May 10, 2018, BARDA is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond current-year amounts from congressionally approved annual appropriations. To the extent that BARDA ceases to provide funding of the program to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our BARDA subcontract is for up to $41.6 million from the initial contract date through May 10, 2018, of which $33.7 million had been received through June 30, 2017.

Similarly, although the NIAID contract and our subcontract with CUBRC under the NIAID contract have terms which currently expire on December 31, 2018, NIAID is entitled to terminate the project for convenience at any time, and is not obligated to provide continued funding beyond December 31, 2018. To the extent NIAID ceases to provide funding of the programs to CUBRC, CUBRC has the right to cease providing funding to us. Committed funding from CUBRC under our subcontract with respect to the NIAID contract is for up to $15.1 million, of which $11.5 million had been received through June 30, 2017. In addition, the NIAID Grant and our subaward from CUBRC expired on May 31, 2017. Committed funding from CUBRC under our subaward with respect to the NIAID Grant was $0.9 million from the initial grant date through May 31, 2017, of which $0.9 million had been received through June 30, 2017.

Similarly, although the CARB-X A ward has a term which currently expires on December 31, 2018, CARB-X is entitled to terminate the project for convenience at any time. Commit ted funding from the CARB-X A ward is for up to $4.0 million from the initial award date through December 31, 2018, of which none had been received through June 30, 2017.

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

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

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

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

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

**Risks Related to Product Development and Commercialization**

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

We currently have no products approved for sale and have invested a significant portion of our efforts and financial resources in the development of eravacycline for use as a first-line empiric monotherapy for the treatment of multidrug-resistant infections. In July 2017, we announced positive top-line data from IGNITE4. We plan to use the results from IGNITE1 and IGNITE4 to support submission of an NDA for IV eravacycline for the treatment of cIAI. We are also conducting our IGNITE3 phase 3 clinical trial evaluating the safety and efficacy of eravacycline with IV administration for the treatment of cUTI. If IGNITE3 is successful, we plan to use the results from IGNITE3 to support submission of an sNDA for IV eravacycline for the treatment of cUTI, assuming approval first of IV eravacycline for the treatment of cIAI.

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

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

- successful outcome of discussions with regulatory agencies regarding our planned marketing applications;
- successful completion and favorable results of IGNITE3, and any additional clinical trials involving eravacycline that we may conduct;
- timely filing for and receipt of marketing approvals from applicable regulatory authorities;
- establishment of arrangements with third-party manufacturers to obtain manufacturing supply;

- obtainment and maintenance of patent and trade secret protection and regulatory exclusivity;
- protection of our rights in our intellectual property portfolio;
- successful manufacturing of commercial scale batches of eravacycline;
- commercial launch of eravacycline, if and when approved, whether alone or in collaboration with others;
- acceptance of eravacycline, if and when approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- a continued acceptable safety profile of eravacycline following approval.

Successful development of the oral formulation of eravacycline and of eravacycline for additional indications will be subject to these same risks.

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

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

We are not permitted to commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA or in other countries without obtaining approvals from comparable foreign regulatory authorities, such as the EMA, and we may never receive such approvals. We must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We have not previously submitted an NDA to the FDA, an MAA to the EMA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates.

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

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

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. In addition, in the case of our clinical trials, results may differ on the basis of the type of bacteria with which patients are infected. We cannot be certain that IGNITE3 or other clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

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

- clinical trials of our product candidates may produce unfavorable or inconclusive results;

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

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

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

Our product development costs will also increase if we experience delays in testing or marketing approvals and we may be required to obtain additional funds to complete clinical trials. We cannot be certain that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of eravacycline or any other product candidate.

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

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

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

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

Serious adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, an institutional review board, or regulatory authorities to interrupt, delay or halt our clinical trials and could result in a more restrictive label, the imposition of distribution or use restrictions or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. If eravacycline or any of our other product candidates are associated with serious adverse events or undesirable side effects or have properties that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound. In our clinical trials of eravacycline, some treatment-related adverse events have been reported. The most common treatment-related adverse events observed in clinical trials of eravacycline have been nausea and emesis. Additional adverse events, undesirable side effects or other unexpected properties of eravacycline or any of our other product candidates could arise or become known either during clinical development or, if approved, after the approved product has been marketed. If such an event occurs during development, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, eravacycline or our other product candidates. If such an event occurs after eravacycline or such other product candidates are approved, a number of potentially significant negative consequences may result, including:

- regulatory authorities may withdraw the approval of such product;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- regulatory authorities may require one or more postmarketing studies;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating revenues from the sale of our products and harm our business and results of operations.

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

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

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

In addition, the potential market opportunity for eravacycline is difficult to estimate. Our estimates of the potential market opportunity are predicated on several key assumptions such as industry knowledge, third-party research reports and other surveys. While we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain and the reasonableness of these assumptions has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, then the actual market for eravacycline could be smaller than our estimates of the potential market opportunity. If the actual market for eravacycline is smaller than we expect, or if the product fails to achieve an adequate level of acceptance by physicians, health care payors and patients, our product revenue may be limited and it may be more difficult for us to achieve or maintain profitability.

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

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

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

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

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

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

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

The development and commercialization of new drug products is highly competitive. We face competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to eravacycline and our other product candidates that we may seek to develop or commercialize in the future. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of multidrug-resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than any product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete or noncompetitive.

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

There are also a number of products currently in phase 3 development by third parties to treat multidrug-resistant infections, including meropenem/vaborbactam, which is being developed by The Medicines Company as Vavomere, plazomicin, which is being developed by Achaogen, Inc., imipenem/relebactam, which is being developed by Merck & Co., Inc., and cefiderocol, which is being

developed by Shionogi. Some of these companies may obtain marketing approval from the FDA or comparable foreign regulatory authorities for their product candidates more rapi dly than we do, which could result in our competitors establishing a strong market position before we are able to enter the market.

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

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

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

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

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

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Moreover, obtaining coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based in part on existing reimbursement amounts for lower cost drugs or may be bundled into the payments for other services.

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

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

We face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we commercially sell eravacycline or any other product candidate that we develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product

liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, str ict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercia lization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

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

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

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

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

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

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

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

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

**Risks Related to Our Dependence on Third Parties**

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

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

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

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or in compliance with applicable regulatory requirements;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

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

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

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

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

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

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

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

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

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

Our reliance on these third parties for clinical development activities limits our control over these activities but we remain responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards. For example, notwithstanding the obligations of a contract research organization for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may

be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will det ermine that any of our clinical trials comply with cGCPs. We are also required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

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

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

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

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

If any of our product candidates are approved by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

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

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

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

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

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

Our development of eravacycline for the treatment of disease caused by bacterial biothreat pathogens and certain life-threatening multidrug-resistant bacteria is currently being partially funded through a subcontract with funding from BARDA. In addition, our development of TP-271 is being funded through a subcontract from the NIH's NIAID division. Contracts and grants funded by the U.S. government and its agencies, including our agreements funded by BARDA and NIAID, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including, but not limited to powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason;
- reduce or modify the government's obligations under such agreements without the consent of the other party;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- suspend the contractor or grantee from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;
- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- control and potentially prohibit the export of products;

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

We may not have the right to prohibit the U.S. government from using certain technologies developed by us, and we may not be able to prohibit third-party companies, including our competitors, from using those technologies in providing products and services to the U.S. government. The U.S. government generally takes the position that it has the right to royalty-free use of technologies that are developed under U.S. government contracts.

In addition, government contracts and grants, and subcontracts and subawards awarded in the performance of those contracts and grants, normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions.

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

**Risks Related to Our Intellectual Property**

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary chemistry technology and product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. The patent application and approval process is expensive and time consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

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

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings which may be brought by us related to our patent rights.

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

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

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

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

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

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

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

***If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.***

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

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

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

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

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

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

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

***If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.***

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

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

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

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

**Risks Related to Regulatory Approval and Other Legal Compliance Matters**

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

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

We are not permitted to market our product candidates in the United States until we receive approval of a n NDA from the FDA. We have not submitted an NDA for any of our product candidates. An NDA must include extensive preclinical and clinical data and supporting information to establish the product candidate's safety and efficacy for each desired indication. The NDA must also include significant information regarding the chemistry, manufacturing and controls for the product candidate. Obtaining approval of an NDA is a lengthy, expensive and uncertain process. The FDA review process typically takes years to co mplete. The FDA has substantial discretion in the approval process and may refuse to accept for filing any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies or additional inf ormation regarding chemistry, manufacturing and controls for the product candidate. For example, our progress in the development and commercialization of eravacycline has been significantly delayed as a result of the failure of eravacycline to achieve the primary endpoint in IGNITE2 and may be further delayed as a result of additional clinical outcomes, manufacturing process challenges or other unforeseeable causes. Foreign regulatory authorities have differing requirements for approval of drug candidates w ith which we must comply prior to marketing. Obtaining marketing approval for marketing of a product candidate in one country does not ensure that we will be able to obtain marketing approval in other countries, but the failure to obtain marketing approval in one jurisdiction could negatively impact our ability to obtain marketing approval in other jurisdictions. Delays in approvals or rejections of marketing applications in the United States or foreign countries may be based upon many factors, including re gulatory requests for additional analyses, reports, data and studies, regulatory questions regarding, or different interpretations of, data and results, changes in regulatory policy during the period of product development and the emergence of new informat ion regarding product candidates or related products. The FDA or equivalent foreign regulatory authorities may determine that eravacycline or any other product candidate that we develop is not effective, or is only moderately effective, or has undesirable or unintended side effects, toxicities, safety profile or other characteristics that preclude marketing approval or prevent or limit commercial use. The FDA may also find during its pre-approval inspection that the facilities identified in our NDA fail to comply with cGMP requirements, thereby delaying or preventing approval. In addition, any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable . If we experience delays in obtaining approval or if we fail to obtain approval of eravacycline or any other product candidate that we develop, the commercial prospects for eravacycline or such other product candidate may be harmed and our ability to gene rate revenues will be materially impaired.

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

If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for that condition, the treatment sponsor may apply for FDA fast track designation. The FDA granted eravacycline fast track designation as a qualified infectious disease product in April 2014, granted fast track designation as a qualified infectious disease product for the IV formulation of TP-271 in September 2015, and granted fast track designation as a qualified infectious disease product for the oral formulation of TP-271 in February 2017. Fast track designation does not ensure approval or a faster development, regulatory review or approval process compared to conventional FDA procedures. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

***If we are unable to obtain marketing approval in international jurisdictions, we will not be able to market our product candidates abroad.***

In order to market and sell eravacycline and any other product candidate that we develop in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis or at all.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withd raw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with r espect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If

any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

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

Any product candidate, including eravacycline, for which we obtain marketing approval, will also be subject to ongoing regulatory requirements for labeling, manufacturing, packaging, storage, distribution, advertising, promotion, record-keeping and submission of safety and other post-market information. For example, approved products, manufacturers and manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs. As such, we and our contract manufacturers will be subject to continual review and periodic inspections to assess compliance with cGMPs. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. We will also be required to report certain adverse reactions and production problems, if any, to the FDA and to comply with requirements concerning advertising and promotion for our products.

In addition, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed, may be subject to significant conditions of approval or may impose requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling and regulatory requirements. The FDA also imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not restrict the marketing of our products only to their approved indications, we may be subject to enforcement action for off-label marketing.

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

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

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

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

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

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Even then, governmental authorities may conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Recent healthcare reform legislation has strengthened these federal and state healthcare laws. For example, the ACA amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or a specific intent to violate them. In addition, the ACA provides that the government may assert that a claim that includes items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act. If governmental authorities find that our operations violate any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud and abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

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

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

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

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

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

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 which reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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

**Risks Related to Employee Matters and Managing Growth**

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

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

We do not have formal employment agreements with any of our other employees. If we lose one or more of our executive officers or key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore , replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval o f and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and c linical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other en tities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize drug candidates will be limited.

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

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

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

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

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

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

Data privacy, security breaches or service interruptions may pose a risk that sensitive data including intellectual property, trade secrets or personal information belonging to us or our business partners may be exposed to unauthorized persons or to the public. Cyber-attacks are growing in their frequency, sophistication and intensity. Our third-party vendors face similar risks and any security breach of their systems could adversely affect us. While we have not yet experienced cyber-attacks and intrusions into our information

technology infrastructure, there can be no assurance that our efforts will prevent or detect future service interruptions or breaches in our systems. Any such future breach may adversely affect our business and operations.

**Risks Related to Our Common Stock**

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

Our stock price may be volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. For example, our stock traded within a range of a high price of $52.90 per share and a low price of $3.11 per share for the period beginning March 20, 2013, our first day of trading on the NASDAQ Global Select Market, through August 1, 2017. As a result of this volatility, investors may not be able to sell their common stock at or above the prices they paid for it. The market price for our common stock may be influenced by many factors, including:

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

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

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

2016, two class action lawsuits were filed against us, our chief executive officer and certain former exec utives in the United States District Court for the District of Massachusetts. In addition, in May 2016, a shareholder derivative action was filed against our chief executive officer, certain former executive officers, all the members of our current board o f directors, a former board member, and against us as nominal defendant, in Massachusetts Superior Court (Suffolk County). This case was subsequently dismissed by the court without prejudice due to the plaintiff's failure to properly perfect service of pro cess. Due to the volatility in our stock price, we may be the target of similar litigation in the future.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

**Item 6. Exhibits**

See the Exhibit Index on the page immediately preceding the exhibits for a list of exhibits filed as part of this quarterly report on Form 10-Q, which Exhibit Index is incorporated herein by reference.

**SIGNAT URES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: August 2, 2017

**TETRAPHASE PHARMACEUTICALS, INC.**

By: /s/ Christopher Watt
Christopher Watt
Senior Vice President, Finance

## EXHIBIT INDEX

| Exhibit Number | Description of Document | Incorporated by Reference from | | | | Filed Herewith |
|---|---|---|---|---|---|---|
| | | Registrant's Form | Form No. | Date Filed with the SEC | Exhibit Number | |
| 10.1+ | Master Manufacturing Services Agreement, dated June 14, 2017, by and between the Registrant and Patheon UK Limited. | | | | | X |
| 31.1 | Certification of Chief Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | | X |
| 31.2 | Certification of Principal Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. | | | | | X |
| 32.1 | Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | | X |
| 32.2 | Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. | | | | | X |
| 101.INS | XBRL Instance Document | | | | | X |
| 101.SCH | XBRL Taxonomy Extension Schema Document | | | | | X |
| 101.CAL | XBRL Taxonomy Extension Calculation Linkbase Document | | | | | X |
| 101.DEF | XBRL Taxonomy Extension Definition Linkbase Document | | | | | X |
| 101.LAB | XBRL Taxonomy Extension Label Linkbase Document | | | | | X |
| 101.PRE | XBRL Taxonomy Extension Presentation Linkbase Document | | | | | X |

+ Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. Double asterisks denote omission.

Exhibit 10.1

# Master Manufacturing Services Agreement

## 14 JUNE 2017

Table of Contents


ARTICLE 1 1

STRUCTURE OF AGREEMENT AND INTERPRETATION 1

1.1 MASTER AGREEMENT. 1
1.2 PRODUCT AGREEMENTS. 1
1.3 DEFINITIONS. 1
1.4 CURRENCY. 7
1.5 SECTIONS AND HEADINGS. 7
1.6 SINGULAR TERMS. 7
1.7 APPENDIX 1, SCHEDULES AND EXHIBITS. 7

ARTICLE 2 8

PATHEON'S MANUFACTURING SERVICES 8

2.1 MANUFACTURING SERVICES. 8
2.2 ACTIVE MATERIAL YIELD. 10

ARTICLE 3 11

CLIENT'S OBLIGATIONS 11

3.1 PAYMENT. 11
3.2 ACTIVE MATERIALS AND QUALIFICATION OF ADDITIONAL SOURCES OF SUPPLY. 12

ARTICLE 4 12

CONVERSION FEES AND COMPONENT COSTS 12

4.1 FIRST YEAR PRICING. 12
4.2 PRICE ADJUSTMENTS – SUBSEQUENT YEARS' PRICING. 13
4.3 PRICE ADJUSTMENTS – CURRENT YEAR PRICING. 14
4.4 ADJUSTMENTS DUE TO TECHNICAL CHANGES OR REGULATORY AUTHORITY REQUIREMENTS. 15
4.5 MULTI-COUNTRY PACKAGING REQUIREMENTS. 15

ARTICLE 5 15

ORDERS, SHIPMENT, INVOICING, PAYMENT 15

5.1 ORDERS AND FORECASTS. 15
5.2 RELIANCE BY PATHEON. 16
5.3 MINIMUM ORDERS. 17
5.4 DELIVERY AND SHIPPING. 17
5.5 INVOICES AND PAYMENT. 17

ARTICLE 6 17

PRODUCT CLAIMS AND RECALLS 17

6.1 PRODUCT CLAIMS. 17
6.2 PRODUCT RECALLS AND RETURNS. 18
6.3 PATHEON'S RESPONSIBILITY FOR DEFECTIVE AND RECALLED PRODUCTS. 19
6.4 DISPOSITION OF DEFECTIVE OR RECALLED PRODUCTS. 20
6.5 HEALTHCARE PROVIDER OR PATIENT QUESTIONS AND COMPLAINTS. 20
6.6 SOLE REMEDY. 20

ARTICLE 7 22
CO-OPERATION 22
7.1 QUARTERLY REVIEW. 22
7.2 GOVERNMENTAL AGENCIES. 22
7.3 RECORDS AND ACCOUNTING BY PATHEON. 22
7.4 INSPECTION. 22
7.5 ACCESS. 22
7.6 NOTIFICATION OF REGULATORY INSPECTIONS. 23
7.7 REPORTS. 23
7.8 REGULATORY FILINGS. 23
ARTICLE 8 24
TERM AND TERMINATION 24
8.1 INITIAL TERM. 24
8.2 TERMINATION FOR CAUSE. 25
8.3 PRODUCT DISCONTINUATION. 25
8.4 OBLIGATIONS ON TERMINATION. 25
ARTICLE 9 26
REPRESENTATIONS, WARRANTIES AND COVENANTS 26
9.1 AUTHORITY. 26
9.2 CLIENT WARRANTIES. 27
9.3 PATHEON WARRANTIES. 27
9.4 PERMITS. 28
9.5 NO WARRANTY. 29
ARTICLE 10 29
REMEDIES AND INDEMNITIES 29
10.1 CONSEQUENTIAL AND OTHER DAMAGES. 29
10.2 LIMITATION OF LIABILITY. 29
10.3 PATHEON INDEMNITY. 29
10.4 CLIENT INDEMNITY. 30
10.5 REASONABLE ALLOCATION OF RISK. 30
ARTICLE 11 31
CONFIDENTIALITY 31
11.1 CONFIDENTIAL INFORMATION. 31
11.2 USE OF CONFIDENTIAL INFORMATION. 31
11.3 EXCLUSIONS. 31
11.4 PHOTOGRAPHS AND RECORDINGS. 32
11.5 PERMITTED DISCLOSURE. 32
11.6 MARKING. 33
11.7 RETURN OF CONFIDENTIAL INFORMATION. 33
11.8 REMEDIES. 33
ARTICLE 12 33
DISPUTE RESOLUTION 33
12.1 COMMERCIAL DISPUTES. 33
12.2 TECHNICAL DISPUTE RESOLUTION. 34

| | | |
|---|---|---|
| **ARTICLE 13** | | **34** |
| **MISCELLANEOUS** | | **34** |
| **13.1** | **INVENTIONS.** | **34** |
| **13.2** | **INTELLECTUAL PROPERTY.** | **34** |
| **13.3** | **INSURANCE.** | **35** |
| **13.4** | **INDEPENDENT CONTRACTORS.** | **35** |
| **13.5** | **NO WAIVER.** | **35** |
| **13.6** | **ASSIGNMENT.** | **35** |
| **13.7** | **FORCE MAJEURE.** | **36** |
| **13.8** | **ADDITIONAL PRODUCT.** | **36** |
| **13.9** | **NOTICES.** | **36** |
| **13.10** | **SEVERABILITY.** | **37** |
| **13.11** | **ENTIRE AGREEMENT.** | **37** |
| **13.12** | **OTHER TERMS.** | **37** |
| **13.13** | **NO THIRD PARTY BENEFIT OR RIGHT.** | **37** |
| **13.14** | **EXECUTION IN COUNTERPARTS.** | **37** |
| **13.15** | **USE OF CLIENT NAME.** | **37** |
| **13.16** | **TAXES.** | **38** |
| **13.17** | **GOVERNING LAW.** | **39** |

# MASTER MANUFACTURING SERVICES AGREEMENT

**THIS MASTER MANUFACTURING SERVICES AGREEMENT (the "Agreement")** is made as of 14 June 2017 (the " **Effective Date** ")

B E T W E E N:

**PATHEON UK LIMITED** , a corporation existing under the laws of England of Kingfisher Drive, Covingham, Swindon, SN3 5BZ
(" **Patheon** "),

- and –

**TETRAPHASE PHARMACEUTICALS, INC.** ,
a corporation existing under the laws of Delaware
of 480 Arsenal Street, Suite 100, Watertown, Massachusetts 02472, USA
(" **Client** ").

THIS AGREEMENT WITNESSES THAT in consideration of the rights conferred and the obligations assumed herein, and for other good and valuable consideration (the receipt and sufficiency of which are acknowledged by each party), and intending to be legally bound the parties agree as follows:

## ARTICLE 1

## STRUCTURE OF AGREEMENT AND INTERPRETATION

**1.1 Master Agreement** .

This Agreement establishes the general terms and conditions under which Patheon or any Affiliate of Patheon may perform Manufacturing Services for Client or any Affiliate of Client, at the manufacturing site where Patheon or the Affiliate of Patheon resides. This "master" form of agreement is intended to allow the parties, or any of their Affiliates, to contract for the manufacture of multiple Products through Patheon's global network of manufacturing sites through the issuance of site specific Product Agreements without having to re-negotiate the basic terms and conditions contained herein.

**1.2 Product Agreements** .

This Agreement is structured so that a Product Agreement may be entered into by the parties for the manufacture of a particular Product or multiple Products at a Patheon manufacturing site. Each Product Agreement will be governed by the terms and conditions of this Agreement unless the parties to the Product Agreement expressly modify the terms and conditions of this Agreement in the Product Agreement. Unless otherwise agreed by the parties, each Product Agreement will be in the general form and contain the information set forth in Appendix 1 hereto.

