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

FORM 10-Q

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2019

OR

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

COMMISSION FILE NUMBER 001-36279

CARA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**75-3175693**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
4 Stamford Plaza **107 Elm Street, 9th Floor** **Stamford, Connecticut**	**06902**
(Address of registrant's principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (203) 406-3700

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.001 per share	CARA	The Nasdaq Stock Market LLC

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

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

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

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

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

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

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of August 2, 2019 was: 46,417,700.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2019

PART I –FINANCIAL INFORMATION

PART I
FINANCIAL INFORMATION

Item 1. ***Financial Statements.***

CARA THERAPEUTICS, INC.

CONDENSED BALANCE SHEETS
(amounts in thousands, excluding share and per share data)
(unaudited)

	June 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 18,494	$ 15,081
Marketable securities	96,815	146,302
Income tax receivable	984	664
Other receivables	605	926
Prepaid expenses	7,512	4,805
Restricted cash, current	361	361
Total current assets	124,771	168,139
Operating lease right-of-use asset	3,344	—
Marketable securities, non-current	20,320	21,396
Property and equipment, net	798	880
Restricted cash	408	408
Total assets	$ 149,641	$ 190,823
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 12,766	$ 13,622
Operating lease liability, current	923	—
Current portion of deferred revenue	26,473	26,825
Total current liabilities	40,162	40,447
Operating lease liability, non-current	3,849	—
Deferred revenue, non-current	6,085	15,184
Deferred lease obligation	—	1,562
Commitments and contingencies (Note 15)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at June 30, 2019 and December 31, 2018, zero shares issued and outstanding at June 30, 2019 and December 31, 2018	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at June 30, 2019 and December 31, 2018, 40,027,916 shares and 39,547,558 shares issued and outstanding at June 30, 2019 and December 31, 2018, respectively	40	39
Additional paid-in capital	438,614	428,059
Accumulated deficit	(339,274)	(294,354)
Accumulated other comprehensive income (loss)	165	(114)
Total stockholders' equity	99,545	133,630
Total liabilities and stockholders' equity	$ 149,641	$ 190,823

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

CONDENSED STATEMENTS OF COMPREHENSIVE LOSS
(amounts in thousands, excluding share and per share data)
(unaudited)

	Three Months Ended		Six Months Ended	
	June 30, 2019	June 30, 2018	June 30, 2019	June 30, 2018
Revenue:				
License and milestone fees	$ 5,208	$ 2,874	$ 9,450	$ 2,874
Clinical compound revenue	—	—	140	—
Total revenue	5,208	2,874	9,590	2,874
Operating expenses:				
Research and development	24,356	17,002	47,964	30,429
General and administrative	4,994	3,685	8,902	7,382
Total operating expenses	29,350	20,687	56,866	37,811
Operating loss	(24,142)	(17,813)	(47,276)	(34,937)
Other income	947	467	2,036	778
Loss before benefit from income taxes	(23,195)	(17,346)	(45,240)	(34,159)
Benefit from income taxes	235	152	320	198
Net loss	$ (22,960)	$ (17,194)	$ (44,920)	$ (33,961)
Net loss per share:				
Basic and Diluted	$ (0.58)	$ (0.52)	$ (1.13)	$ (1.03)
Weighted average shares:				
Basic and Diluted	39,818,162	33,315,809	39,685,954	33,000,487
Other comprehensive income, net of tax of $0:				
Change in unrealized gains (losses) on available-for-sale marketable securities	92	57	279	13
Total comprehensive loss	$ (22,868)	$ (17,137)	$ (44,641)	$ (33,948)

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

CONDENSED STATEMENTS OF STOCKHOLDERS' EQUITY
(amounts in thousands except share and per share data)
(unaudited)

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2017	32,662,255	$ 33	$ 307,158	$ (220,341)	$ (70)	$ 86,780
Stock-based compensation expense	—	—	1,871	—	—	1,871
Shares issued upon exercise of stock options	37,688	—	263	—	—	263
Net loss	—	—	—	(16,767)	—	(16,767)
Other comprehensive loss	—	—	—	—	(44)	(44)
Balance at March 31, 2018	32,699,943	33	309,292	(237,108)	(114)	72,103
Sale of common stock under license agreement	1,174,827	1	14,555	—	—	14,556
Stock-based compensation expense	—	—	2,069	—	—	2,069
Shares issued upon exercise of stock options	184,444	—	1,485	—	—	1,485
Net loss	—	—	—	(17,194)	—	(17,194)
Other comprehensive income	—	—	—	—	57	57
Balance at June 30, 2018	34,059,214	$ 34	$ 327,401	$ (254,302)	$ (57)	$ 73,076

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2018	39,547,558	$ 39	$ 428,059	$ (294,354)	$ (114)	$ 133,630
Stock-based compensation expense	—	—	2,234	—	—	2,234
Shares issued upon exercise of stock options	17,291	—	234	—	—	234
Shares issued for consulting services	10,195	—	197	—	—	197
Net loss	—	—	—	(21,960)	—	(21,960)
Other comprehensive income	—	—	—	—	187	187
Balance at March 31, 2019	39,575,044	39	430,724	(316,314)	73	114,522
Stock-based compensation expense	—	—	2,681	—	—	2,681
Shares issued upon exercise of stock options	378,706	1	3,974	—	—	3,975
Shares issued upon vesting of restricted stock units	74,166	—	1,235	—	—	1,235
Net loss	—	—	—	(22,960)	—	(22,960)
Other comprehensive income	—	—	—	—	92	92
Balance at June 30, 2019	40,027,916	$ 40	$ 438,614	$ (339,274)	$ 165	$ 99,545

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

CONDENSED STATEMENTS OF CASH FLOWS
(amounts in thousands)
(unaudited)