**1.3 Definitions** .

The following terms will, unless the context otherwise requires, have the respective meanings set out below and grammatical variations of these terms will have corresponding meanings:

" **Active Materials** ", **"Active Pharmaceutical Ingredients" or "API"** means the materials listed in a Product Agreement on Schedule D;

" **Active Materials Credit Value** " means the value of the Active Materials for certain purposes of this Agreement, as set forth in a Product Agreement on Schedule D;

" **Actual Annual Yield** " or " **AAY** " has the meaning specified in Section 2.2(a);

" **Actual Yearly Volume** " or " **AYV** " has the meaning specified in Section 4.2.1;

" **Affiliate** " means:

(a) a business entity which owns, directly or indirectly, a controlling interest in a party to this Agreement, by stock ownership or otherwise; or

(b) a business entity which is controlled by a party to this Agreement, either directly or indirectly, by stock ownership or otherwise; or

(c) a business entity, the controlling interest of which is directly or indirectly common to the majority ownership of a party to this Agreement;

For this definition, "control" means the ownership of shares carrying at least a majority of the votes for the election of the directors;

**"Annual Product Review Report"** means the annual product review report prepared by Patheon or an Affiliate of Patheon as described in Title 21 of the United States Code of Federal Regulations, Section 211.180(e);

" **Annual Report"** means the annual report to the FDA prepared by Client regarding the Product as described in Title 21 of the United States Code of Federal Regulations, Section 314.81(b)(2);

" **Annual Volume** " means the minimum volume of Product to be manufactured in any Year of this Agreement as set forth in Schedule B of the applicable Product Agreement;

" **Applicable Laws** " means (i) for Patheon, the Laws of the jurisdiction where the Manufacturing Site is located and all other Laws applicable to the Manufacturing Services; and (ii) for Client and the Products, the Laws of all jurisdictions where the Products are manufactured, distributed, and marketed by or on behalf of Client as these are agreed and understood by the parties in this Agreement;

" **Authority** " means any governmental or regulatory authority, department, body or agency or any court, tribunal, bureau, commission or other similar body, whether federal, state, provincial, county or municipal;

" **Breach Notice** " has the meaning specified in Section 8.2(a);

" **Business Day** " means a day other than a Saturday, Sunday or a day that is a statutory holiday in the United Kingdom or a federal or state holiday in Boston, Massachusetts, USA or the jurisdiction where the Manufacturing Site is located;

" **Capital Equipment Agreement** " means a separate agreement that the parties may enter into that will address responsibility for the purchase of capital equipment and facility modifications that may be required to perform the Manufacturing Services under a particular Product Agreement;

" **Certificate of Analysis** " means a document prepared by Patheon, signed by an authorized representative of Patheon, describing Specifications for, and testing methods applied to each

batch of Product, and the results thereof and (a) listing the manufacturing date, unique b atch number, and quantity of Product in such Batch , and (b) certifying that such b atch was manufactured in accordance with Applicable Laws , including, without limitation cGMP.

" **Certificate of Compliance** " means a document, signed by an authorized representative of Patheon, attesting that a particular batch of Product was manufactured, filled, packaged and held in accordance with Applicable Laws, including, without limitation cGMP, and the Specifications.

**" cGMPs "** means, as applicable, current good manufacturing practices, including as described in:

(a) Parts 210 and 211 of Title 21 of the United States' Code of Federal Regulations;

(b) EC Directive 2003/94/EC;

(c) ICH Q7A "ICH Good Manufacturing Practices Guide for Active Pharmaceutical Ingredients"; and

(d) Division 2 of Part C of the *Food and Drug Regulations* (Canada);

together with the latest Health Canada, Japanese PMDA (to the extent applicable), FDA and EMA guidance documents pertaining to manufacturing and quality control practice, all as updated, amended and revised from time to time;

**"Client Intellectual Property"** means Intellectual Property (a) generated or derived by or on behalf of Client (i) before entering into this Agreement or (ii) during the Term and outside the performance of this Agreement, or (b) by Patheon while performing any Manufacturing Services or otherwise generated or derived by Patheon in its business which Intellectual Property is specific to, or is dependent upon, Client's Active Material or Product;

" **Client Property** " has the meaning specified in Section 8.4(a)(v);

" **Client-Supplied Components** " means those Components to be supplied by Client as set forth in a Product Agreement or that have been supplied by Client;

**" Components "** means, collectively, all packaging components, raw materials, ingredients, and other materials (including labels, product inserts and other labelling for the Products) required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

" **Confidential Information** " has the meaning specified in Section 11.1;

" **CTD** " has the meaning specified in Section 7.8(c);

" **Deficiencies** " have the meaning specified in Section 7.8(d);

**" Deficiency Notice "** has the meaning specified in Section 6.1(a);

**"Delivery Date"** means the date scheduled for shipment of Product under a Firm Order as set forth in Section 5.1(d);

**"Disclosing Party** " has the meaning specified in Section 11.1;

**" EMA "** means the European Medicines Agency, or any successor agency thereto;

" **FDA** " means the United States Food and Drug Administration , or any successor agency thereto ;

" **Firm Orders** " have the meaning specified in Section 5.1(c);

" **Force Majeure Event** " has the meaning specified in Section 13.7;

" **GST** " has the meaning specified in Section 13.16(a)(iii);

" **Health Canada** " means the section of the Canadian Government known as Health Canada, or any successor agency thereto, and includes, among other departments, the Therapeutic Products Directorate and the Health Products and Food Branch Inspectorate;

" **Importer of Record** " has the meaning specified in Section 3.2(a);

" **Initial Product Term** " has the meaning specified in Section 8.1;

" **Initial Term** " has the meaning specified in Section 8.1;

" **Intellectual Property** " means (a) ideas, concepts, discoveries, inventions, developments, know-how, trade secrets, techniques, methodologies, formulae, processing parameters, designs, modifications, innovations, improvements, writings, documentation, electronic code, data and rights (whether or not protectable under state, federal or foreign patent, trademark, copyright or similar laws) or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which contained and whether or not patentable or copyrightable and (b) any and all rights in any of the foregoing, including without limitation, patents, trademarks, copyrights and trade secrets;

" **Invention** " means any innovation, improvement, modification, development, discovery, computer program, device, trade secret, method, know-how, process, technique or the like, whether or not written or otherwise fixed in any form or medium, regardless of the media on which it is contained and whether or not patentable or copyrightable;

" **Inventory** " means all inventories of Components and work-in-process produced or held by Patheon for the manufacture of the Products but, for greater certainty, does not include the Active Materials;

**"Japanese PMDA"** means the Japan Pharmaceuticals and Medical Devices Agency or any successor agency thereto;

" **Laws** " means all laws, statutes, ordinances, regulations, rules, by-laws, judgments, decrees or orders of any Authority;

**"Long Term Forecast** " has the meaning specified in Section 5.1(a);

" **Manufacturing Services** " means the manufacturing, quality control, quality assurance, stability testing, packaging, and related services, as set forth in this Agreement, required to manufacture and supply Product or Products using the Active Materials and Components;

" **Manufacturing Site** " means the facility owned and operated by Patheon or an Affiliate of Patheon where the Manufacturing Services will be performed as identified in a Product Agreement;

**"Master Batch Record" or "MBR"** shall mean the document containing the complete process for manufacturing the Product, including process parameters and process specifications.

**"Materials"** means all Components required to manufacture the Products in accordance with the Specifications, other than the Active Materials;

" **Minimum Order Quantity** " means the minimum number of batches of a Product to be produced during the same cycle of manufacturing as set forth in a Product Agreement on Schedule B;

" **Maximum Credit Value** " means the maximum value of Active Materials that may be credited by Patheon under this Agreement, as set forth in a Product Agreement on Schedule D;

" **Obsolete Stock** " has the meaning specified in Section 5.2(b);

" **Patheon Competitor** " means an entity that derives greater than [**] percent ([**]%) of its revenues from performing contract pharmaceutical development or commercial manufacturing services pursuant to agreements with unrelated third party entities;

**"Patheon Intellectual Property"** means Intellectual Property generated or derived by Patheon before performing any Manufacturing Services, developed by Patheon while performing the Manufacturing Services, or otherwise generated or derived by Patheon in its business which Intellectual Property is not specific to, or dependent upon, Client's Active Material or Product including, without limitation, Inventions and Intellectual Property which may apply to manufacturing processes or the formulation or development of drug products, drug product dosage forms or drug delivery systems unrelated to the specific requirements of the Product(s);

**"Price"** means the price set forth in the applicable Product Agreement, measured in U.S. dollars (if the Manufacturing Site is located in North America) or Euros (if the Manufacturing Site is located outside North America) unless agreed otherwise in a Product Agreement, to be charged by Patheon for performing the Manufacturing Services, and includes the cost of Components (other than Client-Supplied Components), certain cost items as set forth in a Product Agreement on Schedule B, and annual stability testing costs as set forth in a Product Agreement on Schedule C;

" **Product(s)** " means the product(s) listed in a Product Agreement on Schedule A;

" **Product Agreement** " means the agreement between Patheon and Client issued under this Agreement in the form set forth in Appendix 1 (including Schedules A to D) under which Patheon will perform Manufacturing Services at a particular Manufacturing Site;

" **Product Claims** " have the meaning specified in Section 6.3(c);

" **Quality Agreement** " means the agreement (the general form of which is set forth in Exhibit B) between the parties entering a Product Agreement, or between the applicable Affiliate of Patheon and Client if the Manufacturing Services are subcontracted to such Affiliate by Patheon, that sets out the quality assurance standards for the Manufacturing Services to be performed by Patheon for Client;

" **Recall** " has the meaning specified in Section 6.2(a);

" **Recipient** " has the meaning specified in Section 11.1;

" **Regulatory Authority** " means the FDA, EMA, Health Canada , Japanese PMDA (to the extent applicable) and any other foreign regulatory agencies competent to grant marketing approvals for pharmaceutical products including the Products in the Territory;

" **Regulatory Approval** " has the meaning specified in Section 7.8(a);

" **Remediation Period** " has the meaning specified in Section 8.2(a);

" **Representatives** " means a party's directors, officers, employees, advisers, agents, consultants, subcontractors (only to the extent approved by Client with respect to Patheon subcontractors), professional advisors, or other representatives;

**"Resident Jurisdiction "** has the meaning specified in Section 13.16(a)(i);

" **Shortfall Credit** " has the meaning specified in Section 2.2(b);

" **Specifications** " means the file, for each Product, which is given by Client to Patheon in accordance with the procedures listed in a Product Agreement on Schedule A and which contains documents relating to each Product, including, without limitation:

(a) specifications for Active Materials and Components;

(b) manufacturing specifications, directions, and processes;

(c) storage requirements;

(d) all environmental, health and safety information for each Product including material safety data sheets; and

(e) the finished Product specifications, packaging specifications and shipping requirements for each Product;

all as updated, amended and revised from time to time by Client in accordance with the terms of this Agreement;

" **Target Yield** " has the meaning specified in Section 2.2(a);

" **Target Yield Determination Batches** " has the meaning specified in Section 2.2(a);

" **Tax** " or " **Taxes** " have the meaning specified in Section 13.16(a);

" **Technical Dispute** " has the meaning specified in Section 12.2;

" **Territory** " means the geographic area described in a Product Agreement where Products manufactured by Patheon will be distributed by Client;

" **Third Party** " means a party other than Patheon or its Affiliates or Client or its Affiliates.

" **Third Party Rights** " means the Intellectual Property of any Third Party;

" **VAT** " has the meaning specified in Section 13.16(d);

" **Year** " means in the first year of this Agreement or in the first year of a Product Agreement, the period from the Effective Date up to and including December 31 of the same calendar year, and thereafter will mean a calendar year ;

" **Yearly Forecast Volume** " or " **YFV** " has the meaning specified in Section 4.2.1;

" **Zero Forecast Period** " has the meaning specified in Section 5.1(f).

**1.4 Currency** .

Unless otherwise agreed in a Product Agreement, all monetary amounts expressed in this Agreement are in United States dollars (USD) (if the Manufacturing Site is located in North America) or Euros (if the Manufacturing Site is located outside North America).

**1.5 Sections and Headings** .

The division of this Agreement into Articles, Sections, Subsections, an Appendix, Schedules and Exhibits and the insertion of headings are for convenience of reference only and will not affect the interpretation of this Agreement. Unless otherwise indicated, any reference in this Agreement to a Section, Appendix, Schedule or Exhibit refers to the specified Section, Appendix, Schedule or Exhibit to this Agreement. In this Agreement, the terms " **this Agreement** ", " **hereof** ", " **herein** ", " **hereunder** " and similar expressions refer to this Agreement as a whole and not to any particular part, Section, Appendix, Schedule or Exhibit of this Agreement.

**1.6 Singular Terms** .

Except as otherwise expressly stated or unless the context otherwise requires, all references to the singular will include the plural and vice versa.

**1.7 Appendix 1, Schedules and Exhibits** .

Appendix 1 (including the Schedules thereto) and the following Exhibits are attached to, incorporated in, and form part of this Agreement:

Appendix 1 - Form of Product Agreement (Including Schedules A to D)

Exhibit A - Technical Dispute Resolution
Exhibit B - Commercial Quality Agreement
Exhibit C - Quarterly Active Materials Inventory Report
Exhibit D - Report of Annual Active Materials Inventory Reconciliation and Calculation of Actual Annual Yield

## ARTICLE 2

## PATHEON'S MANUFACTURING SERVICES

**2.1 Manufacturing Services** .

Patheon will perform the Manufacturing Services for the Territory for the fees specified in a Product Agreement in Schedules B and C to manufacture Products for Client or its Affiliate (which shall mean that either Client or its Affiliate would enter into a Product Agreement with Patheon). Schedule B to a Product Agreement sets forth a list of cost items that are included in the Price for Products; all cost items that are not included in the Price are subject to additional fees to be paid by the Client. Amendments to the fees set out in Schedules B and C to a Product Agreement will be performed in accordance with the price adjustment mechanisms as set forth in Article 4. Patheon may change the Manufacturing Site for the Products only with the prior written consent of Client. In performing the Manufacturing Services, Patheon and Client agree that:

(a) Conversion of Active Materials and Components . Patheon will convert Active Materials and Components into Products.

(b) Master Batch Record . The Master Batch Record shall be reviewed and approved in writing by Patheon and by Client prior to commencement of Manufacturing Services. Any material change to an approved Master Batch Record shall be reviewed and approved in writing by Patheon and by Client prior to said change being implemented. Each batch of Product shall be manufactured by using a copy of the Master Batch Record. Each copy of the Master Batch Record for such batch of Product shall be assigned a unique batch number. Any deviation from the manufacturing process specified in the Master Batch Record must be documented in the batch record for that batch.

(c) Quality Control and Quality Assurance . Patheon will perform the quality control and quality assurance testing specified in the Quality Agreement and otherwise as required to comply with cGMP. Batch review and release to Client will be the responsibility of Patheon’s quality assurance group. Patheon will perform its batch review and release responsibilities in accordance with Patheon’s standard operating procedures. Each time Patheon ships Products to Client, it will give Client a Certificate of Analysis and Certificate of Compliance, BSE/BTE and melamine statement, and a statement that the batch has been manufactured and tested in accordance with Specifications and cGMPs. Client will have sole responsibility for the release of Products to the market. The form and style of batch documents, including, but not limited to, batch production records, lot packaging records, equipment set up control, operating parameters, and data printouts, raw material data, and laboratory notebooks are the exclusive property of Patheon. Specific Product related information contained in those batch documents is the exclusive property of Client.

(d) Components . Patheon will purchase and test all Components (with the exception of Client-Supplied Components) at Patheon's expense and as required by the Specifications.

(e) Stability Testing . Patheon will conduct stability testing on the Products in accordance with the protocols set out in the Specifications for the separate fees and during the time periods set out in Schedule C to a Product Agreement. Patheon will not make any changes to these testing protocols without prior written approval from Client. If a confirmed stability test failure occurs, Patheon will notify Client within [**], after which Patheon and Client will jointly determine the proceedings and methods to be undertaken

to investigate the cause of the failure, including which party will bear the cost of the investigation . Patheon will not be liable for these costs unless it has failed to perform the Manufacturing Services or testing in accordance with the Specifications and cGMPs. Client shall own all stability test data and results and Patheon will give Client all stability test data and results at Client's request .

(f) Packaging and Artwork . Patheon will package the Products in accordance with the Specifications. Client will own all artwork and shall be responsible for the cost of artwork development. Specifically, Client will be responsible for supplying Patheon with digital artwork necessary to enable Patheon to supply Products fully finished ready for sale by the Client, incorporating Client's trademark(s), livery and text. The Client will also be responsible for the cost of proofing and of production of the printing plates required by Patheon to assemble, package and supply the Products and for the approval of final proofs generated by the printer. All such artwork, trademarks, livery and text shall be the property of Client and Patheon shall obtain no rights therein. Patheon will determine and imprint the batch numbers and expiration dates for each Product shipped. The batch numbers and expiration dates will be affixed on the Products and on the shipping carton of each Product as outlined in the Specifications and as required by cGMPs. Client may, in its sole discretion, make changes to labels, product inserts, and other packaging for the Products. Those changes will be submitted by Client to all applicable Regulatory Authorities and other third parties responsible for the approval of the Products to the extent required by Applicable Law. Client will be responsible for the cost of labelling obsolescence when changes occur, as contemplated in Section 4.4. Patheon's name will not appear on the label or anywhere else on the Products unless: (i) required by any Laws; or (ii) Patheon consents in writing to the use of its name. If necessary, at least [**] days prior to the Delivery Date of Product for which new or modified artwork is required, Client will provide at no cost to Patheon, final artwork for all packaging Components to be used in the manufacture of the Product that meet the Specifications. For the avoidance of doubt, the parties acknowledge and agree that Client will be responsible for complying with any and all regulatory requirements for the labeling of the Product.

(g) Active Materials and Client-Supplied Components . At least [**] days before the scheduled production date, Client will deliver the Active Materials and any Client-Supplied Components to the Manufacturing Site DDP (Incoterms 2010), at no cost to Patheon, with any VAT paid by Client, to enable Patheon to manufacture the desired quantities of Product and to ship Product on the Delivery Date. If the Active Materials and/or Client-Supplied Components are not received [**] days before the scheduled production date, Patheon may delay the shipment of Product by the same number of days as the delay in receipt of the Active Materials and/or Client-Supplied Components. But if Patheon is unable to manufacture Product to meet this new shipment date due to prior third party production commitments, Patheon may delay the shipment until a later date as agreed to by the parties. All shipments of Active Material will be accompanied by certificate(s) of analysis from the Active Material manufacturer and the Client, confirming the identity and purity of the Active Materials and its compliance with the Active Material specifications. For Active Materials or Client-Supplied Components which may be subject to import or export, Client agrees that it shall use commercially reasonable efforts to cause its vendors and carriers to comply with applicable requirements of the U.S. Customs and Border Protection Service and the Customs Trade Partnership Against Terrorism.

(h) Validation Activities (if applicable) . Patheon may assist in the development and approval of the validation protocols for analytical methods and manufacturing procedures (including packaging procedures) for the Products. The fees for this service are not included in the Price and will be set out separately in Schedule C to a Product Agreement.

(i) Storage and Handling . Patheon shall store and handle Components under appropriate GMP conditions for temperature, humidity, light and cleanliness and in accordance with any storage specifications agreed between the parties . Patheon shall store and handle the Active Material Product in accordance with the Specifications and under appropriate GMP conditions for temperature, humidity, light and cleanliness. In addition to the foregoing, Patheon shall store and handle the Active Materials and Products so as to prevent the commingling of same with Patheon's own inventories and supplies, or those held by Patheon for Third Parties.

(j) Subcontracting. Patheon shall not subcontract or otherwise delegate any portion of its obligations under this Agreement without Client's prior written approval other than to its Affiliates as provided for in Section 13.6(a).

(k) Additional Services . If Client requests services other than those expressly set forth herein or in any Product Agreement (such as qualification of a new packaging configuration or shipping studies, or validation of alternative batch sizes), Patheon will provide a good faith and reasonable written quote of the fee for the additional services and Client will advise Patheon whether it wishes to have the additional services performed by Patheon. The scope of work and fees will be set forth in a separate agreement signed by the parties. The terms and conditions of this Agreement will apply to these services.

**2.2 Active Material Yield .**

(a) Reporting . Patheon will give Client a quarterly inventory report of the Active Materials held by Patheon using the inventory report form set out in Exhibit C, which will contain the following information for the quarter:

**Quantity Received:** The total quantity of Active Materials that complies with the Specifications and is received at the Manufacturing Site during the applicable period.

**Quantity Dispensed:** The total quantity of Active Materials dispensed at the Manufacturing Site during the applicable period. The Quantity Dispensed is calculated by adding the Quantity Received to the inventory of Active Materials that complies with the Specifications held at the beginning of the applicable period, less the inventory of Active Materials that complies with the Specifications held at the end of the period. The Quantity Dispensed will only include Active Materials received and dispensed in commercial manufacturing of Products and, for certainty, will not include any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing as required under this Agreement (if applicable), and (iv) Active Materials received or dispensed in technical transfer activities or development activities under this Agreement during the applicable period, including without limitation, any regulatory, stability, validation or test batches manufactured during the applicable period.

**Quantity Converted:** The total amount of Active Materials contained in the Products manufactured with the Quantity Dispensed (including any additional Products produced in accordance with Section 6.3(a) or 6.3(b)), delivered by Patheon, and not rejected, recalled or returned in accordance with Section 6.1or 6.2 because of Patheon's failure to perform the Manufacturing Services and supply Product in accordance with Specifications, cGMPs, and Applicable Laws.

Within [**] days after the end of each Year, Patheon will prepare an annual reconciliation of Active Materials on the reconciliation report form set forth in Exhibit D including the calculation of the " **Actual Annual Yield** " or " **AAY** " for the Product at the Manufacturing Site during the Year . AAY is the percentage of the Quantity Dispensed that was converted to Products and is calculated as follows:

Quantity Converted during the Year x 100%
Quantity Dispensed during the Year

After Patheon has produced a minimum of [**] successful commercial production batches if the Manufacturing Site is outside of North America or [**] successful commercial production batches if the Manufacturing Site is in North America of Product and has produced commercial production batches for at least [**] months at the Manufacturing Site (collectively, the " **Target Yield Determination Batches** "), the parties will agree on the target yield for the Product at the Manufacturing Site (each, a " **Target Yield** "). The Target Yield will be revised annually to reflect the actual manufacturing experience as agreed to by the parties, such agreement not to be unreasonably withheld.

(b) Shortfall Credit Calculation . If the Actual Annual Yield falls more than [**] percent ([**]%) below the respective Target Yield in a Year, then the shortfall for the Year (the " **Shortfall** ") will be calculated as follows:

Shortfall Credit = [**]

( c ) Credit for Shortfall . If there is a Shortfall for a Product in a Year, then Patheon will credit Client's account for the amount of the Shortfall not later than [**] days after the end of the Year. Each credit under this Section 2.2(c) will be summarized on the reconciliation report form set forth in Exhibit D. Upon expiration or termination of a Product Agreement, any remaining credit owing under this Section will be paid to Client. The Annual Shortfall, if any, will be disclosed by Patheon on the reconciliation report form.

(d) Maximum Credit . Patheon's liability for Active Materials calculated in accordance with this Section 2.2 for any Product in a Year will not exceed, in the aggregate, the Maximum Credit Value set forth in Schedule D to a Product Agreement.

( e ) No Material Breach . It will not be a material breach of this Agreement by Patheon under Section 8.2(a) if the Actual Annual Yield is less than the Target Yield.

## ARTICLE 3

## CLIENT'S OBLIGATIONS

**3.1 Payment** .

Client will pay Patheon for performing the Manufacturing Services according to the Prices specified in Schedules B and C in a Product Agreement. These Prices may be subject to adjustment under other parts of this Agreement.

**3.2 Active Materials and Qualification of A dditional Sources of Supply .**

(a) Client will at its sole cost and expense deliver the Active Materials to Patheon in accordance with Section 2.1(g). If applicable, Patheon and the Client will reasonably cooperate to permit the import of the Active Materials to the Manufacturing Site. Client's obligation will include obtaining the proper release of the Active Materials from the applicable Customs Agency and Regulatory Authority. Client or Client's designated broker will be the " **Importer of Record** " for Active Materials imported to the Manufacturing Site. The Active Materials will be held by Patheon on behalf of Client as set forth in this Agreement. Title to the Active Materials will at all times remain the property of Client. Any Active Materials received by Patheon will only be used by Patheon to perform the Manufacturing Services for Client hereunder. Client will be responsible for paying for all rejected Product that arises from defects in the Active Materials which (i) could not be reasonably discoverable by Patheon using the test methods set forth in the Specifications; and (ii) are not due to the failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws or the wilful misconduct of Patheon.

(b) If Client asks Patheon to qualify an additional source for the Active Material or any Component, Patheon shall evaluate the Active Material or Component to be supplied by the additional source to determine if it is suitable for use in the Product. The parties will agree on the scope of work to be performed by Patheon at Client's cost. For an Active Material, this work at a minimum will include: (i) laboratory testing to confirm the Active Material meets existing specifications; (ii) manufacture of an experimental batch of Product that will be placed on [**] months accelerated stability; and (iii) manufacture of [**] full-scale validation batches that will be placed on concurrent stability (one batch may be the registration batch if manufactured at full scale).

(c) Patheon will promptly advise Client if it encounters supply problems, including delays and/or delivery of non-conforming Active Material or Components from a Client designated additional source; and Patheon and Client will cooperate to reduce or eliminate any supply problems from these additional sources of supply. Client will be obligated to certify all Client designated sources of supply on an annual basis at its expense and will provide Patheon with copies of these annual certifications. If Patheon agrees to certify a Client designated additional sources of supply on behalf of Client, it will do so at Client's expense.

## ARTICLE 4

## CONVERSION FEES AND COMPONENT COSTS

**4.1 First Year Pricing .**

The Price for the first Year will be listed in Schedules B and C in a Product Agreement and will be subject to the adjustments set forth in Sections 4.2 and 4.3. Either party may, upon written notice to the other party, request that the Price be increased or decreased if there are changes to the underlying manufacturing, packaging or testing assumptions set forth in Schedule B of the Product Agreement that result in an increase or decrease in the cost of performing the Manufacturing Services. Within [**] days after receipt of such notice, the parties shall meet and negotiate in good faith an adjustment to the Price to reflect such increase or decrease due to the change in assumptions. The party requesting such adjustment shall provide the other party supporting documentation to substantiate the requested adjustment to Price.

**4.2 Price Adjustments – Subsequent Years' Pricing** .

After the first Year of the Product Agreement, Patheon may adjust the Price effective January 1 st of each Year as follows:

(a) Manufacturing and Stability Testing Costs . Patheon may adjust the conversion component of the Price and the annual stability testing costs for inflation, based upon the preliminary number for any increase in the inflation index stated in the Product Agreement in August of the preceding Year compared to the final number for the same month of the Year prior to that, unless the parties otherwise agree in writing. On or before [**] of each Year, Patheon will give Client a statement setting forth the calculation for the inflation adjustment to be applied in calculating the Price for the next Year. In no event shall any increase over the preceding Year pursuant to this Section 4.2(a) exceed [**] percent ([**]%) during the first [**] Years of a Product Agreement. Thereafter, this restriction shall not apply.

(b) Component Costs . If Patheon incurs an increase in Component costs during the Year, it may increase the Price for the next Year to pass through the additional Component costs at Patheon's cost. On or before [**] of each Year, Patheon will give Client information about the increase in Component costs which will be applied to the calculation of the Price for the next Year to reasonably demonstrate that the Price increase is justified. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(c) Pricing Basis . Client acknowledges that the Price in any Year is quoted based upon the Minimum Order Quantity and the Annual Volume specified in Schedule B to a Product Agreement. The Price is subject to change if the specified Minimum Order Quantity changes or if the Annual Volume is not ordered in a Year. For greater certainty, if Patheon and Client agree that the Minimum Order Quantity will be reduced or the Annual Volume in the lowest tier will not be ordered in a Year whether as a result of a decrease in estimated Annual Volume or otherwise and, as a result of the reduction, Patheon demonstrates to Client that its costs to perform the Manufacturing Services or to acquire the Components for the Product will increase on a per unit basis (including the amount of the increase), then Patheon may increase the Price by an amount sufficient to absorb the documented increased costs. On or before [**] of each Year, Patheon will give Client a statement setting forth the information to be applied in calculating those cost increases for the next Year. But Patheon will not be required to give information to Client that is subject to obligations of confidentiality between Patheon and its suppliers.

(d) Tier Pricing (if applicable) . The pricing in Schedule B of a Product Agreement is set forth in Annual Volume tiers based upon the Client's volume forecasts under Section 5.1. The Client will be invoiced during the Year for the unit price set forth in the Annual Volume tier based on the [**] month forecast provided in September of the previous Year. Within [**] days after the end of each Year or of the termination of the Agreement, Patheon will send Client a reconciliation of the actual volume of Product ordered by the Client during the Year with the pricing tiers. If Client has overpaid during the Year, Patheon will issue a credit to the Client for the amount of the overpayment within [**] days after the end of the Year or will issue payment to the Client for the overpayment within [**] days after the termination of the Agreement. If Client has underpaid during the Year, Patheon will issue an invoice to the Client under Section 5.5 for the amount of the underpayment within [**] days after the end of the Year or termination of the Agreement. If Client disagrees with the reconciliation, the parties will work in good faith to resolve the disagreement amicably. If the parties are unable to resolve the disagreement within [**] days, the matter will be handled under Section 12.1.

( e ) For all Price adjustments under this Section 4.2 , Patheon will deliver to Client on or before [**] of each Year a revised Schedule B to the Product Agreement to be effective for Product delivered on or after the first day of the next Year. If in any Year Patheon would have been entitled to increase the Price based on any of the provisions of this Section 4.2 but Patheon did not exercise its right to do so, then at the expiry of any subsequent Year, Patheon will be entitled to make cumulative adjustments as set out in Section 4.2 based on changes during all of the preceding Years since Patheon last adjusted the Price.

**4.2.1** **Price Adjustment due to Volume Changes from Yearly Forecast Volumes for Sterile Products** .

On the execution of a Product Agreement, Client will give to Patheon a forecast of the volume of Product required for the first [**] Years of the Product Agreement (the " **Yearly Forecast Volume** " or " **YFV** ") that will become part of the Product Agreement. If at the end of the first Year the aggregate actual volume of Product ordered by Client and invoiced by Patheon under Section 5.5 (" **Actual Yearly Volume** " or " **AYV** ") during the Year is less than the YFV as set out in the Product Agreement, then Client will pay Patheon for its non-absorbed fixed manufacturing costs incurred during the Year in an amount to be determined as follows:

Amount due to Patheon = [**].

On or before [**] of each Year, the parties will agree on the YFV for the next [**] Years of the Product Agreement on a rolling forward basis. The forecast of the volume of Product for the [**] Year may not vary by more than [**]% from the original YFV for the [**] Year. Once agreed, the YFV for the next Year will become binding on the parties and any amount due to Patheon will be determined as set forth above.

**4.3** **Price Adjustments – Current Year Pricing** .

During any Year, the Prices set out in Schedule B of a Product Agreement will be adjusted as follows:

Extraordinary Increases in Component Costs . If, at any time, market conditions result in Patheon's cost of Components being materially greater than normal forecasted increases, then Patheon will be entitled to adjust the Price for any affected Product to compensate it for the increased Component costs. Changes materially greater than normal forecasted increases will have occurred if: (i) the cost of a Component increases by [**]% of the cost for that Component upon which the most recent Price or fee quote was based; or (ii) the aggregate cost for all Components required to manufacture a Product increases by [**]% of the total Component costs for the Product upon which the most recent fee quote was based. If Component costs have been previously adjusted to reflect an increase in the cost of one or more Components, the adjustments set out in (i) and (ii) above will operate based on the last cost adjustment for the Components.

For a Price adjustment under this Section 4.3, Patheon will deliver to Client a revised Schedule B to the Product Agreement and budgetary pricing information, adjusted Component costs or other documents reasonably sufficient to demonstrate that a Price adjustment is justified. Patheon will have no obligation to deliver any supporting documents that are subject to obligations of confidentiality between Patheon and its suppliers. The revised Price will be effective for any Product delivered on or after the first day of the month following Client's receipt of the revised Schedule B to the Product Agreement.

**4.4 Adjustments Due to Technical Changes or Regulatory Authority Re q uirements** .

Amendments to the Specifications or the Quality Agreement requested by Client will be implemented only following a technical and cost review that Patheon will perform at Client's cost and are subject to Client and Patheon reaching agreement on Price changes required because of the amendment. Amendments to the Specifications, the Quality Agreement, or the Manufacturing Site requested by Patheon will only be implemented following the written approval of Client, the approval not to be unreasonably withheld, conditioned or delayed. If Client accepts a proposed Price change, the proposed change in the Specifications or the Quality Agreement and the associated scope of work will be implemented with the costs to be allocated between the parties as mutually agreed in writing, and the Price change will become effective, only for those orders of Product that are manufactured under the revised Specifications; provided that the parties agree that if such changes are implemented due to a regulatory requirement that applies generally to the Product as well as to other products manufactured by Patheon for itself or for third parties, then Client shall pay a pro rata amount of the reasonable cost of such regulatory changes. In addition, Client agrees to purchase, at the price paid by Patheon (including all costs incurred by Patheon for the purchase, handling and transport of the Inventory), all Inventory held under the "old" Specifications and purchased or maintained by Patheon in order to fill Firm Orders or under Section 5.2, if the Inventory can no longer be used under the revised Specifications; provided that Patheon shall use reasonable efforts to mitigate such costs. Patheon shall, where possible, cancel open purchase orders for Components no longer required under any revised Specifications that were placed by Patheon with suppliers in order to fill Firm Orders or under Section 5.2, but if the orders may not be cancelled without penalty, Client shall pay the lesser of the price for such order or such penalty . Additional payments or price increases may also be agreed to by the parties to compensate Patheon for fees and other expenses incurred by Patheon to comply with Regulatory Authority requirements which apply to the Manufacturing Services.

**4.5 Multi-Country Packaging Requirements . _**

If Client decides to have Patheon perform Manufacturing Services for the Product for countries outside the Territory, then Client will inform Patheon of the packaging requirements for each new country and Patheon will prepare a quotation for consideration by Client of any additional costs for Components (other than Client-Supplied Components) and the change over fees for the Product destined for each new country. The agreed additional packaging requirements and related packaging costs and change over fees will be set out in a written amendment to this Agreement.

## ARTICLE 5

## ORDERS, SHIPMENT, INVOICING, PAYMENT

**5.1 Orders and Forecasts** .

(a) Long Term Forecast . When each Product Agreement is executed, Client will give Patheon a non-binding [**] year forecast of Client's estimated volume requirements for the Product for each Year during the term of the Product Agreement (the " **Long Term Forecast** "). The Long Term Forecast will thereafter be updated every [**] during the Initial Product Term. If Patheon is unable to accommodate any portion of the Long Term Forecast, it will notify Client and the parties will agree on any revisions to the forecast.

(b) Rolling [**] Forecast . When each Product Agreement is executed, Client will give Patheon a non-binding [**] forecast of the estimated volume of Product that Client expects to order in the first [**] of commercial manufacture of the Product (" **Rolling Forecast** "). The Rolling Forecast will then be updated by Client on or before the [**] on a rolling forward basis. Client will update the Rolling Forecast if it determines that the volumes estimated in the most recent Rolling Forecast have changed by more than [**] percent ([**]%). The most recent [**] forecast will prevail.

(c) Firm Orders. Unless otherwise agreed in the Product Agreement, t he first [**] of the Rolling F orecast will be considered binding firm orders . The remaining [**] of each Rolling Forecast submitted by Client shall be for planning purposes only, and thus shall not be binding. Concurrent with the [**] forecast, Client will issue a new firm written order in the form of a purchase order or otherwise (" **Firm Order** ") by Client to purchase and, when accepted by Patheon, for Patheon to manufacture and deliver the agreed quantity of the Products . The D elivery D ate will not be less than [**] days following the date that the Firm Order is submitted. Firm Orders submitted to Patheon will specify Client's purchase order number, quantities by Product type, monthly delivery schedule, and any other elements necessary to ensure the timely manufacture and shipment of the Products. The quantities of Products ordered in those written orders will be firm and binding on Client and may not be reduced by Client. Expedited Firm Orders will be subject to additional fees.

(d) Acceptance of Firm Order . Patheon will accept Firm Orders by sending an acknowledgement to Client within [**] Business Days of its receipt of the Firm Order; provided that Patheon may only reject a Firm Order which fails to comply with the requirements of this Article 5 or that is not consistent with the Long Term Forecast. The acknowledgement will include, subject to confirmation from the Client, the Delivery Date for the Product ordered. The Delivery Date may be amended by agreement of the parties. If Patheon fails to acknowledge receipt of a Firm Order within the [**] Business Day period, the Firm Order will be deemed to have been accepted by Patheon.

(e) Cancellation of a Firm Order . If Client cancels a Firm Order, Client, as its sole liability for such cancellation, will pay Patheon 100% of the Price for the Firm Order.

(f) Zero Volume Forecast . Once Client has commenced issuing Firm Orders for Product, if Client subsequently forecasts zero volume for [**] period during the term of a Product Agreement (the " **Zero Forecast Period** "), then Patheon will have the option, at its sole discretion, to provide a [**] day notice to Client of Patheon's intention to terminate the Product Agreement on a stated day within the Zero Forecast Period. Client thereafter will have [**] days to either (i) withdraw the zero forecast and re-submit a reasonable volume forecast, or (ii) negotiate other terms and conditions on which the Product Agreement will remain in effect. Otherwise, Patheon will have the right to terminate the Product Agreement at the end of the [**] day notice period.

**5.2 Reliance by Patheon** .

(a) Client understands and acknowledges that Patheon will rely on the Firm Orders and Rolling Forecasts submitted under Section 5.1(b) in ordering the Components (other than Client-Supplied Components) required to meet the Firm Orders. In addition, Client understands that to ensure an orderly supply of the Components **,** Patheon may want to purchase the Components in sufficient volumes to meet the production requirements for Products during part or all of the Rolling Forecast or to meet the production requirements of any longer period agreed to by Patheon and Client in writing. Accordingly, Client authorizes Patheon to, and Patheon shall purchase Components to satisfy the Manufacturing Services requirements for Products for the first [**] contemplated in the most recent Rolling Forecast. Patheon may make other purchases of Components to meet Manufacturing Services requirements for longer periods if agreed to in writing by the parties. Client will give Patheon written authorization to order Components for any launch quantities of Product requested by Client which will be considered a Firm Order when accepted by Patheon.

(b) Client will reimburse Patheon for the cost of Components that have expired or that are rendered obsolete due to changes in artwork or applicable regulations during the period (collectively, " **Obsolete Stock** "). This reimbursement will include Patheon's cost to purchase (plus a [**] % handling fee) and destroy the Obsolete Stock.

(c) If Client fails to take delivery of conforming finished Product within [**] of manufacture and release testing, Client will pay Patheon $[**] / EURO [**] per pallet, per month thereafter for storing the finished Product. Storage fees for Product which contain controlled substances or require refrigeration will be charged at $[**] / EURO [**] per pallet per month. Storage fees are subject to a one pallet minimum charge per month.

**5.3 Minimum Orders** .

Client may order Manufacturing Services for batches of Products only in multiples of the Minimum Order Quantities as set out in Schedule B to a Product Agreement.

**5.4 Delivery and Shipping** .

The Product will be delivered to Client after it has been manufactured and released to the Client by Patheon. Delivery of Products will be made EXW (Incoterms 2010) Patheon's shipping point unless otherwise agreed in a Product Agreement. Risk of loss or of damage to Products will remain with Patheon until Patheon loads the Products onto the carrier's vehicle for shipment at the shipping point at which time risk of loss or damage will transfer to Client. Patheon will, in accordance with Client's instructions and as agent for Client, at Client's risk, arrange for shipping to be paid by Client. Client will arrange for insurance and will select the freight carrier used by Patheon to ship Products and may monitor Patheon's shipping and freight practices as they pertain to this Agreement. Products will be transported in accordance with the Specifications.

**5.5 Invoices and Payment** .

Invoices will be sent by email to the email address given by Client to Patheon in writing. Invoices will be issued when the Product is manufactured and released by Patheon to the Client. Patheon will also submit to Client, with each shipment of Products, a duplicate copy of the invoice covering the shipment. Patheon will also give Client an invoice covering any Inventory or Components which are to be purchased by Client under Section 5.2 of this Agreement. Each invoice will, to the extent applicable, identify Client's Manufacturing Services purchase order number, Product numbers, names and quantities, unit price, freight charges, and the total amount to be paid by Client. Client will pay all undisputed invoices within [**] days after electronic receipt thereof. If any portion of an invoice is disputed, the Client will pay Patheon for the undisputed amount and the parties will use good faith efforts to reconcile the disputed amount as soon as practicable. Interest on undisputed past due accounts will accrue at [**] percent ([**]%) per month which is equal to an annual rate of [**] percent ([**]%).

## ARTICLE 6

## PRODUCT CLAIMS AND RECALLS

**6.1 Product Claims** .

(a) Product Claims . Client has the right to reject any portion of any shipment of Products that deviate from the Specifications, cGMPs, or Applicable Laws, without invalidating any remainder of the shipment. Client will inspect the Products manufactured by Patheon promptly upon receipt and will give Patheon written notice (a " **Deficiency Notice** ") of all claims for Products that deviate from the Specifications, cGMPs, or Applicable Laws, within [**] days after Client's receipt thereof (or, in the case of

any defects not reasonably susceptible to discovery upon receipt of the Product, within [**] days after discovery by Client , but not after [**] months following the expiration date of the Product , provided that any notification after the expiration date relates to an underlying event giving rise to a claim that occurred on or before the expiration date ). Should Client fail to give Patheon the Deficiency Notice within the applicable [**] day period, then the delivery will be deemed to have been accepted by Client on the [**] day after delivery or discovery, as applicable.

(b) Determination of Deficiency . Upon receipt of a Deficiency Notice, Patheon will have [**] days to advise Client by notice in writing that it disagrees with the contents of the Deficiency Notice. If Client and Patheon fail to agree within [**] days after Patheon's notice to Client as to whether any Products identified in the Deficiency Notice deviate from the Specifications, cGMPs, or Applicable Laws, then the parties will mutually select an independent laboratory to evaluate if the Products deviate from the Specifications, cGMPs, or Applicable Laws. This evaluation will be binding on the parties. If the evaluation certifies that any Products deviate from the Specifications, cGMPs, or Applicable Laws, Client may reject those Products in the manner contemplated in this Section 6.1 and Patheon will be responsible for the cost of the evaluation. If the evaluation does not so certify for any of the Products, then Client will be deemed to have accepted delivery of the Products and Client will be responsible for the cost of the evaluation.

(c) Shortages . Claims for shortages in the amount of Products shipped by Patheon will be dealt with by reasonable agreement of the parties.

(d) Product Rejection for Finished Product Specification Failure . Internal process specifications will be defined and agreed upon. If Patheon manufactures Product in accordance with the agreed upon process specifications, the batch production record, and Patheon's standard operating procedures for manufacturing, and a batch or portion of batch of Product does not meet a finished Product specification, Client will pay Patheon the applicable fee per unit for the non-conforming Product. The API in the non-conforming Product will be included in the "Quantity Converted" for purposes of calculating the "Actual Annual Yield" under Section 2.2(a).

**6.2 Product Recalls and Returns** .

(a) Records and Notice . Client shall be solely responsible for determining that a Recall of any Product is appropriate. Patheon and Client will each maintain records necessary to permit a Recall of any Products delivered to Client or customers of Client. Patheon will promptly notify Client by telephone (to be confirmed in writing) of any information which might affect the marketability, safety, quality or effectiveness of the Products or which might result in the Recall or seizure of the Products. Client will promptly notify Patheon by telephone (to be confirmed in writing) of any information Client receives which Client reasonably believes may result in the Recall or seizure of the Products. Upon receiving this notice from Client, Patheon will stop making any further shipments of any Products in its possession or control until a decision has been made whether a Recall or some other corrective action is necessary. The decision to initiate a Recall or to take some other corrective action, if any, will be made and implemented by Client. " **Recall** " will mean any action (i) by Client to recover title to or possession of quantities of the Products sold or shipped to Third Parties (including, without limitation, the voluntary withdrawal of Products from the market); or (ii) by any regulatory authorities to detain or destroy any of the Products. Recall will also include any action by either party to refrain from selling or shipping quantities of the Products to Third Parties which would be subject to a Recall if sold or shipped.

(b) Recalls . If (i) any Regulatory Authority issues a directive, order or, following the issuance of a safety warning or alert about a Product, a written request that any Product be Recalled, (ii) a court of competent jurisdiction orders a Recall, or (iii) Client determines that any Product should be Recalled or that a "Dear Doctor" letter is required relating to restrictions on the use of any Product, Patheon will co-operate as reasonably required by Client, having regard to all applicable laws and regulations.

(c) Product Returns . Client will have the responsibility for handling customer returns of the Products. Patheon will give Client any assistance that Client may reasonably require to handle the returns.

**6.3 Patheon's Responsibility for Defective and Recalled Products .**

(a) Defective Product . If Client rejects Products under Section 6.1 and the deviation is determined to have arisen from Patheon's failure to provide the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, Patheon will credit Client's account for Patheon's invoice price for the defective Products. If Client previously paid for the defective Products, Patheon will promptly, at Client's election, either: (i) refund the invoice price for the defective Products; (ii) offset the amount paid against other amounts due to Patheon hereunder; or (iii) replace the Products with conforming Products, (provided that Patheon is able to manufacture replacement Product at the same Manufacturing Site as that of the rejected Products), without Client being liable for payment therefor under Section 3.1, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. For greater certainty, Patheon's responsibility for any loss of Active Materials in defective Product will be captured and calculated in the Active Materials Yield under Section 2.2.

(b) Recalled Product . If a Recall or return results from, or arises out of, a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws, Patheon will be responsible for the documented out-of-pocket expenses of the Recall or return and will replace the Recalled or returned Products with new Products, contingent upon the receipt from Client of all Active Materials and Client-Supplied Components required for the manufacture of the replacement Products. For greater certainty, Patheon's responsibility for any loss of Active Materials in Recalled Product will be captured and calculated in the Active Materials Yield under Section 2.2. If Patheon is unable to replace the Recalled or returned Products (except where this inability results from a failure to receive the required Active Materials and Client-Supplied Components), then Client may request Patheon to reimburse Client for the price that Client paid to Patheon for Manufacturing Services for the affected Products. In all other circumstances, Recalls, returns, or other corrective actions will be made at Client's cost and expense.

(c) Except as set forth in Sections 6.3(a) and (b) above and Sections 6.4 and 6.5 below, Patheon will not be liable to Client nor have any responsibility to Client for any deficiencies in, or other liabilities associated with, any Product manufactured by it, (collectively, " **Product Claims** "). For greater certainty but not limitation, Patheon will have no obligation for any Product Claims to the extent the Product Claim solely (i) is caused by deficiencies in the Specifications, the safety, efficacy, or marketability of the Products or any distribution thereof, (ii) results from a defect in a Component that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications and not otherwise due to Patheon's failure to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws or wilful misconduct prior to use of the applicable Component in the performance of the Manufacturing Services, (iii) results from a defect in the Active Materials, Client-Supplied Components or Components supplied by a Client designated additional source that is not reasonably discoverable by Patheon using the test methods set forth in the Specifications and not otherwise due to Patheon's failure to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws or wilful misconduct, (iv) is caused by actions of Client or Third Parties occurring after the Product is shipped by Patheon under Section 5.4, (v) is due to packaging design or labelling defects or omissions for which Patheon has no responsibility, or (vi) is due to any other breach by Client of its obligations under this Agreement.

**6.4 Disposition of Defective or Recalled Products** .

Client will not dispose of any damaged, defective, returned, or Recalled Products for which it intends to assert a claim against Patheon without Patheon's prior written authorization to do so. Alternatively, Patheon may instruct Client to return the Products to Patheon. Patheon will bear the cost of disposition for any damaged, defective, returned or Recalled Products for which it bears responsibility under Section 6.3. In all other circumstances, Client will bear the cost of disposition, including all applicable fees for Manufacturing Services, for any damaged, defective, returned, or Recalled Products.

**6.5 Healthcare Provider or Patient Questions and Complaints** .

Client will have the sole responsibility for responding to questions and complaints from its customers. Questions or complaints received by Patheon from Client's customers, healthcare providers or patients will be promptly referred to Client. Patheon will co-operate as reasonably required to allow Client to determine the cause of and resolve any questions and complaints. This assistance will include follow-up investigations, including testing. In addition, Patheon will give Client all agreed upon information that will enable Client to respond properly to questions or complaints about the Products as set forth in the Quality Agreement. Unless it is determined that the cause of the complaint resulted from a failure by Patheon to perform the Manufacturing Services and supply Product in accordance with the Specifications, cGMPs, and Applicable Laws, all costs incurred under this Section 6.5 will be borne by Client.

**6.6 Shortage of Supply; Supply Failure** .

(a) Patheon shall notify Client immediately upon becoming aware of an event that would render Patheon unable to supply any quantity of the Product required to be supplied hereunder. If the event is caused by a breach of this Agreement by Patheon, Patheon shall use commercially reasonable efforts to remedy such shortage, including allocating a pro-rata portion of any available materials or capacity based on the production of the Product for Client and Patheon's other uses according to the relative quantities used by each during the immediately preceding [**] prior to such shortage without regard to price; provided, however, that Client shall receive treatment proportionately no less favorable than any of Patheon's other supply arrangements with respect to allocation of such materials or capacity.

(b) If there is a Supply Deficiency, then, if requested by Client, Patheon shall promptly take one (1) or more of the following steps to remedy the Supply Deficiency, in the following order of preference whenever practicable (i.e., with highest preference given to the remedy in paragraph (i) and the lowest preference given to the remedy in paragraph (iv)): (i) increase the length of a manufacturing campaign at the Manufacturing Site in order to manufacture for Client additional batches that are manufactured in accordance with the Specifications, cGMPs and Applicable Laws to remedy the Supply Deficiency (each such Batch, a " **Deficiency Cure Batch** "); (ii) utilize any appropriately qualified capacity at the Manufacturing Site which is not then contractually committed to the performance of services for Third Party customers during the applicable quarter to manufacture for Client Deficiency Cure Batches; (iii) coordinate and cooperate with Client to re-schedule manufacture batches of Product ordered hereunder in order to maximize Patheon's ability to manufacture for Client Deficiency Cure Batches while minimizing the disruption of manufacture at the Manufacturing Site then in force and any contractual commitments to Third P arty customers; and (iv) use commercially reasonable efforts to remedy the Supply Deficiency in subsequent quarters, if any, by utilizing and dedicating excess capacity not contractually committed to Third Party customers to manufacture Deficiency Cure Batches and to reserve such capacity for Client's requirements until the issues surrounding the Supply Deficiency have been remedied. For purposes of this Section 6.6(b), **"Supply Deficiency** " shall mean the difference between the Product manufactured under Firm Order(s) accepted by Patheon that meet the requirements under this Agreement and the number specified in such Firm Order(s) in the event that Patheon has failed to manufacture the quantities specified in the relevant Firm Order(s) solely as a result of a breach of this Agreement by Patheon (but excluding any failure that relates to a Shortfall provided that Patheon complies with its obligations in Section 2.2(c)).

(c) If Patheon delivers less than [**] percent ( [**] %) of the Product ordered by Client pursuant to a Firm Order within [**] days of the agreed-upon D elivery D ate(s) in any Rolling Forecast in any [**] periods (calculated on the basis of the aggregate quantity of Product delivered during [**] periods) solely as a result of a breach of this Agreement by Patheon but excluding any failure that relates to a Shortfall provided that Patheon complies with its obligations in Section 2.2(c) ( " **Supply Failure** " ), then (x) obligations relating to the minimum purchase and binding portion of such forecast will cease to apply with respect to the current Rolling Forecast and any subsequent Rolling Forecast and (y) Client shall have the right to purchase all of its requirements of the Product from an alternative supplier, in each case until Patheon has satisfied the requirements of sub-section (i), below. For purposes of this definition, any Product that is non-conforming Product at the time of delivery as a result of a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, or Applicable Laws shall be considered not delivered.

(i) If, after a Supply Failure, Patheon delivers [**]% of the aggregate quantity of Product ordered by Client under Firm Orders within [**] days of the agreed-upon delivery date(s) during a consecutive [**] period as determined by the Firm Order date (the " **Cure Period** "), the minimum purchase and binding portion obligations will be re-instated, beginning with the first Rolling Forecast delivered by Client after the Cure Period.

(ii) Should Patheon fail to remedy any Supply Failure during the Cure Period, Client may in its sole discretion, transfer any and all volume of the Product previously reflected in the binding portion of its forecast to an alternate supplier.

(d) Section 6.6 shall not apply if the Supply Deficiency, Supply Failure or any other Product shortage is caused by a Force Majeure Event or is attributable in whole or in part to Client or its contractors or to a breach of this Agreement by Client.

**6.7 Alternative Supplier .**

(a) Subject to the provisions of Section 2.1 , nothing in this Agreement shall preclude Client, at anytime during this Agreement, from qualifying an alternate supplier to provide manufacturing services for Product(s); *provided, however* , that Client otherwise complies all of its obligations under this Agreement.

(b) If Client exercises its option to transfer the manufacture of the Product to an alternate supplier in accordance with Section 6.6(c) Patheon shall reasonably assist Client for a reasonable period of time in such transfer, including providing all Product data and any non-Confidential Information regarding the manufacturing process provided that Client will reimburse Patheon for its fees and all documented costs and out-of-pocket expenses incurred in connection with such assistance (Patheon would provide a quotation for the services that Client requires pursuant to this Section 6.7 and on acceptance by Client of the same and signature by the parties, Patheon will provide the services stated therein).

**6.8 Sole Remedy** .

Except for the indemnity set forth in Section 10.3 and subject to the limitations set forth in Sections 10.1 and 10.2, the remedies described in this Article 6 will be Client's sole remedy for any failure by Patheon to provide the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws.

## ARTICLE 7

## CO-OPERATION

**7.1 Quarterly Review** .

Each party will forthwith upon execution of this Agreement appoint one of its employees to be a relationship manager responsible for liaison between the parties. The relationship managers will meet not less than quarterly to review the current status of the business relationship and manage any issues that have arisen.

**7.2 Governmental Agencies** .

Subject to Section 7.8, each party may communicate with any governmental agency, including but not limited to governmental agencies responsible for granting Regulatory Approval for the Products, regarding the Products if, in the opinion of that party's counsel, the communication is necessary to comply with the requirements of any law, governmental order or regulation; provided that, to the extent reasonably practicable, Patheon shall provide Client prompt notice upon its determination and discuss with Client such proposed communication. Unless, in the reasonable opinion of its counsel, there is a legal prohibition against doing so, Patheon will permit Client to accompany and take part in any communications with the agency, and to receive copies of all communications from the agency.

**7.3 Records and Accounting by Patheon** .

Patheon will keep records of the Manufacturing Services, including the manufacture, testing, and shipping of the Products, and retain samples of the Products as are necessary to comply with cGMP and other manufacturing regulatory requirements applicable to Patheon, as well as to assist with resolving Product complaints and other similar investigations. Unless otherwise agreed to in the Quality Agreement, copies of the records and samples will be retained for one year following the date of Product expiry, or longer if required by law or regulation, following which time Client will be contacted in writing concerning the delivery and destruction of the documents and/or samples of Products. Patheon reserves the right to destroy or return to Client, at Client's sole expense, any document or samples for which the retention period has expired if Client fails to arrange for destruction or return within [**] days of receipt of written notice from Patheon. Client is responsible for retaining samples of the Products necessary to comply with the legal/regulatory requirements applicable to Client.

**7.4 Inspection** .

Client may inspect Patheon reports and records relating to the Product(s) and this Agreement during normal business hours and with reasonable advance notice, but a Patheon representative must be present during the inspection.

**7.5 Access** .

Patheon will give Client reasonable access at agreed times to the areas of the Manufacturing Site in which the Products are manufactured, stored, handled, or shipped to permit Client to verify that the Manufacturing Services are being performed in accordance with this Agreement, the Specifications, cGMPs, and Applicable Laws. But, with the exception of "for-cause" audits, Client or designee will be limited each Year to [**], each audit lasting no more than [**] days, and involving no more than [**]. Client may request additional cGMP-type audits, additional audit days, or the participation of additional auditors subject to payment to Patheon of a fee of $[**] / EUR [**] for each additional audit day and $[**] / EUR [**] per audit day for each additional auditor. The right of access set forth in Sections 7.4 and 7.5 will not include a right to access or inspect Patheon's financial records. For each Product,

Patheon will support the first pre- Approval Inspection by the FDA (" **PAI** ") and all subsequent routine non-PAI FDA inspections or equivalent routine non-PAI regulatory inspection for other jurisdictions (where applicable) and provide a copy of the resulting report at no cost. Additional PAI s or equivalent support will be subject to additional fees.

**7.6 Notification of Regulatory Inspections** .

Patheon will notify Client within [**] of any inspections by any Authority or other governmental agency involving the Products. Patheon will also notify Client of receipt of any form 483's or warning letters or any other significant regulatory action which Patheon's quality assurance group determines could impact the regulatory status of the Products and shall promptly provide Client with Patheon's plan to correct any deficiencies identified by such Authority (which may be redacted to protect any confidential information of Patheon or any Third Party) and diligently pursue such corrections.

**7.7 Reports** .

Upon Client's reasonable request, Patheon will supply all Product data in its control, including release test results, complaint test results, and all investigations (in manufacturing, testing, and storage), that Client reasonably requires in order to complete any filing under any applicable regulatory regime, including any Annual Report that Client is required to file with the FDA. Any additional data or report requested by Client beyond the scope of cGMPs and customary FDA, EMA or Japanese PMDA requirements will be subject to an additional fee to be agreed upon between Patheon and the Client.

**7.8 Regulatory Filings** .

(a) Regulatory Authority . Client will have the sole responsibility at Client's expense for filing all documents with all Regulatory Authorities and taking any other actions that may be required for the receipt and/or maintenance of Regulatory Authority approval for the commercial manufacture, distribution and sale of the Products (" **Regulatory Approval** "). Patheon will assist Client, to the extent consistent with Patheon's obligations under this Agreement, to obtain Regulatory Authority approval for the commercial manufacture, distribution and sale of all Products as quickly as reasonably possible.

(b) Verification of Data . Prior to filing any documents with any Regulatory Authority that incorporate data generated by Patheon, Client will give Patheon a copy of the documents incorporating this data to give Patheon the opportunity to verify the accuracy and regulatory validity of those documents as they relate to Patheon generated data. Patheon requires [**] days to perform this review but the parties may agree to a shorter time for the review as needed.

(c) Verification of CTD . Prior to filing with any Regulatory Authority any documentation which is or is equivalent to the Quality Module (Drug Product Section) of the Common Technical Document (all such documentation herein referred to as " **CTD** ") related to any Marketing Authorization, such as a US New Drug Application, US Abbreviated New Drug Application, US Biologics Licence Application, or EU Marketing Authorisation Application, Client will give Patheon a copy of the CTD as well as all supporting documents which have been relied upon to prepare the CTD. This disclosure will permit Patheon to verify that the CTD accurately describes the validation or scale-up work that Patheon has performed and the manufacturing processes that Patheon will perform under this Agreement. Patheon requires [**] days to perform this review but the parties may agree to a shorter time for the review as needed. Client will give Patheon copies of all relevant filings which contain CTD information regarding the Product.

(d) Deficiencies . If, in Patheon's sole discretion, acting reasonably, Patheon determines that any of the information given by Client under clauses (b) and (c) above is inaccurate or deficient in any

manner whatsoever (the " **Deficiencies** "), Patheon will promptly (within [**] business days of discovery ) notify Client in writing of the Deficiencies. The parties will work together to have the Deficiencies resolved prior to the date of filing of the relevant application and in any event before any pre-approval inspection or before the Product is placed on the market if a pre-approval inspection is not performed .

(e) Client Responsibility . For clarity, the parties agree that in reviewing the documents referred to in clause (b) above, Patheon's role will be limited to verifying the accuracy of the description of the work undertaken or to be undertaken by Patheon. Subject to the foregoing, Patheon will not assume any responsibility for the accuracy of any application for receipt of an approval by a Regulatory Authority. The Client is solely responsible for the preparation and filing of the application for approval by the Regulatory Authority and any relevant costs will be borne by the Client.

(f) Inspection by Regulatory Authorities . If Client does not give Patheon the documents requested under subsections (b) and (c) above within the time specified and if Patheon reasonably believes that Patheon's standing with a Regulatory Authority may be jeopardized, Patheon (i) shall so notify Client in writing and (ii) may, in its sole discretion, upon written notice to Client, delay or postpone any inspection by the Regulatory Authority with respect to the Product that is the subject of such documents until Patheon has reviewed the requested documents and is satisfied with their contents.

(g) Pharmacovigilance. Client will be responsible, at its expense, for all pharmacovigilance obligations for the Products pursuant to Applicable Laws; Patheon shall provide Client any safety information it receives related to the Product on a prompt basis. Unless required by Applicable Law, Client will not be obliged to exchange with the other party any information or data which it compiles pursuant to pharmacovigilance obligations or activities.

(h) No Patheon Responsibility . Patheon will not assume any responsibility for the accuracy or cost of any application for Regulatory Approval. If a Regulatory Authority, or other governmental body, requires Patheon to incur fees, costs or activities in relation to the Products which Patheon considers unexpected and extraordinary, then Patheon will notify Client in writing and the parties will discuss in good faith appropriate mutually acceptable actions, including fee/cost sharing, or termination of all or any part of this Agreement.

## ARTICLE 8

## TERM AND TERMINATION

**8.1 Initial Term** .

This Agreement will become effective as of the Effective Date and will continue until December 31, 2022 (the " **Initial Term** "), unless terminated earlier by one of the parties in accordance herewith. This Agreement will automatically renew after the Initial Term for successive terms of two Years each if there is a Product Agreement in effect, unless either party gives written notice to the other party of its intention to terminate this Agreement at least eighteen (18) months prior to the end of the then current term. In any event, the legal terms and conditions of this Agreement will continue to govern any Product Agreement in effect as provided in Section 1.2. Each Product Agreement will have an initial term of two (2) Years from the start of commercial manufacture at the Manufacturing Site for the Product unless the parties agree to a different number of Years in the applicable Product Agreement (each, an " **Initial Product Term** "). Product Agreements will automatically renew after the Initial Product Term for successive terms of two Years each unless either party gives written notice to the other party of its intention to terminate the Product Agreement at least eighteen (18) months prior to the end of the then current term.

**8.2 Termination for Cause** .

(a) Either party at its sole option may terminate this Agreement or a Product Agreement upon written notice where the other party has failed to remedy a material breach of any of its representations, warranties, or other obligations under this Agreement or the Product Agreement within [**] days following receipt of a written notice (the " **Remediation Period** ") of the breach from the aggrieved party that expressly states that it is a notice under this Section 8.2(a) (a " **Breach Notice** "). The aggrieved party's right to terminate this Agreement or a Product Agreement under this Section 8.2(a) may only be exercised for a period of [**] days following the expiry of the Remediation Period (where the breach has not been remedied). The termination of a Product Agreement under this Section 8.2(a) will not affect this Agreement or any other Product Agreements where there has been no material breach of the other Product Agreements.

(b) Either party at its sole option may immediately terminate this Agreement or a Product Agreement upon written notice, but without prior advance notice, to the other party if: (i) the other party is declared insolvent or bankrupt by a court of competent jurisdiction; (ii) a voluntary petition of bankruptcy is filed in any court of competent jurisdiction by the other party; or (iii) this Agreement or a Product Agreement is assigned by the other party for the benefit of creditors.

(c) Client may terminate a Product Agreement upon thirty (30) days' prior written notice if any Authority takes any action, or raises any objection, that prevents Client from importing, exporting, purchasing, or selling the Product. But if this occurs, Client must still fulfill all of its obligations under Section 8.4 below and under any Capital Equipment Agreement regarding the Product.

(d) Patheon may terminate this Agreement or a Product Agreement upon six months' prior written notice if Client assigns under Section 13.6 any of its rights under this Agreement or a Product Agreement to an assignee that, in the opinion of Patheon acting reasonably, is a Patheon Competitor or is not a creditworthy substitute for Client.

**8.3 Product Discontinuation** .

Client will use reasonable efforts to give Patheon at least [**] advance written notice if it intends to no longer order Manufacturing Services for a Product due to the Product's discontinuance in the market.

**8.4 Obligations on Termination** .

(a) If a Product Agreement is completed, expires, or is terminated in whole or in part for any reason, then:

(i) Subject to Article 6, Client will take delivery of and pay for all undelivered Products that are manufactured and/or packaged under a Firm Order in accordance with this Agreement, at the Price in effect at the time the Firm Order was placed;

(ii) Client will purchase, at Patheon's cost (including all costs incurred by Patheon for the purchase and handling of the Inventory), the Inventory applicable to the Products which was purchased, produced or maintained by Patheon as reasonably necessary to fill Firm Orders or in accordance with Section 5.2;

(iii) Client will satisfy the purchase price payable under Patheon's orders with suppliers of Components, if the orders were made by Patheon in reliance on Firm Orders or in accordance with Section 5.2;

(iv) Client acknowledges th at no Patheon Competitor will be permitted access to the Manufacturing Site ; and

(v) Client will make commercially reasonable efforts, at its own expense, to remove from Patheon site(s), within [**] days, all unused Active Material and Client-Supplied Components, all applicable Inventory and Materials (whether current or obsolete), supplies, undelivered Product, chattels, equipment or other moveable property owned by Client, related to the Agreement and located at a Patheon site or that is otherwise under Patheon's care and control (" **Client Property** "). If Client fails to remove the Client Property within [**] days following the completion, termination, or expiration of the Product Agreement, Client will pay Patheon $[**] / EUR [**] per pallet, per month, one pallet minimum (except that Client will pay $[**] / EUR [**] per pallet, per month, one pallet minimum, for any of the Client Property that contains controlled substances, requires refrigeration or other special storage requirements) thereafter for storing the Client Property and will assume any third party storage charges invoiced to Patheon regarding the Client Property. Patheon will invoice Client for the storage charges as set forth in Section 5.5 of this Agreement.

(b) Upon Client's request Patheon shall reasonably assist Client for a reasonable period of time in the transfer of the manufacture to a Third Party, including providing all Product data and any non-Confidential Information regarding the manufacturing process provided that Client will reimburse Patheon for its fees and all documented costs and out-of-pocket expenses incurred in connection with such assistance (Patheon would provide a quotation for the services that Client requires pursuant to this Section 8.4(b) and on acceptance by Client of the same and signature by the parties, Patheon will provide the services stated therein.

(c) Any completion, termination or expiration of this Agreement or a Product Agreement will not affect any accrued rights or outstanding obligations or payments due prior to the completion, termination or expiration, nor will it prejudice any other remedies that the parties may have under this Agreement or a Product Agreement or any related Capital Equipment Agreement. For greater certainty, completion, termination or expiration of this Agreement or of a Product Agreement for any reason will not affect the obligations and responsibilities of the parties under Articles 10 and 11 and Sections 5.4, 5.5, 8.4, 13.1, 13.2, 13.3 , 13.16 and 13.17, all of which survive any completion, termination or expiration.

## ARTICLE 9

## REPRESENTATIONS, WARRANTIES AND COVENANTS

**9.1 Authority** .

Each party covenants, represents, and warrants that it has the full right and authority to enter into this Agreement and that it is not aware of any impediment that would inhibit its ability to perform its obligations hereunder.

**9.2 Client Warranties** .

Client covenants, represents, and warrants that:

(a) Non-Infringement .

(i) the Specifications for each of the Products are its or its Affiliate's property and that Client may lawfully disclose the Specifications to Patheon;

(ii) any Client Intellectual Property, used by Patheon in performing the Manufacturing Services according to the Specifications (A) is Client's or its Affiliate's property or Client or its Affiliate otherwise has a right to use such Client Intellectual Property, and (B) to the knowledge of Client, does not infringe any Third Party Rights;

(iii) the performance of the Manufacturing Services by Patheon for any Product under this Agreement or any Product Agreement or the use or other disposition of any Product by Patheon as may be required to perform its obligations under this Agreement or under any Product Agreement does not knowingly infringe any Third Party Rights;

(iv) there are no actions or other legal proceedings involving the Client that concerns the infringement of Third Party Rights related to any of the Specifications, or any of the Active Materials and the Components, or the sale, use, or other disposition of any Product made in accordance with the Specifications;

(b) Quality and Compliance .

(i) the Specifications for all Products conform to all applicable cGMPs and Applicable Laws;

(ii) the Products, after approval, and if labelled and manufactured in accordance with the Specifications and in compliance with applicable cGMPs and Applicable Laws may be lawfully sold and distributed in every jurisdiction in which Client markets the Products;

(iii) on the date of shipment, the API will conform to the specifications for the API that Client has given to Patheon and that the API will be adequately contained, packaged, and labelled and will conform to the affirmations of fact on the container.

**9.3 Patheon Warranties** .

Patheon covenants, represents, and warrants that:

(a) it will perform the Manufacturing Services in accordance with this Agreement, the Specifications, Master Batch Record, cGMPs, and Applicable Laws;

(b) all Product Patheon delivers to Client pursuant to this Agreement shall be transferred to Client free and clear of any liens or encumbrances of any kind provided that Client pays all invoices in accordance with Section 5.5;

(c) all Product Patheon delivers to Client pursuant to this Agreement shall, at the time of delivery, not be adulterated or misbranded as a result of a failure by Patheon to perform the Manufacturing Services in accordance with this Agreement, the Specifications, cGMPs and Applicable Laws within the meaning of adulterated or misbranded as set out in the United States *Federal Food, Drug, and Cosmetic Act* or within the meaning of all Applicable Law in which the definitions of adulteration and misbranding are substantially the same as those contained in United States *Federal Food, Drug, and Cosmetic Act* , as such act and such laws are constituted and effective at the time of delivery, and will not be an article which may not under the provisions of Sections 404 and 505 of the United States *Federal Food, Drug, and Cosmetic Act* be introduced into interstate commerce as a result of a failure by Patheon to perform the Manufacturing Services in accordance with this Agreement, the Specifications, cGMPs and Applicable Laws ;

(d) it has obtained and will remain in compliance with during the term of this Agreement, all permits, licenses and other authorizations which are required under federal, state and local laws, rules and regulations applicable to the Manufacturing Services at the Manufacturing Site;

(e) any Patheon Intellectual Property used by Patheon to perform the Manufacturing Services (i) is Patheon's or its Affiliate's property or Patheon or its Affiliate otherwise has a right to use such Patheon Intellectual Property, and (ii) to the knowledge of Patheon does not infringe any Third Party Rights. In its performance of its obligations under this Agreement, Patheon will not knowingly incorporate into the manufacturing process any Third Party Rights for which it does not have a license that permits it to do so and/or to be able to grant to Client the licenses and other rights otherwise required to be granted to Client hereunder;

(f) Patheon's performance of its obligations under this Agreement will not result in a material violation or breach of any agreement, contract, commitment or obligation to which Patheon is a party or by which it is bound and will not conflict with or constitute a default under its corporate charter or bylaws;

(g) it will not in the performance of its obligations under this Agreement use the services of any person it knows is debarred or suspended under 21 U.S.C. §335(a) or (b); and

(h) it does not currently have, and it will not hire, as an officer or an employee any person whom it knows has been convicted of a felony under the laws of the United States for conduct relating to the regulation of any drug product under the United States *Federal Food, Drug, and Cosmetic Act* .

**9.4** **Permits** .

(a) Client will be solely responsible for obtaining or maintaining, on a timely basis, any permits or other regulatory approvals for the Products or the Specifications, including, without limitation, all marketing and post-marketing approvals.

(b) Patheon will be solely responsible for and will maintain at all relevant times all governmental permits, licenses, approval, and authorities required to enable it to lawfully and properly perform the Manufacturing Services and operate the Manufacturing Site.

**9.5 No Warranty** .

**NEITHER PARTY MAKES ANY WARRANTY OR CONDITION OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, OTHER THAN THOSE EXPRESSLY SET FORTH IN THIS AGREEMENT. NEITHER PARTY MAKES ANY WARRANTY OR CONDITION OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY WARRANTY OR CONDITION OF MERCHANTABILITY FOR THE PRODUCTS.**

## ARTICLE 10

## REMEDIES AND INDEMNITIES

**10.1 Consequential and Other Damages** .

Except with respect to a breach of the confidentiality and non-use obligations of Article 11, under no circumstances whatsoever will either party be liable to the other in contract, tort, negligence, breach of statutory duty, or otherwise for (i) any (direct or indirect) loss of profits, of production, of anticipated savings, of business, or goodwill or (ii) any reliance damages, including but not limited to costs or expenditures incurred to evaluate the viability of entering into this Agreement or to prepare for performance under this Agreement, or (iii) for any other liability, damage, costs, or expense of any kind incurred by the other party of an indirect or consequential nature, including regardless of any notice of the possibility of these damages.

**10.2 Limitation of Liability** .

(a) Active Materials . Except as expressly set forth in Section 2.2, under no circumstances will Patheon be responsible for any loss or damage to the Active Materials. Patheon's maximum responsibility for loss or damage to the Active Materials will not exceed the Maximum Credit Value set forth in Schedule D of a Product Agreement.

(b) Defective or Recalled Product . Patheon's maximum aggregate liability to Client for any obligation to (i) refund, offset or replace any defective Product under Section 6.3(a) or (ii) replace any recalled Products under Section 6.3(b), will not exceed [**]% of the Price for the defective or recalled Product as applicable. This Section 10.2(b) will not be subject to Section 10.2(c).

(c) Maximum Liability . Except as stated in Section 10.2(b), Patheon's maximum aggregate liability to Client in any Year under this Agreement or any Product Agreement for any reason whatsoever, including, without limitation, any liability arising under Section 6.3(b) relating to the expenses of a Recall or Product return, Section 2.2 or Section 10.3 hereof or resulting from any and all breaches of its representations, warranties, or any other obligations under this Agreement or any Product Agreement (but excluding Patheon's obligations described in Section 10.2(b)) will not exceed on a per Product basis [**]% of the revenue paid by Client to Patheon (and its Affiliates) per Year under the applicable Product Agreement during the Year in which the underlying event occurred that gave rise to the liability (e.g. the date of the incident or manufacture).

(d) Death, Personal Injury and Fraudulent Misrepresentation . Nothing contained in this Agreement shall act to exclude or limit either party's liability for personal injury or death caused by the negligence of either party or fraudulent misrepresentation.

**10.3 Patheon Indemnity** .

Patheon agrees to defend, indemnify and hold harmless Client, its Affiliates and each of their officers, employees, and agents (" **Client Indemnitees** ") against all losses, damages, costs, claims,

demands, judgments and liability to, from and in favour of T hird P arties resulting from or arising out of: (i) any claim of personal injury or property damage to the extent that the injury or damage is the result of the negligence or wilful misconduct of any Patheon Indemnitee; or (ii) any claim of personal injury or property damage to the extent that the injury or damage is the result of a breach of this Agreement by Patheon, including a failure by Patheon to perform the Manufacturing Services in accordance with the Specifications, cGMPs, and Applicable Laws , except to the extent th at the losses, damages, costs, claims, demands, judgments , and lia bility are due to the negligence or wrongful act(s) of any Client Indemnitee .

**10.4 Client Indemnity** .

Client agrees to defend, indemnify and hold harmless Patheon, its Affiliates and each of their officers, employees, and agents (" **Patheon Indemnitees** ") against all losses, damages, costs, claims, demands, judgments and liability to, from and in favour of Third Parties resulting from, or relating to (i) any claim of infringement or alleged infringement of any Third Party Rights arising from the manufacture, storage, promotion, labeling, marketing, distribution, use or sale of Product, or (ii) any claim of personal injury or property damage to the extent that the injury or damage arises other than from a breach of the relevant agreement by Patheon, including, without limitation, any representation or warranty contained herein, except to the extent that the losses, damages, costs, claims, demands, judgments, and liability are due to the negligence or wrongful act(s) of any Patheon Indemnitee.

**10.5 Indemnification Procedure** .

A party that makes a claim for indemnification under this Article 10 shall promptly notify the other party (the " **Indemnitor** ") in writing of any action, claim or other matter in respect of which such party, intends to claim such indemnification; *provided, however,* that failure to provide such notice within a reasonable period of time shall not relieve the Indemnitor of any of its obligations hereunder except to the extent the Indemnitor is prejudiced by such failure. The indemnified party shall permit the Indemnitor, at its discretion, to settle any such action, claim or other matter, and the indemnified party agrees to the complete control of such defense or settlement by the Indemnitor. Notwithstanding the foregoing, the Indemnitor shall not enter into any settlement that would adversely affect the indemnified party's rights hereunder, or impose any obligations on the indemnified party in addition to those set forth herein, in order for it to exercise such rights, without the indemnified party's prior written consent, which shall not be unreasonably withheld or delayed. No such action, claim or other matter shall be settled without the prior written consent of the Indemnitor, which shall not be unreasonably withheld or delayed. The indemnified party shall fully cooperate with the Indemnitor and its legal representatives in the investigation and defense of any action, claim or other matter covered by the indemnification obligations of this Article 10. The indemnified party shall have the right, but not the obligation, to be represented in such defense by counsel of its own selection and at its own expense.

**10.6 Reasonable Allocation of Risk** .

This Agreement (including, without limitation, this Article 10) is reasonable and creates a reasonable allocation of risk for the relative profits the parties each expect to derive from the Products. Patheon assumes only a limited degree of risk arising from the manufacture, distribution, and use of the Products because Client has developed and holds the marketing approval for the Products, Client requires Patheon to manufacture and label the Products strictly in accordance with the Specifications, and Client, not Patheon, is best positioned to inform and advise potential users about the circumstances and manner of use of the Products.

## ARTICLE 11

## CONFIDENTIALITY

**11.1 Confidential Information** .

**"Confidential Information"** means any non-public information disclosed by the Disclosing Party to the Recipient (whether disclosed in oral, written, electronic or visual form) that is confidential or proprietary including, without limitation, information relating to the Disclosing Party's patent and trademark applications, process designs, process models, drawings, plans, designs, data, databases and extracts therefrom, formulae, methods, know-how and other intellectual property, its clients or client confidential information, finances, marketing, products and processes and all price quotations, manufacturing or professional services proposals, information relating to composition, proprietary technology, and all other information relating to manufacturing capabilities and operations. In addition, all analyses, compilations, studies, reports or other documents prepared by any party's Representatives containing the Confidential Information will be considered Confidential Information. Samples or materials provided hereunder as well as any and all information derived from the approved analysis of the samples or materials will also constitute Confidential Information. The terms of this Agreement shall be deemed the Confidential Information of both parties. For the purposes of this ARTICLE 11, a party or its Representative receiving Confidential Information under this Agreement is a " **Recipient** ," and a party or its Representative disclosing Confidential Information under this Agreement is the " **Disclosing Party** ."

**11.2 Use of Confidential Information** .

The Recipient will use the Confidential Information of the Disclosing Party solely for the purpose of meeting its obligations under this Agreement or exercising its rights under this Agreement. The Recipient will keep the Confidential Information of the Disclosing Party confidential and will not disclose such Confidential Information to any Third Party in any manner whatsoever, in whole or in part, other than to those of its Representatives who (i) have a need to know the Confidential Information for the purpose of this Agreement; (ii) have been advised of the confidential nature of the Confidential Information and (iii) have obligations of confidentiality and non-use to the Recipient no less restrictive than those of this Agreement. Recipient will protect the Confidential Information of the Disclosing Party disclosed to it hereunder by using reasonable precautions to prevent the unauthorized disclosure, dissemination or use of such Confidential Information, which precautions will in no event be less than those exercised by Recipient with respect to its own confidential or proprietary information of a similar nature.

**11.3 Exclusions** .

The obligations of confidentiality and non-use will not apply to the extent that the Recipient can establish that the information:

(a) is or becomes publicly known through no breach of this Agreement or fault of the Recipient or its Representatives;

(b) is in the Recipient's possession at the time of disclosure by the Disclosing Party other than as a result of the Recipient's breach of any legal obligation;

(c) is or becomes known to the Recipient on a non-confidential basis through disclosure by sources, other than the Disclosing Party, having the legal right to disclose the Confidential Information, provided that the other source is not known by the Recipient to be bound by any obligations (contractual, legal, fiduciary, or otherwise) of confidentiality to the Disclosing Party with respect to the Confidential Information;

(d) is independently developed by the Recipient without use of or reference to the Disclosing Party's Confidential Information as evidenced by Recipient's contemporaneous written records; or

(e) is expressly authorized for release by the written authorization of the Disclosing Party.

Any combination of information which comprises part of the Confidential Information is not exempt from the obligations of confidentiality merely because individual parts of that Confidential Information were publicly known, in the Recipient's possession, or received by the Recipient, unless the combination itself was publicly known, in the Recipient's possession, or received by the Recipient.

**11.4 Photographs and Recordings** .

Neither party will take any photographs or videos of the other party's facilities, equipment or processes, nor use any other audio or visual recording equipment (such as camera phones) while at the other party's facilities, without that party's express written consent; provided, however, that Client may photograph or video the Product at any Patheon facility provided that any photograph or video is treated as Confidential Information of Patheon.

**11.5 Permitted Disclosure; Publicity** .

(a) Notwithstanding any other provision of this Agreement, the Recipient may disclose Confidential Information of the Disclosing Party to the extent required, as advised by counsel, in response to a valid order of a court or other governmental body or as required by law, regulation or stock exchange rule; provided that (i) the Recipient will advise the Disclosing Party in advance of the disclosure to the extent practicable and permissible by the order, law, regulation or stock exchange rule and any other applicable law, (ii) will reasonably cooperate with the Disclosing Party, at the Disclosing Party's expense, if required, in seeking an appropriate protective order or other remedy, and (iii) will otherwise continue to perform its obligations of confidentiality set out herein. If any public disclosure is required by law, the parties will consult concerning the form of announcement prior to the public disclosure being made.

(b) All publicity, press releases and other announcements relating to this Agreement shall be reviewed in advance by, and subject to the approval of, both parties (which approval shall not be unreasonably withheld); *provided, however,* that either party may, to the extent required (i) disclose the terms of this Agreement (with appropriate redactions as described below) insofar as required to comply with applicable securities laws, *provided* that in the case of such disclosures the Party proposing to make such disclosure notifies the other Party reasonably in advance of such disclosure and cooperates to minimize the scope and content of such disclosure, and (ii) disclose the terms of this Agreement to such party's professional advisors or existing or potential licensees, investors, acquirers, or merger candidates who are bound by obligations of confidentiality and non-use consistent with those set forth herein. The failure of a Party to respond in writing to a publication proposal from the other party within [**] working days of such party's receipt of such publication shall be deemed as such party's approval of such publication as received by such party. Each party agrees that it shall cooperate fully and in a timely manner with the other with respect to any disclosures to the Securities and Exchange Commission and any other governmental or regulatory agencies, including requests for confidential treatment of Confidential Information of either party included in any such disclosure. For each such disclosure, (a) the filing party will provide the other party at least [**] business days to review a draft redacted version of this Agreement, and (b) both Parties shall work together in good faith to agree on the disclosure to be made, having due and proper regard to their legal obligations; provided that the filing party shall ultimately retain control over what information to disclose to any securities authority or stock exchange. Each filing party shall use reasonable efforts to seek confidential treatment for terms proposed to be redacted.

**11.6 Marking** .

The Disclosing Party agrees to use reasonable efforts to summarize in writing the content of any oral disclosure or other non-tangible disclosure of its Confidential Information within [**] days of the disclosure, but failure to provide this summary will not affect the nature of the Confidential Information disclosed if the Confidential Information was identified as confidential or proprietary when disclosed orally or in any other non-tangible form.

**11.7 Return of Confidential Information** .

Upon the written request of the Disclosing Party, the Recipient will promptly return the Confidential Information to the Disclosing Party or, if the Disclosing Party directs, destroy all Confidential Information disclosed in or reduced to tangible form including any copies thereof and any summaries, compilations, analyses or other notes derived from the Confidential Information except for one copy which may be maintained by the Recipient for its records. The retained copy will remain subject to all confidentiality provisions contained in this Agreement.

**11.8 Remedies** .

The parties acknowledge that monetary damages may not be sufficient to remedy a breach by either party of this Agreement and agree that the non-breaching party will be entitled to seek specific performance, injunctive and/or other equitable relief to prevent breaches of this Agreement and to specifically enforce the provisions hereof in addition to any other remedies available at law or in equity. These remedies will not be the exclusive remedies for breach of this Agreement but will be in addition to any and all other remedies available at law or in equity.

**11.9 Confidentiality Term** .

All obligations of confidentiality and non-use imposed upon the parties under this Agreement shall expire [**] years after the expiration or earlier termination of this Agreement; *provided, however,* that Confidential Information which constitutes the trade secrets of a party (and is labelled as a trade secret or is otherwise identified in writing as being a trade secret at the time of disclosure or within [**] days thereafter) shall be kept confidential indefinitely, subject to the limitations set forth in Sections 11.3 and 11.5.

## ARTICLE 12

## DISPUTE RESOLUTION

**12.1 Commercial Disputes** .

(a) If any dispute arises out of this Agreement or any Product Agreement (other than a dispute under Section 6.1(b) or a Technical Dispute, as defined herein), the parties will first try to resolve it amicably. In that regard, any party may send a notice of dispute to the other, and each party will appoint, within [**] Business Days from receipt of the notice of dispute, a single representative having full power and authority to resolve the dispute. The representatives will meet as necessary in order to resolve the dispute. If the representatives fail to resolve the matter within [**] from their appointment, or if a party fails to appoint a representative within the [**] Business Day period set forth above, the dispute will immediately be referred to the Chief Operating Officer (or another officer as he/she may designate) of each party who will meet and discuss as necessary to try to resolve the dispute amicably within [**] days of referral of the matter to the Chief Operating Officer or his/her designee. Should the parties fail to reach a resolution under this Section 12.1(a), the dispute will be referred to a court of competent jurisdiction in accordance with Section 13.17.

**12.2 Technical Dispute Resolution** .

If a dispute arises (other than disputes under Sections 6.1(b) or 12.1) between the parties that is exclusively related to technical aspects of the manufacturing, packaging, labelling, quality control testing, handling, storage, or other activities under this Agreement (a " **Technical Dispute** "), the parties will make reasonable efforts to resolve the dispute by amicable negotiations. In that regard, senior representatives of each party will, as soon as possible and in any event no later than [**] Business Days after a written request from either party to the other, meet in good faith to resolve any Technical Dispute. If, despite this meeting, the parties are unable to resolve a Technical Dispute within a reasonable time, and in any event within [**] Business Days of the written request, the Technical Dispute will, at the request of either party, be referred for determination to an expert in accordance with Exhibit A. If the parties cannot agree that a dispute is a Technical Dispute, Section 12.1 will prevail. For greater certainty, the parties agree that the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

## ARTICLE 13

## MISCELLANEOUS

**13.1 Inventions** .

(a) For the term of this Agreement, Client hereby grants to Patheon a non-exclusive, paid-up, royalty-free, non-transferable license of Client's Intellectual Property which Patheon must use in order to perform the Manufacturing Services for Client in accordance with this Agreement.

(b) All Client Intellectual Property will be the exclusive property of Client. Patheon hereby assigns, and to the extent it cannot presently assign, will assign, to Client all of Patheon's and its Affiliates' worldwide right, title and interest, if any, in Client Intellectual Property. Patheon shall provide reasonable assistance to Client in securing for Client any patents, copyrights or other proprietary rights in such Client Intellectual Property, and shall take such reasonable actions and execute such documents as Client may reasonably request in connection with providing such assistance or otherwise to vest in Client all right, title and interest in such Inventions, including without limitation any and all applications, assignments or other instruments each of the foregoing at the cost of Client.

(c) All Patheon Intellectual Property will be the exclusive property of Patheon. Patheon hereby grants to Client a perpetual, irrevocable, non-exclusive, paid-up, royalty-free, transferable license to use the Patheon Intellectual Property used by Patheon to perform the Manufacturing Services to enable Client to manufacture the Product(s).

(d) Each party will be solely responsible for the costs of filing, prosecution, and maintenance of patents and patent applications on its own Inventions.

(e) Patheon will give the Client written notice, as promptly as practicable, of all Inventions which can reasonably be deemed to constitute improvements or other modifications of the Products or processes or technology owned or otherwise controlled by Client .

**13.2 Intellectual Property** .

Neither party has, nor will it acquire, any interest in any of the other party's Intellectual Property unless otherwise expressly agreed to in writing. Neither party will use any Intellectual Property of the other party, except as specifically authorized by the other party or as required for the performance of its obligations under this Agreement.

**13.3 Insurance** .

Each party will maintain commercial general liability insurance, including blanket contractual liability insurance covering the obligations of that party under this Agreement through the term of this Agreement and for a period of [**] thereafter. This insurance will have policy limits of not less than (i) EUR [**] for each occurrence for personal injury or property damage liability; and (ii) EUR [**] in the aggregate per annum for product and completed operations liability. If requested, each party will give the other a certificate of insurance evidencing the above and showing the name of the issuing company, the policy number, the effective date, the expiration date, and the limits of liability. If a party is unable to maintain the insurance policies required under this Agreement through no fault of its own, then the party will forthwith notify the other party in writing and the parties will in good faith negotiate appropriate amendments to the insurance provision of this Agreement in order to provide adequate assurances.

**13.4 Independent Contractors** .

The parties are independent contractors and this Agreement and any Product Agreement will not be construed to create between Patheon and Client any other relationship such as, by way of example only, that of employer-employee, principal agent, joint-venturer, co-partners, or any similar relationship, the existence of which is expressly denied by the parties.

**13.5 No Waiver** .

Either party's failure to require the other party to comply with any provision of this Agreement or any Product Agreement will not be deemed a waiver of the provision or any other provision of this Agreement or any Product Agreement.

**13.6 Assignment** .

(a) Patheon may not assign this Agreement or any Product Agreement or any of its associated rights or obligations without the written consent of Client. Further it is specifically agreed that Patheon may subcontract any part of the Manufacturing Services under a Product Agreement to any of its Affiliates; provided that such Affiliate is identified in the applicable Product Agreement. Patheon will remain solely liable to Client for its obligations under this Agreement, and for the obligations of the applicable Affiliate of Patheon under the Quality Agreement, if the Manufacturing Services are subcontracted.

(b) Subject to Section 8.2(d), Client may assign this Agreement or any Product Agreement or any of its associated rights or obligations without approval from Patheon. But Client will give Patheon prior written notice of any assignment, any assignee will covenant in writing with Patheon to be bound by the terms of this Agreement or the Product Agreement. Client may not perform any partial assignment of this Agreement or any Product Agreement or any of its associated rights or obligations to more than [**] assignees without the consent of Patheon (with assignment to the first [**] assignees not requiring the consent of Patheon).

(c) Despite the foregoing provisions of this Section 13.6, either party may assign this Agreement or any Product Agreement to any of its Affiliates or to a successor to or purchaser of all or substantially all of its business; provided that the assignee agrees to be bound by the terms of this Agreement, the Quality and the Product Agreement, as applicable.

**13.7 Force Majeure** .

Neither party will be liable for the failure to perform its obligations under this Agreement or any Product Agreement if the failure is caused by an event beyond that party's reasonable control, including, but not limited to, strikes or other labor disturbances, lockouts, riots, quarantines, communicable disease outbreaks, wars, acts of terrorism, fires, floods, storms, interruption of or delay in transportation, defective equipment, lack of or inability to obtain fuel, power or components, or compliance with any order or regulation of any government entity acting within colour of right (a " **Force Majeure Event** "). A party claiming a right to excused performance under this Section 13.7 will immediately notify the other party in writing of the extent of its inability to perform, which notice will specify the event beyond its reasonable control that prevents the performance. Neither party will be entitled to rely on a Force Majeure Event to relieve it from an obligation to pay money (including any interest for delayed payment) which would otherwise be due and payable under this Agreement or any Product Agreement. If Patheon becomes subject to a Force Majeure Event which interferes with production of the Product at the Manufacturing Site for more than 30 days, the parties shall mutually agree on implementation of an agreed-upon action plan to transfer production of the Product to another Patheon plant or location at Client's cost. The parties shall, after the execution of this Agreement and at the request of either party, meet to discuss and define such an action plan .

**13.8 Additional Product** .

Additional Products may be added to, or existing Products deleted from, any Product Agreement by amendments to the Product Agreement including Schedules A, B, C, and D as applicable.

**13.9 Notices** .

Unless otherwise agreed in a Product Agreement, any notice, approval, instruction or other written communication required or permitted hereunder will be sufficient if made or given to the other party by personal delivery, by telecopy, facsimile communication, or confirmed receipt email or by sending the same by first class mail, postage prepaid to the respective addresses, telecopy or facsimile numbers or electronic mail addresses set forth below:

If to Client:

Tetraphase Pharmaceuticals, Inc.
480 Arsenal Way
Watertown
Massachusetts 02472
USA

Attention: General Counsel
Facsimile No.: [**]
Email address: [**]

If to Patheon:

Patheon UK Limited
Kingfisher Drive
Covingham
Swindon Wiltshire SN3 5BZ
England

Attention: Legal Director
Email address: [**]

or to any other addresses, telecopy or facsimile numbers or electronic mail addresses given to the other party in accordance with the terms of this Section 13.9. Notices or written communications made or given by personal delivery, telecopy, facsimile, or electronic mail will be deemed to have been sufficiently made or given when sent (receipt acknowledged), or if mailed, five days after being deposited in the United States, Canada, or European Union mail, postage prepaid or upon receipt, whichever is sooner.

**13.10 Severability**.

If any provision of this Agreement or any Product Agreement is determined by a court of competent jurisdiction to be invalid, illegal, or unenforceable in any respect, that determination will not impair or affect the validity, legality, or enforceability of the remaining provisions, because each provision is separate, severable, and distinct. With respect to any such invalid, illegal, or unenforceable provision, the parties shall consult and use their best efforts to agree upon a valid and enforceable provision which shall be a reasonable substitute for such invalid, illegal, or unenforceable provision in light of the intent of this Agreement.

**13.11 Entire Agreement**.

This Agreement, together with the applicable Product Agreement and the Quality Agreement, constitutes the full, complete, final and integrated agreement between the parties relating to the subject matter hereof and supersedes all previous written or oral negotiations, commitments, agreements, transactions, or understandings concerning the subject matter hereof. Any modification, amendment, or supplement to this Agreement or any Product Agreement must be in writing and signed by authorized representatives of both parties. In case of conflict, the prevailing order of documents will be this Agreement, the Product Agreement, and the Quality Agreement.

**13.12 Other Terms**.

No terms, provisions or conditions of any purchase order or other business form or written authorization used by Client or Patheon will have any effect on the rights, duties, or obligations of the parties under or otherwise modify this Agreement or any Product Agreement, regardless of any failure of Client or Patheon to object to the terms, provisions, or conditions unless the document specifically refers to this Agreement or the applicable Product Agreement and is signed by both parties.

**13.13 No Third Party Benefit or Right**.

For greater certainty, nothing in this Agreement or any Product Agreement will confer or be construed as conferring on any Third Party any benefit or the right to enforce any express or implied term of this Agreement or any Product Agreement.

**13.14 Execution in Counterparts**.

This Agreement and any Product Agreement may be executed in two or more counterparts, by original, facsimile or “pdf” signature, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

**13.15 Use of Client Name**.

Patheon will not make any use of Client’s name, trademarks or logo or any variations thereof, alone or with any other word or words, without the prior written consent of Client.

**13.16 Taxes** .

(a) The Client will bear all taxes, duties, levies and similar charges (and any related interest and penalties) (" **Tax** " or " **Taxes** "), however designated, imposed as a result of the provision by the Patheon of Services under this Agreement, except:

(i) any Tax based on net income or gross income that is imposed on Patheon by its jurisdiction of formation or incorporation (" **Resident Jurisdiction** ");

(ii) any Tax based on net income or gross income that is imposed on Patheon by jurisdictions other than its Resident Jurisdiction; and

(iii) any Tax that is recoverable by Patheon in the ordinary course of business for purchases made by Patheon in the course of providing its Services, such as Value Added Tax (as more fully defined in subparagraph (d) below), Goods & Services Tax (" **GST** ") and similar taxes.

(b) If the Client is required to bear a tax, duty, levy or similar charge under this Agreement by any state, federal, provincial or foreign government, including, but not limited to, Value Added Tax, the Client will pay the tax, duty, levy or similar charge and any additional amounts to the appropriate taxing authority as are necessary to ensure that the net amounts received by Patheon hereunder after all such payments or withholdings equal the amounts to which Patheon is otherwise entitled under this Agreement as if the tax, duty, levy or similar charge did not exist. The parties will cooperate reasonably in completing and filing documents required under the provisions of any applicable tax laws or under any other applicable law, in connection with the making of any required tax payment or withholding payment, or in connection with any claim to a refund of or credit for any such payment. The parties will cooperate to minimize such taxes in accordance with applicable laws.

(c) Patheon will not collect an otherwise applicable tax if the Client's purchase is exempt from Patheon's collection of the tax and a valid tax exemption certificate is furnished by the Client to Patheon.

(d) If Section 13.16 (a)(iii) does not apply, any payment due under this Agreement for the provision of Services to the Client by Patheon is exclusive of value added taxes, turnover taxes, sales taxes or similar taxes, including any related interest and penalties (hereinafter all referred to as " **VAT** "). If any VAT is payable on a Service supplied by Patheon to the Client under this Agreement, this VAT will be added to the invoice amount and will be for the account of (and reimbursable to Patheon by) the Client. If VAT on the supplies of Patheon is payable by the Client under a reverse charge procedure (i.e., shifting of liability, accounting or payment requirement to recipient of supplies), the Client will ensure that Patheon will not effectively be held liable for this VAT by the relevant taxing authorities or other parties. Where applicable, Patheon will ensure that its invoices to the Client are issued in such a way that these invoices meet the requirements for deduction of input VAT by the Client, if the Client is permitted by law to do so.

(e) Any Tax that Client pays, or is required to pay, but which Client believes should properly be paid by Patheon pursuant hereto may not be offset against sums due by Client to Patheon whether due pursuant to this Agreement or otherwise.

**13.17 Governing Law** .

This Agreement and any Product Agreement, unless otherwise agreed by the parties in the Product Agreement and then only for the purposes of that Product Agreement, will be construed and enforced in accordance with the laws of the State of Delaware and subject to the exclusive jurisdiction of the courts thereof. The parties expressly waive their respective rights to a jury trial in respect of any matter relating to this Agreement or its formation. The UN Convention on Contracts for the International Sale of Goods will not apply to this Agreement.

[Signature page to follow]

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Agreement as of the Effective Date .

**PATHEON UK LIMITED**

By: /s/ Nick Plummer
Name: Nick Plummer
Title: Director & Company Secretary

**TETRAPHASE PHARMACEUTICALS, INC.**

By: /s/ Guy Macdonald
Name: Guy Macdonald
Title: CEO

## APPENDIX 1

## FORM OF PRODUCT AGREEMENT

## (Includes Schedules A to D)

## PRODUCT AGREEMENT

This Product Agreement (this " **Product Agreement** ") is issued under the Master Manufacturing Services Agreement dated 9 June 2017 between Patheon UK Limited and Tetraphase Pharmaceuticals, Inc. (the " **Master Agreement** "), and is entered into **[insert effective date]** (the " **Effective Date** "), between Patheon UK Limited **[or applicable Patheon Affiliate]** , a corporation existing under the laws of England **[or applicable founding jurisdiction for Patheon Affiliate]** , having a principal place of business at Kingfisher Drive, Covingham, Swindon, Wiltshire SN3 5BZ, England **[or Patheon Affiliate address]** (" **Patheon** ") and **[insert Client name, legal entity, founding jurisdiction and address]** (" **Client** ").

The terms and conditions of the Master Agreement are incorporated herein except to the extent this Product Agreement expressly references the specific provision in the Master Agreement to be modified by this Product Agreement. All capitalized terms that are used but not defined in this Product Agreement will have the respective meanings given to them in the Master Agreement.

The Schedules to this Product Agreement are incorporated into and will be construed in accordance with the terms of this Product Agreement.

1. **Product List and Specifications** (See Schedule A attached hereto)

2. **Minimum Order Quantity, Annual Volume, and Price** (See Schedule B attached hereto)

3. **Annual Stability Testing and Validation Activities (if applicable)** (See Schedule C attached hereto)

4. **Active Materials, Active Materials Credit Value and Maximum Credit Value** (See Schedule D attached hereto)

5. **Yearly Forecasted Volume:**

**6. Territory** : (insert the description of the Territory here)

**7 . Manufacturing Site** :

Subcontractor: Patheon Italia SpA. Address: 2 Trav. SX, Via Morolense 5, 03013, Ferentino, Italy

Subcontractor: Patheon Manufacturing Services LLC. Address: 5900 Martin Luther King Jr. Highway, Greenville, NC 27834, USA

**8** . **Inflation Index:** pursuant to Section 4.2(a) of the Master Agreement, the inflation index is:

Italy: the **Consumer Price Index,** published by ISTAT. This index is set forth at the following web address: [details to be included]

North America : Producer Price Index pcu325412325412 for Pharmaceutical Preparation Manufacturing (“PPI”) published by the United States Department of Labor, Bureau of Labor Statistics

**9** . **Currency** : (if applicable under Section 1.4 of the Master Agreement)

**1 0** . **Initial Set Exchange Rate** (if applicable – if Currency included above)

**1 1** . **Initial Product Term:** (if applicable under Section 8.1 of the Master Agreement)

**12** . **Notices** : (if applicable under Section 13.9 of the Master Agreement)

**13 . Other Modifications to the Master Agreement** : (if applicable under Section 1.2 of the Master Agreement)

**Sole Manufacturer**

Patheon shall be the sole manufacturer for at least [**]% of the volumes of the Product set out in the forecast in Schedule [ ]. With respect to those countries in the Territory that are member states of the EEA (“ **EEA Countries** ”), [**] years after the Effective Date, Client’s commitment in the preceding sentence will be reduced automatically to a commitment to purchase no more than [**]% of its requirements of Products for distribution and sale in those EEA Countries. The parties may, however, agree to extend the period of exclusivity for the EEA Countries for an additional period by mutual written consent.

**Adjustments Due to Currency Fluctuations** . [delete this section if pricing will be in Euros]

If the parties agree in this Product Agreement [Item 10 of Product Agreement] to invoice in a currency other than the local currency for the Manufacturing Site, Patheon will adjust the Price to reflect currency fluctuations. The adjustment will be calculated after all other annual Price adjustments under this Section [ ] have been made. The adjustment will proportionately reflect the increase or decrease, if any, in the Set Exchange Rate compared to the Set Exchange Rate established for the prior Year or the Initial Set Exchange Rate, as the case may be.

“ **Initial Set Exchange Rate** ” means as of the Effective Date of a Product Agreement, the initial exchange rate set forth in the Product Agreement to convert one unit of the billing currency into the Patheon Manufacturing Site local currency, calculated as the daily average interbank exchange rate for conversion of one unit of the billing currency into the Patheon Manufacturing Site local currency during the 90 day period immediately preceding the Effective Date as published by OANDA.com “The Currency Site” under the heading “FxHistory: historical currency exchange rates” at www.OANDA.com/convert/fxhistory ;

**“Set Exchange Rate”** means the exchange rate to convert one unit of the billing currency into the Patheon Manufacturing Site local currency for each Year, calculated as the average daily interbank exchange rate for conversion of one unit of the billing currency into the Patheon Manufacturing Site local currency during the full year period (October 1 st [preceding year] to September 30 th ) as published by OANDA.com “The Currency Site” under the heading “FxHistory: historical currency exchange rates” at www.OANDA.com/convert/fxhistory ;

IN WITNESS WHEREOF, the duly authorized representatives of the parties have executed this Product Agreement as of the Effective Date set forth above.

**PATHEON UK LIMITED [or applicable Patheon Affiliate]**

By: _____
Name: _____
Title: _____

**TETRAPHASE PHARMACEUTICALS, INC.**

By: _____
Name: _____
Title: _____

## SCHEDULE A

## PRODUCT LIST AND SPECIFICATIONS

**Product List**

eravacycline for injection

**Specifications**

Prior to the start of commercial manufacturing of Product under this Agreement Client will give Patheon the originally executed copies of the Specifications as approved by the applicable Regulatory Authority. If the Specifications received are subsequently amended, then Client will give Patheon the revised and originally executed copies of the revised Specifications. Upon acceptance of the revised Specifications, Patheon will give Client a signed and dated receipt indicating Patheon's acceptance of the revised Specifications.

## SCHEDULE B

## MINIMUM ORDER QUANTITY, ANNUAL VOLUME, AND PRICE

**[Insert Price Table]**

**Manufacturing Assumptions :**

**Packaging Assumptions :**

**Testing Assumptions :**

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of two pages were omitted. [**]

## SCHEDULE C

## ANNUAL STABILITY TESTING [and VALIDATION ACTIVITIES (if applicable)]

Patheon and Client will agree in writing on any stability testing to be performed by Patheon on the Products. This agreement will specify the commercial and Product stability protocols applicable to the stability testing and the fees payable by Client for this testing.

## SCHEDULE D

## ACTIVE MATERIALS

| Active Materials | Supplier |
|---|---|
| • | • |
| • | • |

## ACTIVE MATERIALS CREDIT VALUE

The Active Materials Credit Value will be as follows:

| PRODUCT | ACTIVE MATERIALS | ACTIVE MATERIALS CREDIT VALUE |
|---|---|---|
| | | Client's actual cost for Active Materials not to exceed $ / EUR_____per kilogram |
| | | |

## MAXIMUM CREDIT VALUE

Patheon's liability for Active Materials calculated in accordance with Section 2.2 of the Master Agreement **[for any Product]** in a Year will not exceed, in the aggregate, the maximum credit value set forth below:

| PRODUCT | MAXIMUM CREDIT VALUE |
|---|---|
| | [**]% of revenues (being payments of the Price) per Year received by Patheon under this Product Agreement, |
| | |

**[End of Product Agreement]**

## EXHIBIT A

## TECHNICAL DISPUTE RESOLUTION

Technical Disputes which cannot be resolved by negotiation as provided in Section 12.2 will be resolved in the following manner:

1. **Appointment of Expert**. Within [**] Business Days after a party requests under Section 12.2 that an expert be appointed to resolve a Technical Dispute, the parties will jointly appoint a mutually acceptable independent expert with experience and expertise in the subject matter of the dispute. If the parties are unable to so agree within the [**] Business Day period, or if there is a disclosure of a conflict by an expert under Paragraph 2 hereof which results in the parties not confirming the appointment of the expert, then an expert (willing to act in that capacity hereunder) will be appointed by an experienced arbitrator on the roster of the American Arbitration Association.

2. **Conflicts of Interest**. Any person appointed as an expert will be entitled to act and continue to act as an expert even if at the time of his appointment or at any time before he gives his determination, he has or may have some interest or duty which conflicts or may conflict with his appointment if before accepting the appointment (or as soon as practicable after he becomes aware of the conflict or potential conflict) he fully discloses the interest or duty and the parties will, after the disclosure, have confirmed his appointment.

3. **Not Arbitrator**. No expert will be deemed to be an arbitrator and the provisions of the American Arbitration Act or of any other applicable statute (foreign or domestic) and the law relating to arbitration will not apply to the expert or the expert's determination or the procedure by which the expert reaches his determination under this Exhibit A.

4. **Procedure**. Where an expert is appointed:

(a) Timing. The expert will be so appointed on condition that (i) he promptly fixes a reasonable time and place for receiving representations, submissions or information from the parties and that he issues the authorizations to the parties and any relevant third party for the proper conduct of his determination and any hearing and (ii) he renders his decision (with full reasons) within [**] Business Days (or another other date as the parties and the expert may agree) after receipt of all information requested by him under Paragraph 4(b) hereof.

(b) Disclosure of Evidence. The parties undertake one to the other to give to any expert all the evidence and information within their respective possession or control as the expert may reasonably consider necessary for determining the matter before him which they will disclose promptly and in any event within [**] Business Days of a written request from the relevant expert to do so.

(c) Advisors. Each party may appoint any counsel, consultants and advisors as it feels appropriate to assist the expert in his determination and so as to present their respective cases so that at all times the parties will co-operate and seek to narrow and limit the issues to be determined.

(d) Appointment of New Expert . If within the time specified in P aragraph 4(a) above the expert will not have rendered a decision in accordance with his appointment, a new expert may (at the request of either party) be appointed and the appointment of the existing expert will thereupon cease for the purposes of determining the matter at issue between the parties except if the existing expert renders his decision with full reasons prior to the appointment of the new expert, then this decision will have effect and the proposed appointment of the new expert will be withdrawn.

(e) Final and Binding . The determination of the expert will, except for fraud or manifest error, be final and binding upon the parties.

(f) Costs . Each party will bear its own costs for any matter referred to an expert hereunder and, in the absence of express provision in the Agreement to the contrary, the costs and expenses of the expert will be shared equally by the parties.

For greater certainty, the release of the Products for sale or distribution under the applicable marketing approval for the Products will not by itself indicate compliance by Patheon with its obligations for the Manufacturing Services and further that nothing in this Agreement (including this Exhibit A) will remove or limit the authority of the relevant qualified person (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

**EXHIBIT B**

**COMMERCIAL QUALITY AGREEMENT**

# QUALITY AGREEMENT
## Commercial Product

Between

**TETRAPHASE PHARMACEUTICALS, INC.**
a corporation existing under the laws of Delaware, USA

(" **Client** ")

-and-

**PATHEON ITALIA S.p.A.**
a corporation existing under the laws of Italy

**Ferentino Operations (FRT)**
2° Trav. SX Via Morolense 5, 03013 Ferentino, Italy

(" **Patheon** ")

**Effective Date** : <ENTER EFFECTIVE DATE HERE>

**TABLE OF CONTENTS**


| | | |
|---|---|---|
| SECTION 1 | BACKGROUND AND AGREEMENT | 3 |
| SECTION 2 | RESPONSIBILITIES TABLE | 4 |
| SECTION 3 | GENERAL | 6 |
| SECTION 4 | DESCRIPTION OF RESPONSIBILITIES | 7 |
| SECTION 5 | APPENDICES | 20 |
| | APPENDIX A: PRODUCT(S) | |
| | APPENDIX B: QUALITY CONTACTS | |
| | APPENDIX C: PATHEON APPROVED VENDOR LIST | |
| | APPENDIX D: CLIENT APPROVED VENDOR LIST | |
| | APPENDIX E: PATHEON APPROVED CONTRACT LABORATORIES AND MANUFACTURERS LIST | |
| | APPENDIX F: API STARTING MATERIAL EU REQUIREMENTS | |

**SECTION 1: BACKGROUND AND AGREEMENT**

**BACKGROUND**. Under a manufacturing services agreement dated <ENTER MSA DATE HERE> between Patheon UK Limited (the " **Contract Acceptor** ") and the Client (the " **MSA** "), the Contract Acceptor agreed to sub-contract the performance of pharmaceutical manufacturing services for certain marketed products in certain countries (as set forth in Appendix A hereto) (" **Products** ") to Patheon. The parties agreed that the Contract Acceptor will remain solely liable to the Client for any breach of the duties and responsibilities assumed by Patheon under this Agreement. The Client is required to give the Contract Acceptor certain Specifications in order for Patheon to perform the manufacturing services. Under the MSA, the Contract Acceptor is required to ensure that Patheon operates within the Specifications and in accordance with cGMP. The Client and Patheon, as provider of the manufacturing services on behalf of the Contract Acceptor for the benefit of the Client, desire to allocate the responsibility for procedures and Specifications impacting on the identity, strength, quality and purity of the Products by entering into this Quality Agreement (this **"Agreement** ").

**AGREEMENT**. NOW THEREFORE in consideration of the rights conferred and the obligations assumed under the MSA and herein, and for other good and valuable consideration (the receipt and sufficiency of which are acknowledged by each party), and intending to be legally bound, the parties agree as follows:

**SECTION 2: RESPONSIBILITIES TABLE**

Patheon will be responsible for all the operations that are marked with "X" in the column titled "Patheon" and the Client will be responsible for all the operations that are marked with "X" in the column titled "Client". If marked with "(X)", cooperation is required from the designated party. If more than one Patheon site is involved the “X” representing Patheon will be replaced with the three letter acronym(s) on the title page applicable to each site.

| Section No. | Subject / Terms | Client | Patheon |
|---|---|---|---|
| **4.1 Quality Management** | | | |
| 4.1.1 | cGMP, Health and Safety Compliance | X | X (or PPP) |
| 4.1.2 | Client Audit Rights | X | |
| 4.1.3 | Subcontracting | (X) | X |
| 4.1.4 | Self-Inspection | | X |
| **4.2 Regulatory Requirements** | | | |
| 4.2.1 | Permits | X | |
| 4.2.2 | Regulatory Filing / Registration Change Control | X | (X) |
| 4.2.3 | Regulatory Compliance | | X |
| 4.2.4 | Government Agency Inspections, Communications and Requisitions | (X) | X |
| **4.3 Incoming Material Control** | | | |
| 4.3.1 | Test Methods and Specifications | X | |
| 4.3.2 | Material Destruction | (X) | X |
| 4.3.3 | Vendor Audit Responsibility | X | X |
| 4.3.4 | Client Furnished Materials | X | |
| 4.3.5 | Temperature Monitoring Devices for In-Coming Materials | X | |
| 4.3.6 | Incoming Material Release | | X |
| 4.3.7 | Packaging Component Qualification | X | |
| **4.4 Building, Facilities, Utilities and Equipment** | | | |
| 4.4.1 | General | | X |
| 4.4.2 | Equipment, Calibration and Preventative Maintenance | | X |
| 4.4.3 | Environmental Monitoring Program | | X |
| **4.5 Product Controls** | | | |
| 4.5.1 | Technical Transfer | X | |
| 4.5.2 | Master Batch Record | (X) | X |
| 4.5.3 | Reprocessing and Rework | (X) | X |
| 4.5.4 | Personnel Training | | X |
| **4.6 Packaging, Labeling and Printed Materials** | | | |
| 4.6.1 | Master Batch Packaging Records | (X) | X |
| 4.6.2 | Printed Material and Artwork | X | |
| 4.6.3 | Test Methods and Method Validation | X | (X) |
| **4.7 Deviation Reports (DRs)** | | | |
| 4.7.1 | Deviations | | X |
| 4.7.2 | Notification of Deviations | | X |
| 4.7.3 | Client Support | X | |
| **4.8 Release of Product** | | | |
| 4.8.1 | Test Methods and Specifications | X | |
| 4.8.2 | Batch Release for Shipment | | X |
| 4.8.3 | Certificate of Manufacture | | X |

| Section No. | Subject / Terms | Client | Patheon |
|---|---|---|---|
| 4.8.4 | Certificate of Analysis | | X |
| 4.8.5 | Product Release | X | |
| **4.9 Validation** | | | |
| 4.9.1 | Master Validation Plan | (X) | X |
| 4.9.2 | Cleaning Validation Program | (X) | X |
| 4.9.3 | Analytical Method and Procedure Validation | X | (X) |
| 4.9.4 | Process Validation | X | (X) |
| **4.10 Change Control** | | | |
| 4.10.1 | General | X | X |
| **4.11 Documentation** | | | |
| 4.11.1 | Record Retention | | X |
| 4.11.2 | Batch Document Requisition | | X |
| 4.11.3 | Record Destruction | (X) | X |
| **4.12 Laboratory Controls** | | | |
| 4.12.1 | Specifications and Test Methods | X | X |
| 4.12.2 | Out of Specifications (OOS) / Out of Trend (OOT) | | X |
| **4.13 Stability** | | | |
| 4.13.1 | Sample Storage | | X |
| 4.13.2 | Stability Studies | X | X |
| 4.13.3 | Stability Failures | | X |
| 4.13.4 | API and Product Retest and Expiry Date | X | |
| **4.14 Annual Product Review** | | | |
| 4.14.1 | Annual Report | X | (X) |
| 4.14.2 | Product Quality Report | (X) | X |
| **4.15 Storage and Distribution** | | | |
| 4.15.1 | General | | X |
| 4.15.2 | Product Storage and Shipment Changes | (X) | X |
| 4.15.3 | Product Quarantine | | X |
| **4.16 Product Complaints** | | | |
| 4.16.1 | Complaint Investigation | X | (X) |
| 4.16.2 | Complaint Sample Retrieval | X | |
| **4.17 Product Recall** | | | |
| 4.17.1 | Product Recall Notification | X | |
| 4.17.2 | Government Agency Notification | X | |
| **4.18 Reference and Retention Samples** | | | |
| 4.18.1 | Excipient, Primary and Printed Packaging Materials, and Active Ingredient Reference Sample | | X |
| 4.18.2 | Finished Product Retention Sample | X | X |
| 4.18.3 | Sample Destruction | (X) | X |

**SECTION 3: GENERAL**

3.1 Capitalized terms not otherwise defined herein will have the meaning specified in the MSA.

3.2 Any communications about the subject matter of this Agreement will be directed, in the first instance, to the person(s) identified in Appendix B.

3.3 If any provision of this Agreement should be found invalid, or unenforceable by law, the rest of the Agreement will remain valid and binding and the parties will negotiate a valid provision which meets as closely as possible the objective of the invalid provision.

3.4 Any amendment of this Agreement will be made in writing and signed by both parties.

In particular, in the event of a substantial change to cGMPs or regional governances directly impacting Product Quality compliance, it shall be mutually agreed upon prior to implementation.

3.5 If there is any conflict between the terms of this Agreement and the MSA, the MSA will take precedence except for any specific quality-related issue. Notwithstanding anything to the contrary in this Agreement, the MSA will take precedence with respect to any commercial terms, including fees for quality-related services.

3.6 The “Background” provisions of Section 1 are incorporated into this Agreement.

## SECTION 4: DESCRIPTION OF RESPONSIBILITIES

### 4.1 QUALITY MANAGEMENT

4.1.1 c GMP, Health and Safety Compliance

Patheon will conduct operations in compliance with applicable environmental, occupational health and safety laws, and cGMP regulations.

4.1.2 Client Audit Rights

Patheon will permit audits by the Client on reasonable prior written notice, of all relevant premises, procedures and documentation related to Client's Product. Client audits are limited to [**] with a maximum of [**] auditors for [**] per calendar year unless for cause. Client representatives for audits must be preapproved by Patheon.

4.1.3 Subcontractin g

Unless otherwise allowed herein, Patheon will not subcontract tasks to a third party without Client's consent. Patheon may subcontract tasks to the Patheon approved contract manufacturers and laboratories set forth in Appendix E hereto.

4.1.4 Self-Inspection

Patheon will perform self-inspections of its premises, facilities, and processes used to manufacture, package, test, and store the Client's starting, intermediate, and/or finished products in accordance with Patheon's written standard operating procedures (" **SOPs** ") to ensure compliance with cGMP.

### 4.2 REGULATORY REQUIREMENTS

4.2.1 Permits

The Client will be solely responsible for obtaining or maintaining, on a timely basis, any permits or other regulatory approvals for the Products or the Specifications, including, without limitation, all marketing and post-marketing approvals and reporting.

Patheon will obtain and maintain the appropriate manufacturing license(s) to allow for the Manufacturing services.

4.2.2 Regulatory Filing / Registration Change Control

The Client will ensure product filing and registrations are in compliance with all Applicable Laws.

The Client will determine whether changes to the Product or related to the Product will impact a regulatory filing and will apply for and receive approval for any required manufacturing amendment, change or addition to their Product marketing authorization. Upon request, Patheon will provide assistance in the preparation and review of pertinent sections of new or supplemental regulatory applications before filing.

For EU products it is the responsibility of the Client to provide Patheon sites with the accurate Product registration information as per European legislations (cGMPs guide part I - chapters 1,4,6,7 and annex 16 / directives 2001/83/EC – title IV, articles 46, 48, 51 and 2003/94/EC article 5).

Prior to submission of any new, or change to any existing applicable CMC, CTD, Regulatory File, Product Registration, etc., to any Regulatory Authority relating to the Product, the Client will provide Patheon copies of sections of the submissions that are relevant to the services provided.

Specifically, Client will provide Patheon with a copy of any documentation which is or is equivalent to the Quality Module (Drug Product Section) of the Common Technical Document and any

amendments thereto (all such documentation herein referred to as “CTD”) related to any Marketing Authorization, such as a US New Drug Application, US Abbreviated New Drug Application, US Biologics Licence Application, or EU Marketing Authorisation Application at least [**] days prior to filing such information with the Regulatory Authority.

The parties agree that **no inspections by any Regulatory Authority may be scheduled** until Patheon has had an opportunity to review the requested documents and is satisfied with their accuracy.

Patheon will communicate directly with the Regulatory Agency after discussions with Client.

The Client is responsible for all communications with Regulatory Authorities as well as for the approval, maintenance, and updating of marketing approval in a timely manner.

4.2.3 Regulatory Compliance

Patheon will ensure that Product(s) are manufactured and tested in strict compliance with;

- current Canadian regulatory requirements (as defined under Part C, Division 2 of the Food and Drug Regulations),
- US Federal regulatory and statutory requirements relating to Good Manufacturing Practices (cGMP) (US 21 CFR parts 210, 211, 600, 601, 610, etc…)
- EU Directive 2003/94/EC for the Manufacture of Finished Medicinal Products)
- EU Directives 2004/27/EC and 2011/62/EU, as applicable to the Holder of the Manufacturing Authorization.

as applicable, as well as all regulatory approvals and Applicable Laws at the site(s) of manufacture and/or testing.

The Client shall comply with EU Directives 2004/27/EC and 2011/62/EU as applicable to the holder of the relevant marketing authorisation or to the extent that such Directives apply to the supply of API.

4.2.4 Government Agency Inspections, Communication and Requisitions

Each party will permit all relevant inspections by Regulatory Authorities of premises, procedures, and documentation.

The parties will notify each other within [**] Business Days of receipt of any notice of inspection from a Regulatory Authority and within [**] of any regulatory authority request for Product samples, batch documentation, or similar information related to the Product.

Each party reserves the right to be present on site during a regulatory inspection that relates to the Product.

The parties will notify within [**] of receipt of any Form 483's warning letter or similar communication from any Regulatory Authority that relates to the Product; or if the supply of Product will be affected, or if the facilities used to produce, test or package the Product will be affected.

During a regulatory inspection relating to the Product, upon request, a party will provide the requesting party with the applicable Product data for which it is responsible under this Agreement.

Patheon is responsible for responding to all regulatory audits conducted at any Patheon site. Patheon will provide Client with a draft of any responses directly related to the Product prior to submission to the Regulatory Authority. Client must provide approval or request changes in a

timely manner to enable Patheon to respond to the Regulatory Authority by the applicable deadline . Notwithstanding, Patheon reserves the right to respond to the Regulatory Authority without Client's prior approval , if, in the opinion of Patheon's Legal counsel, it is required or reasonable to do so.

Client is responsible for responding to all regulatory audits at any Client site. Client will provide Patheon with a draft of any response directly related to Patheon services prior to submission to the Regulatory Authority. Patheon must provide approval or request changes in a timely manner to enable Client to respond to the Regulatory Authority by the applicable deadline. Notwithstanding, Client reserves the right to respond to the Regulatory Authority without Patheon's prior approval , if, in the reasonable opinion of Client 's Legal counsel, it is required or reasonable to do so.

**4.3 INCOMING MATERIAL CONTROL**

4.3.1 Test Methods and Specifications

The Client will give Patheon a copy of the Specifications and test methods used if the Client issues raw material Specifications.

4.3.2 Material Destruction

Patheon has the right to either return to the Client or dispose of any outdated or rejected material. If the material is disposed of, disposal will be consistent with the nature of the material and sent to a permitted waste disposal facility. Prior to disposal:

(i.) Patheon will send notice to the Client about Patheon's intent to dispose of the material. If no direction is received from the Client, Patheon will dispose of the material no sooner than [**] days after the date of the notice.

(ii.) The materials will be disposed and destroyed in compliance with local environmental regulations and performed in a secure and legal manner that prevents unauthorized use or diversion.

Patheon will maintain destruction records in accordance with Patheon SOPs.

4.3.3 Vendor Audit Responsibility

(For the purposes of this Section the term " **Vendor** " refers to the sites performing the manufacturing and testing of a material).

Excipient, Packaging Component, and API Vendors:

(i.) If the Client stipulates a Vendor, the Client will audit and approve the Vendor and ensure cGMP compliance in accordance with Section 4.3.4 of this Agreement. If Patheon is to release an API or other Client stipulated material based on "ID Only", the Client will ensure the required verification testing by an independent laboratory has been completed. The Client stipulated Vendor(s) will be included on the Client's approved Vendor list (attached hereto as Appendix D).

(ii.) If Patheon stipulates a Vendor, Patheon will audit and approve the manufacturers and ensure cGMP compliance in accordance with Patheon's SOP. The Patheon stipulated Vendor(s) will be included on Patheon's approved Vendor list (attached hereto as Appendix C).

(iii.) Upon request by any regulatory body audits of API manufacturing sites should be available to both parties.

4.3.4 Client Furnished Materials

The Client is responsible for Vendor qualification of Client furnished materials and for providing a certificate of compliance confirming the following as applicable:

(i) That the materials are compliant with the provisions outlined in the "Note for Guidance on minimizing the risk of transmitting spongiform encephalopathy agents via human and veterinary medicinal products" (EMA/410/01, most current revision or equivalent requirement).

(ii) Certification there is no potential for specific toxic solvents listed in the EP / USP / ICH residual solvents Class I, Class II or Class III to be present and the material, if tested, will comply with established EP / USP / ICH requirements. If any of the solvents listed in the EP / USP / ICH residual solvents Class I, Class II or Class III are used in the manufacture or are generated in the manufacturing process, solvents of concern will be indicated.

(iii) A cGMP compliance declaration for the API, assuring compliance with the latest regulatory requirements (e.g. EU directive 2004/27/EC for an API sourced from inside the EU or, ICH Q7 for an API sourced from outside the EU, for API see Appendix F); and

(iv) Any other certification applicable to the furnished material (e. g. Residues of Metals Catalysts & Reagents, Genotoxic Impurities, Kosher, Melamine, Viral Inactivation, etc. ..).

4.3.5 Temperature Monitoring Devices for In-Coming Materials

The Client is responsible for ensuring that the furnished API and all other furnished temperature sensitive materials are shipped to Patheon with the following conditions to ensure no temperature excursions occurred during transportation of the materials:

(i) Ambient or Room Temperature APIs must be transported in a manner that reflects the label requirements. Temperature stability data for the API to support label requirements will be provided to Patheon. If temperature stability data is not available, temperature monitoring devices will need to accompany each API shipment until this data is made available.

(ii) APIs and other materials that require special storage conditions (e.g. 2-8°C, (-15)-(-25°C), "Do Not Freeze", etc.) must be transported in a manner which reflects the label requirements of the material. Temperature stability data for the API to support label requirements will be provided to Patheon. As such, temperature monitoring devices will accompany each shipment of these materials unless validated shipping processes are followed.

4.3.6 In-Coming Material Release

Patheon will use established systems and procedures for the receipt of materials to ensure all incoming materials are checked against receiving documentation and purchase orders, and are properly labeled and identified. Prior to use in the manufacture of any Product, material(s) will be inspected, tested and released by Patheon against the Specification approved by the Client.

4.3.7 Packaging Component Qualification

In all cases the Client is responsible for qualifying any packaging container closure system for use in Product, for example USP<660>, <661>, <670>, <671>, Poison Prevention Act (Child Resistance), etc., unless other provisions are agreed to.

**4.4 BUILDING, FACILITIES , UTILITIES AND EQUIPMENT**

4.4.1 General

All buildings and facilities used in the manufacturing, packaging, testing and storage of any materials and/or Product will be of suitable size, construction and location to facilitate cleaning, and will be maintained in a good state of repair. Maintenance and cleaning records will be kept in accordance with Patheon's SOPs.

4.4.2 Equipment, Calibration and Preventative Maintenance

All equipment used in the manufacturing, packaging, testing and storage of any materials and/or Product will be suitable for its intended use and appropriately located to allow for cleaning and maintenance. Calibration and maintenance records will be kept according to Patheon SOPs for all critical equipment. Patheon will calibrate instrumentation and qualify computer systems used in the manufacture and testing of the Product in accordance with Patheon's SOPs.

4.4.3 Environmental Monitoring Program

Patheon will perform and maintain an environmental monitoring program. The collected data will be reviewed and interpreted by the responsible person within Patheon's quality unit. Any out of limit results will be managed appropriately in accordance with Patheon SOPs.

**4.5 PRODUCTION CONTROLS**

4.5.1 Technical Transfer

For all processes related to the Product developed outside of Patheon, the Client will provide technical information to support a technical transfer, including development reports, critical Deviations and OOS, related CAPA, and other relevant aspects of the product performance history.

4.5.2 Master Batch Record

The Client will provide the Specifications to Patheon and Patheon will manufacture Product in accordance with the Specifications.

Patheon is responsible for preparing the master batch records for the Product, however, the Client is responsible to review and approve the master batch records prior to the manufacture of the Product unless otherwise agreed to in writing.

Patheon will not make changes to master batch records except through the established Patheon change control system, and all master document revisions will be approved by the Client's quality unit unless otherwise agreed to in writing. Any changes made to issued batch records (prior to master revisions) must be reviewed and approved by the Client's quality unit prior to implementation unless otherwise agreed to in writing.

Patheon will maintain a batch numbering system designed to assure traceability of the product and associated documentation.

4.5.3 Reprocessing and Rework

Patheon will not reprocess or rework the Product without the prior written consent of the Client.

Reprocessing is defined as the introduction of material back into the process and repeating a step, (e.g. redrying, remilling) using the same equipment and techniques of the established manufacturing process.

Rework is defined as the introduction of material to one or more processing steps that are different from the established manufacturing process.

4.5.4 Personnel Training

Patheon will provide appropriate training for all employees. Each person engaged in the manufacture, packaging, testing, storage, and shipping of the Product will have the education, training, and experience necessary, consistent with current cGMP and safety training requirements.

**4.6 PACKAGING, LABELING AND PRINTED MATERIALS**

4.6.1 Master Batch Packaging Records

The Client will provide Patheon with the Specifications for all packaging components. Patheon will create, control, issue, and execute in accordance with the master batch packaging record and the Specifications.

Patheon will not make changes to master batch packaging records except through the established Patheon change control system, and all master document revisions will be approved by the Client's quality unit. Any changes made to issued batch records (prior to Master revisions) must be reviewed and approved by the Client's quality unit prior to implementation unless agreed to in writing.

Patheon will maintain a batch numbering system designed to assure traceability of the product and associated documentation.

4.6.2 Printed Material and Artwork

The Client will provide artwork and labelling text (blister, carton, leaflet, label etc.) Specifications to Patheon. The labelling proofs must be reviewed and approved by the Client.

4.6.3 Test Methods and Method Validation

The Client will provide test methods and method validation for packaging components to Patheon. Where applicable, Patheon will provide test methods and validation for packaging components purchased from Vendors on the Patheon approved Vendor list only (Appendix C).

**4.7 DEVIATION REPORTS (DRS)**

4.7.1 Deviations

Patheon will document, investigate and resolve deviations from approved manufacturing/packaging instructions or Specifications in accordance with Patheon's SOPs.

4.7.2 Notification of Deviations

Patheon will notify the Client within [**] Business Days if any significant deviation occurs during manufacture of the Product, where the deviation affects the quality, efficacy or availability of the Product.

4.7.3 Client Support

As part of the written notification acknowledgement, Client will confirm if they require approval of the DR within [**] Business Days. If no response is received, Patheon will proceed to complete in the investigation without Client approval. A copy of the closed DR will be provided to Client if required.

As the Product license holder and technical Product/process expert the Client will provide technical and/or Product quality assessments in support of DRs, if required.

If Client approval is required on a specific DR, Client will provide investigation comments or approval within [**] Business Days of receipt of draft or Patheon approved DR. This Client approval will not be unreasonably withheld.

**4.8 RELEASE OF PRODUCT**

4.8.1 Test Methods and Specifications

The Client will provide to Patheon the finished Product Specifications.

4.8.2 Batch Release for Shipment

Batch review and release for shipment will be the responsibility of Patheon's Quality Assurance department who will act in accordance with Patheon's SOPs.

4.8.3 Certificate of Manufacture (Certificate of Compliance, Conformance, etc.)

For each batch certified by Patheon, Patheon will deliver to the Client a Certificate of Manufacture that will include a statement that the batch has been manufactured in accordance with cGMPs and the Specifications.

4.8.4 Certificate of Analysis

For each batch released by Patheon, Patheon will deliver to the Client a Certificate of Analysis with analytical data showing the batch complies with the Product Specifications.

4.8.5 Product Release

The Client will have sole responsibility for release of the Product to the market. When Patheon EU Qualified Person (" **QP** ") services are employed, Patheon QP may release the Product for distribution on behalf of the Client.

**4.9 VALIDATION**

4.9.1 Master Validation Plan

Patheon will establish applicable master validation plans and maintain a validation program for the Product. The Client will review and approve performance qualification and process validation protocols and reports for the Product.

4.9.2 Cleaning Validation Program

The Client will provide required information (i.e. LD50, toxicity, solubility, batch size, fill volume, product min dose/70Kg patient) to establish cleaning limits.

In addition the Client will inform Patheon of any planned changes in dosing strategies, particularly smallest therapeutic and largest single dose prior to change in clinic or market to ensure cleaning limits justification remain applicable.

Patheon will maintain an appropriate cleaning and cleaning validation program.

4.9.3 Analytical Method and Procedure Validation

The Client will provide to Patheon non-compendial test methods. The Client must ensure that its analytical methods and manufacturing procedures (including packaging procedures) are validated. If the methods and procedures are not validated by the Client, then Patheon may assist in validation.

4.9.4 Process Validation

Subject to the terms of the MSA, Patheon, with technical support from the client, will conduct process validation for commercial products consistent with the regulations and guidelines for the intended market. The Client will support the process validation program by supplying development details, technical Specifications and submission details. Following the initial process and packaging validation, Patheon and the Client will be responsible to periodically assess the validated state of the product and conduct revalidation as necessary.

**4.10 CHANGE CONTROL**

4.10.1 General

Patheon will notify the Client in accordance to Patheon's SOPs before implementing any proposed changes to the process, materials, testing, equipment or premises, where such changes may directly affect the Product.

The Client will be responsible for determining whether or not to initiate registration variation procedures, post approval changes, etc..., and for maintaining adequate control over the quality commitments of the marketing authorization made to the regulatory authorities by the Client for the Products.

The Client will review and provide any comments, regulatory advice, or Product implementation requirements related to any changes within [**] days of notice. Patheon will proceed with implementation of changes if no response is received after [**] days.

Following validation of a process change, Patheon will deliver a copy of the related validation report to the Client and the associated stability data, if applicable, as it becomes available.

**4.11 DOCUMENTATION**

4.11.1 Record Retention

Patheon will maintain all batch records for a minimum of [**] past Product expiry date and supply all these records to the Client upon request. Patheon will maintain records and evidence on the testing of raw materials and packaging/labeling materials for [**] after the materials were last used in the manufacture or packaging/labeling of the Product.

4.11.2 Batch Document Requisition

At the request of the Client, Patheon will provide a copy of any of the executed batch documents relating to Products to the Client as soon as reasonably possible. This does not apply to processes that Patheon considers proprietary (e.g. specific gel capsule technologies).

4.11.3 Record Destruction

Following the expiry of the retention period, Patheon will provide notice to Client in accordance with the contact information set forth in Appendix B (or as updated in writing from time to time) of its intent to destroy the documents. Client will have [**] days from the date of Patheon's notice to notify Patheon in writing if Client wishes to have documents returned. Client will then have up to [**] days from the date of Patheon's notice to remove the documents from Patheon's premises.

Patheon assumes no responsibility for documents destroyed after the expiry of the [**] day limit above. Client will be solely responsible for providing Patheon with up-to-date contact information for notification purposes.

**4.12 LABORATORY CONTROLS**

4.12.1 Specifications and Test Methods

Patheon will test and approve starting material, intermediate, and the finished Product in accordance with the approved Specifications, analytical methods, and Patheon's SOPs.

The Client will provide to Patheon the API Specifications for furnished API, including a certificate of analysis for each batch.

The Client will supply any required reference standards that are not readily available through a commonly recognized source. These reference standards must be accompanied by a Certificate of Analysis listing the expiration date and any correction factors that need to be applied.

4.12.2 Out of Specifications (OOS) / Out of Trend (OOT)

Patheon and Client will notify each others' quality unit of confirmed out-of-Specification (" **OOS** ") or out-of-trend (" **OOT** ") results within [**] Business Days.

If Client approval is required on a specific OOS, Client will provide investigation comments or approval within [**] Business Days of receipt of draft or Patheon approved OOS. This Client approval will not be unreasonably withheld.

For all confirmed OOS results generated by Patheon, Patheon will generate a DR type deviation as per Patheon SOPs and obtain approval of the DR from the Client's responsible person within their quality unit. This Client approval will not be unreasonably withheld.

**4.13 STABILITY**

4.13.1 Sample Storage

Patheon will store stability samples if and as required under the MSA.

4.13.2 Stability Studies

The Client will develop and validate stability indicating assay(s) prior to process validation. If required, Patheon may assist with this activity.

If applicable, Patheon will conduct stability studies in accordance with the agreed and validated stability testing analytical methods at the agreed upon testing points in accordance with the agreed stability protocol.

Patheon will perform the stability testing described in a stability protocol agreed to by both Patheon and the Client. Stability data will be provided by Patheon to the Client on an ongoing basis as agreed to by both parties.

4.13.3 Stability Failures

Patheon will notify the Client of any potential OOS within [**] of the potential OOS being identified.

Client will notify regulatory agencies in accordance with Section 4.17 of this Agreement.

4.13.4 API and Product Retest and Expiry Date

The Client will be responsible for establishing and approving the Retest and Expiry Date for all API and Product in compliance with all applicable regulatory requirements.

**4.14 ANNUAL PRODUCT REVIEW**

4.14.1 Annual Product Review

The Client will complete Annual Product Review (" **APR** ") in accordance with regulatory requirements of the Product marketed authorization, for example 21CFR 314.81(b)(2). Patheon will provide copies of all information and correspondence necessary to support the APR when requested by the Client.

Client will provide a copy of the approved Final APR (redacted as applicable) where required.

4.14.2 Product Quality Report

Patheon will perform annual Product Quality Reports (" **PQR** ") applicable to the Services after commencement of commercial activities in compliance with all applicable regulatory requirements, for example 21CFR211.180e. This will include, for example, status of batches processed, status of product deviations/investigations/CAPA, trending of complaints, status of stability studies maintained by Patheon, status of change controls, statistical trending of the finished product test results performed by Patheon, and a summary report of applicable finished product retained sample inspection. The PQR will be provided [**] after each anniversary date, unless agreed otherwise in writing.

Upon receipt of the PQR from Patheon, the Client will complete the Final PQR with applicable Product information that Patheon does not have. The Client will notify Patheon of any issues detected during the Final PQR potentially affecting processes supported by Patheon and will provide a summary of any related concerns or issues related to the services provided prior to Final PQR completion. Client will provide a copy of the approved Final PQR (redacted as applicable) where required.

**4.15 STORAGE AND DISTRIBUTION**

4.15.1 General

Patheon will store and ship Product in accordance with the agreed qualified (and where required, validated) temperature, packaging, monitoring, and transportation requirements specified by the Client.

4.15.2 Product Storage and Shipment Changes

Patheon will communicate any proposed changes in storage or shipping to the Client for review and approval. Client approval will not be unreasonably withheld.

4.15.3 Product Quarantine

Patheon will have a system in place for assuring that unreleased Product is not shipped unless authorized by the Client's quality unit.

**4.16 PRODUCT COMPLAINTS**

4.16.1 Complaint Investigation

The Client is responsible for investigating and resolving all medical and non-medical Product complaints, adverse events, etc.... Patheon will assist in the investigations involving all Patheon manufacturing and packaging type Product complaints related to the Manufacturing Services provided.

The Client is responsible to comply with all pharmacovigilence legislation.

Patheon will inform the Client within [**] of any complaints Patheon becomes aware of from other sources.

4.16.2 Complaint Sample Retrieval

The Client is responsible for retrieving complaint sample(s) and forwarding them to Patheon in a timely manner to facilitate a complete and comprehensive investigation. If the complaint sample(s) cannot be obtained and provided to Patheon, the Client will provide a written explanation detailing the reasons as to why the complaint sample cannot be obtained.

In order for Patheon to conduct a valid investigation, the Client must provide:

(i) A physical sample of the Product which triggered the Complaint. An alternate option is for the Client to provide clear multiple digital photographs. In those cases where a physical sample or photos are impossible to be retrieved and provided, Client documentation must be provided as evidence that reasonable efforts were made to obtain a sample.

(ii) Special handling instructions for the returned sample (i.e. refrigeration, Health & Safety concerns based on product, security for controlled drugs / narcotic) as applicable.

(iii) Complete, clear concise information from the complainant. This information needs to be reviewed by the Client prior to forwarding to Patheon and assessed on completeness before processing the Complaint to Patheon. These include the following, as applicable

a. Descriptive detailed odour descriptions

b. Full Product Name, Lot number(s) (Patheon and Client), Dosage Form, Strength, pack size, Product Code Number (Patheon and Client), Expiry date

c. Complaint Origin

d. Market Country

e. Client Complaint Number

f. Client Severity Assignment

g. Client Complaint Classification

**4.17 PRODUCT RECALL**

4.17.1 Product Recall Notification

The Client and Patheon will notify each other about a Product Recall or other regulatory type product notification (e.g. US field alert, confirmed stability OOS notifications, suspected falsified product, etc…) related to the Product as soon as possible, but, in any event, prior to informing the appropriate regulatory authorities.

The Client will be responsible for all related Recall activities. In the event of a confirmed falsified Product, the client will take all appropriate measures to physically and securely segregate Product from the legitimate Product supply chain, and the Client will inform the applicable authorities. Patheon will assist in the investigations involving all Patheon manufacturing and packaging type Product complaints related to the Manufacturing Services provided.

Patheon will supply Client any related documentation, as requested, to support the Recall or other actions, including investigating Patheon activities as a deviation as outlined in Section 4.7. Affected products at Patheon's facility will be quarantined and labeled according to Patheon's SOP.

4.17.2 Government Agency Notification

The Client will notify the appropriate regulatory authorities of any Field Alert, Recall, Falsified Product, etc… type quality issues.

The Client will perform the Product recall and will communicate with the appropriate regulatory authorities.

Where legislated, Patheon reserves the right to notify regulatory authorities of Product quality issues. Patheon will inform the Client prior to any notification to the regulatory authorities.

**4.17 REFERENCE AND RETENTION SAMPLES**

4.18.1 Excipient, Primary and Printed Packaging Materials, and Active Ingredient Reference Sample

Patheon will keep a reference sample of each material supplied to Patheon and used to manufacture the Product. The reference sample will consist of at least [**] times the necessary quantity for all Quality Control tests required to determine whether the materials meet required Specifications.

Where applicable each packaging site will keep reference samples of each batch of primary and printed packaging materials.

The reference samples will be stored by Patheon under controlled conditions in accordance with cGMP storage requirements for [**] beyond the expiration date of the last batch of product containing the materials. The reference samples will be made available by Patheon to the Client, if requested.

4.18.2 Finished Product Retention Sample

Retention samples of finished Product will be retained by Patheon for [**] past Product expiry or such longer period as required by law. Where applicable, the legal sample(s) of finished Product must be retained by the Client.

4.18.3 Sample Destruction

Following the expiry of the retention period, Patheon will provide notice to Client in accordance with the contact information set forth in Appendix B (or as updated in writing from time to time) of its intent to destroy the samples. Client will have [**] days from the date of Patheon's notice to notify Patheon in writing if Client wishes to have samples returned. Client will then have up to [**] days from the date of Patheon's notice to remove the samples from Patheon's premises.

Patheon assumes no responsibility for samples destroyed after the expiry of the [**] day limit above. Client will be solely responsible for providing Patheon with up-to-date contact information for notification purposes.

* * *

IN WITNESS WHEREOF, the parties have caused their duly authorized officer to execute and deliver this Quality Agreement as of the Effective Date identified on the first page:

**TETRAPHASE PHARMACEUTICALS, INC.**

By: _____ Date: _____
Name: _____
Title: _____

**PATHEON ITALIA S.p.A**

By: _____ Date: _____
Name: _____
Title: _____

**SECTION 5: APPENDICES**
**NOTE, APPENDICES can change independent of the Quality Agreement upon written confirmation by each party.**

- Appendix A: Product(s)
- Appendix B: Quality Contacts
- Appendix C: Patheon Approved Supplier List
- Appendix D: Client Approved Supplier List
- Appendix E: Patheon Approved Contract Manufacturers and Laboratories List

**APPENDIX A TO THE QUALITY AGREEMENT BETWEEN TETRAPHASE PHARMACEUTICALS, INC. AND PATHEON DATED <EFFECTIVE DATE HERE>:**

**PRODUCT(S)**

| Product (s) | Dosage Form | Dosage (Strength) |
|---|---|---|
| | | |

**APPENDIX B TO THE QUALITY AGREEMENT BETWEEN TETRAPHASE PHARMACEUTICALS, INC. AND PATHEON DATED <EFFECTIVE DATE HERE>:**

**QUALITY CONTACTS**

| | **Patheon** | **(Client)** |
|---|---|---|
| **Responsibility** | QUALITY ASSURANCE | QUALITY ASSURANCE |
| **Name** | | |
| **Title** | | |
| **Phone** | | |
| **E-mail** | | |
| **Address** | | |
| **Responsibility** | QUALITY CONTROL | QUALITY CONTROL |
| **Name** | | |
| **Title** | | |
| **Phone** | | |
| **E-mail** | | |
| **Address** | | |
| **Responsibility** | BUSINESS | BUSINESS |
| **Name** | | |
| **Title** | | |
| **Phone** | | |
| **E-mail** | | |
| **Address** | | |

**APPENDIX C TO THE QUALITY AGREEMENT BETWEEN TETRAPHASE PHARMACEUTICALS, INC. AND PATHEON DATED <EFFECTIVE DATE HERE>:**

**PATHEON APPROVED VENDOR LIST**

| MATERIAL NUMBER | DESCRIPTION | MANUFACTURER NAME | MANUFACTURER CITY/PROVINCE/ STATE |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

**APPENDIX D TO THE QUALITY AGREEMENT BETWEEN TETRAPHASE PHARMACEUTICALS, INC. AND PATHEON DATED <EFFECTIVE DATE HERE>:**

**CLIENT APPROVED VENDOR LIST**

| MATERIAL NUMBER | DESCRIPTION | MANUFACTURER NAME | MANUFACTURER CITY/PROVINCE/ STATE |
|---|---|---|---|
| | | | |
| | | | |
| | | | |
| | | | |
| | | | |

**APPENDIX E TO THE QUALITY AGREEMENT BETWEEN TETRAPHASE PHARMACEUTICALS, INC. AND PATHEON DATED <EFFECTIVE DATE HERE>:**

**PATHEON APPROVED CONTRACT MANUFACTURERS AND LABORATORIES LIST**

| Contractor Name | Address | Contact Information |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

This list does not include any contractors specified by individual clients of Patheon Inc.

In addition to Patheon Inc.'s Quality Control Laboratory, the approved contract labs are used only in situations when:

a) Patheon Inc., does not have the equipment to perform the testing, or,

b) Patheon Inc., does not have enough resources available to perform the testing

**APPENDIX E TO THE QUALITY AGREEMENT BETWEEN TETRAPHASE PHARMACEUTICALS, INC. AND PATHEON DATED <EFFECTIVE DATE HERE>:**

## APPENDIX E: API STARTING MATERIALS EU REQUIREMENTS

The **Customer** is responsible for providing **Patheon** with the following on ***any supplied API*** :

*Registration information*

- all registered API manufacturing sites including addresses & functions;
- approved registered file (CTD module 3.2.S) and any relevant update;
- latest Certificate of suitability to the European Pharmacopoeia (CEP), Active Substance Master File (ASMF) or scientific data in force (as applicable).

*Regulatory compliance information*

- for API sourced from an EU Member State:
  - proof of the manufacturer, distributor & importer registration in the relevant Member State (EUDRA GMDP);
  - manufacturer GMP & distributor GDP certificate from the National Competent Authority as available (EUDRA GMDP);
- for API sourced from a non listed Third country (waiver for listed ones):
  - EU Member State or foreign authority GMP certificate;
  - API EU GMP compliance " ***written confirmation*** " as per official template;
- for all: TSE/ BSE (or viral safety where applicable), Residual Solvents, Genotoxic Impurities, Residues of Metal Catalyst and Reagent information.

*Quality compliance information*

- Proof of the API manufacturer GMP/GDP compliance via ***audit reports*** (on site availability);
- Well identified and documented API supply chain (including API manufacturers, brokers,
  • traders, repackers, relabellers, micronisers and importers).

Current EU regulation references

- **Compilation of the Community Procedures on Inspections and Exchanges of Information** *(version in force)* **:**
  - Union format for registration of Manufacturer, Importer or Distributor of Active Substance;
  - Union format for a GMP certificate [including active substances];
  - Union format for a GDP certificate for active substances to be used as starting materials.
- **GMP Guide Part I:** Basic Requirements for Medicinal Products ( *version in force* ):
  - **Chapter 5:** Production ;
  - **Chapter 7** : Outsourced activities,
- **GMP Guide Part II** : Basic Requirements for Active Substances used as Starting Material ( *version in force* ).
- **GMP Guide Q&As – Part II:** questions 8,9,10 ( *version in force* ).

- **GDP for active substances** : [SANCO/D/6/SF/mg/ddg1.d.6(2013)179367] draft ( *FEB/2013* ).
- **Directive 2011/62/EU** ( *JUL/2011* ) articles 46, 46 b (2), 47, 111b and derivative texts:
    - Implementing decision on the assessment of a third country's regulatory framework applicable to active substances of medicinal products for human use [2013/51/EU] ( *JAN/2013* );
    - Template for ***written confirmation*** [SANCO/SFS/SF/mg/ddg1.d.6(2013)118630] ( *version in force* ) & Q&As [SANCO/D/6/] ( *version in force* );
    - Implementing regulation on principles and guideline for GMP for AS [(EU) n°1252/2014] ( *MAY/2014* )
- **EMA/334808/2014** : Qualified Person's declaration concerning GMP compliance of the active substance manufacture - "The QP declaration template" and guidance for the "QP declaration template **EMA/196292/2014** *(version in force).*
- **EMA/410/01** : Note for guidance on guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal product ( *version in force* ).
- **Ph. Eur. 5.2.8** : Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products.
- **EU EMA/CHMP/ICH/82260/2006** : (ICH topic Q3C R5) Impurities - guideline for residual solvents ( *version in force* ) + annexes I & II **CPMP/QWP/450/03** ( *version in force* )
- **Ph. Eur. Chapter 5.4** : Residual Solvents.
- **EMEA/CHMP/SWP/4446/2000** : Guideline on the specification limits for residues of metal catalysts or metal reagents ( *version in force* ).
- **Ph Eur Chapter 5.20** : Metal catalyst and metal reagents residues .
- **ICHQ3D** Draft guideline for elemental impurities (step 4) ( *DEC/2014* ).
- **CPMP/SWP/5199/02 - EMEA/CHMP/QWP/251344/2006** : Guideline on the limits of genotoxic impurities *(version in force)* + Q&As **EMA/CHMP/SWP/431994/2007** *(version in force).*

## EXHIBIT C

## QUARTERLY ACTIVE MATERIALS INVENTORY REPORT

TO: TETRAPHASE PHARMACEUTICALS, INC.

FROM: PATHEON UK LIMITED [or applicable Patheon Affiliate]

RE: Active Materials quarterly inventory report under Section 2.2(a) of the Master Manufacturing Services Agreement dated • (the "**Agreement**")

Reporting quarter: _____

Active Materials on hand at beginning of quarter: _____ kg (A)

Active Materials on hand at end of quarter: _____ kg (B)

Quantity Received during quarter: _____ kg (C)

Quantity Dispensed [1] during quarter: (A + C – B) _____ kg

Quantity Converted during quarter: (total Active Materials in Products produced and not rejected, recalled or returned) _____ kg

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

PATHEON UK LIMITED
[or applicable Patheon Affiliate]

DATE: _____

Per: _____
Name: _____
Title:

[1] Excludes any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv) Active Materials received or consumed in technical transfer activities or development activities, including, without limitation, any regulatory, stability, validation, or test batches manufactured during the quarter.

**EXHIBIT D**

**REPORT OF ANNUAL ACTIVE MATERIALS INVENTORY RECONCILIATION AND CALCULATION OF ACTUAL ANNUAL YIELD**

TO: TETRAPHASE PHARMACEUTICALS, INC.

FROM: PATHEON UK LIMITED [or applicable Patheon Affiliate]

RE: Active Materials annual inventory reconciliation report and calculation of Actual Annual Yield under Section 2.2(a) of the Master Manufacturing Services Agreement dated • (the " **Agreement** ")

| | | | |
|---|---|---|---|
| Reporting Year ending: | | | |
| Active Materials on hand at beginning of Year: | | kg | (A) |
| Active Materials on hand at end of Year: | | kg | (B) |
| Quantity Received during Year: | | kg | (C) |
| Quantity Dispensed [2] during Year: (A + C – B) | | kg | (D) |
| Quantity Converted during Year: (total Active Materials in Products produced and not rejected, recalled or returned) | | kg | (E) |
| Active Materials Credit Value: | USD/EUR | / kg | (F) |
| Target Yield: | | % | (G) |
| Actual Annual Yield: ((E/D) * 100) | | % | (H) |
| Shortfall: (((G – 5) - H)/100) * F * D | USD/EUR (if a negative number, insert zero) | | (I) |

Based on the foregoing reimbursement calculation Patheon will reimburse Client the amount of USD/EUR _____.

2 Excludes any (i) Active Materials that must be retained by Patheon as samples, (ii) Active Materials contained in Product that must be retained as samples, (iii) Active Materials used in testing (if applicable), and (iv) Active Materials received or consumed in technical transfer activities or development activities, including, without limitation, any regulatory, stability, validation, or test batches manufactured during the Year.

Capitalized terms used in this report have the meanings given to the terms in the Agreement.

DATE: _____

PATHEON UK LIMITED
[or applicable Patheon Affiliate]

Per: _____
Name:
Title:

ActiveUS 163370610

**Exhibit 31.1**

**Certification of Chief Executive Officer**
**pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934,**
**as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Guy Macdonald, certify that:

(1) I have reviewed this quarterly report on Form 10-Q of Tetraphase Pharmaceuticals, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: August 2, 2017

/s/ Guy Macdonald
Guy Macdonald
Chief Executive Officer (Principal Executive Officer)

**Exhibit 31.2**

**Certification of Principal Financial Officer**
**pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934,**
**as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002**

I, Christopher Watt, certify that:

(1) I have reviewed this quarterly report on Form 10-Q of Tetraphase Pharmaceuticals, Inc.;

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

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

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d015(f)) for the registrant and have:

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

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

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

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

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

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

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

Date: August 2, 2017

/s/ Christopher Watt
Christopher Watt
Senior Vice President, Finance
(Principal Financial Officer and Principal Accounting Officer)

**Exhibit 32.1**

**Certification of Chief Executive Officer**
**pursuant to 18 U.S.C. Section 1350, as adopted**
**pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**

In connection with the quarterly report on Form 10-Q of Tetraphase Pharmaceuticals, Inc. (the "Company") for the period ended June 30, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Guy Macdonald, as Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

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

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

Dated: August 2, 2017

/s/ Guy Macdonald
Guy Macdonald
Chief Executive Officer

**Exhibit 32.2**

**Certification of Principal Financial Officer**
**pursuant to 18 U.S.C. Section 1350, as adopted**
**pursuant to Section 906 of the Sarbanes-Oxley Act of 2002**

In connection with the quarterly report on Form 10-Q of Tetraphase Pharmaceuticals, Inc. (the "Company") for the period ended June 30, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Christopher Watt, as Senior Vice President, Finance of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge:

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

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

Dated: August 2, 2017

/s/ Christopher Watt
Christopher Watt
Senior Vice President, Finance