	Six Months Ended	
	June 30, 2019	**June 30, 2018**
Operating activities		
Net loss	$ (44,920)	$ (33,961)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Stock-based compensation expense	6,249	3,940
Depreciation and amortization	100	239
Amortization expense component of lease expense	293	—
Accretion of available-for-sale marketable securities	(803)	(559)
Realized loss on sale of available-for-sale marketable securities	—	15
Deferred rent costs	—	(23)
Deferred revenue	(9,450)	52,569
Changes in operating assets and liabilities:		
Income tax receivable	(320)	258
Other receivables	321	7
Prepaid expenses	(2,609)	(3,980)
Accounts payable and accrued expenses	(856)	4,047
Operating lease liability	(427)	—
Net cash (used in) provided by operating activities	(52,422)	22,552
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	122,881	56,700
Proceeds from sale of available-for-sale marketable securities	—	11,150
Purchases of available-for-sale marketable securities	(71,236)	(98,271)
Purchases of property and equipment	(18)	(21)
Net cash provided by (used in) investing activities	51,627	(30,442)
Financing activities		
Proceeds from the sale of common stock under license agreement	—	14,556
Proceeds from the exercise of stock options	4,208	1,748
Net cash provided by financing activities	4,208	16,304
Net increase in cash, cash equivalents and restricted cash	3,413	8,414
Cash, cash equivalents and restricted cash at beginning of period	15,850	10,157
Cash, cash equivalents and restricted cash at end of period	$ 19,263	$ 18,571
Noncash investing and financing activities		
Shares of common stock issued in exchange for consulting services (recorded as a prepaid expense)	$ 197	$ —

See Notes to Condensed Financial Statements.

1. Business

Cara Therapeutics, Inc., or the Company, is a clinical-stage biopharmaceutical corporation formed on July 2, 2004. The Company is focused on developing and commercializing new chemical entities designed to alleviate pruritus by selectively targeting peripheral kappa opioid receptors. The Company's primary activities to date have been organizing and staffing the Company, developing its product candidates and raising capital.

As of June 30, 2019, the Company had raised aggregate net proceeds of approximately $383,200 from several rounds of equity financing, including its initial public offering, or IPO, which closed in February 2014 and three follow-on public offerings of common stock, which closed in July 2018, April 2017 and August 2015, and the issuance of convertible preferred stock and debt prior to the IPO. The Company had also received $88,900 under its license agreements for CR845/difelikefalin, primarily with Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceutical Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and an earlier product candidate for which development efforts ceased in 2007. Additionally, in May 2018, the Company received net proceeds of $14,556 from the issuance and sale of 1,174,827 shares of the Company's common stock to Vifor (International) Ltd., or Vifor, in connection with the Company's license agreement with VFMCRP (see Note 10, *Collaboration and Licensing Agreements*).

As of June 30, 2019, the Company had unrestricted cash and cash equivalents and marketable securities of $135,629 and an accumulated deficit of $339,274. The Company has incurred substantial net losses and negative cash flows from operating activities in nearly every fiscal period since inception and expects this trend to continue for the foreseeable future. The Company recognized net losses of $22,960 and $17,194 for the three months ended June 30, 2019 and 2018, respectively, and $44,920 and $33,961 for the six months ended June 30, 2019 and 2018, respectively, and had net cash (used in) provided by operating activities of $(52,422) and $22,552 for the six months ended June 30, 2019 and 2018, respectively.

In July 2019, the Company received net proceeds of approximately $136,446 from the issuance and sale of 6,325,000 shares of its common stock in a follow-on public offering, which includes the full exercise of the underwriters' option to purchase 825,000 additional shares of its common stock (see Note 16, *Subsequent Events*).

The Company is subject to risks common to other life science companies including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, product liability, protection of proprietary technology, ability to raise additional financing, and compliance with Food and Drug Administration, or FDA, and other government regulations. If the Company does not successfully commercialize any of its product candidates, it will be unable to generate recurring product revenue or achieve profitability.

2. Basis of Presentation

The unaudited interim condensed financial statements included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission, or SEC. Accordingly, they do not include all information and disclosures necessary for a presentation of the Company's financial position, results of operations and cash flows in conformity with generally accepted accounting principles in the United States of America, or GAAP. In the opinion of management, these unaudited interim financial statements reflect all adjustments, consisting primarily of normal recurring accruals, necessary for a fair presentation of results for the periods presented. The results of operations for interim periods are not necessarily indicative of the results for the full year. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted from this report, as is permitted by SEC rules and regulations; however, the Company believes that the disclosures are adequate to make the information presented not misleading. The condensed balance sheet data as of December 31, 2018 were derived from audited financial statements, but do not include all disclosures required by GAAP. These unaudited interim condensed financial statements should be read in conjunction with the audited financial statements and accompanying notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2018.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities, and disclosure of contingent assets and liabilities, as of the date of the financial statements as well as the reported amounts of revenues and expenses during the reporting period. Actual results could differ materially from the Company's estimates and assumptions. Significant estimates include the fair value of marketable securities that are classified as level 2 of the fair value hierarchy, useful lives of fixed assets, the periods over which certain revenues will be recognized, including licensing and collaborative revenue recognized from non-refundable up-front and milestone payments, the determination of prepaid research and development, or R&D, clinical costs and accrued research projects, the amount of non-cash compensation costs related to share-based payments to employees and non-employees and the periods over which those costs are expensed, the incremental borrowing rate used in lease calculations and the likelihood of realization of deferred tax assets.

Significant Accounting Policies

There have been no material changes to the significant accounting policies previously disclosed in Note 2 to the Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2018, except for the recent adoption of new accounting pronouncements as disclosed below.

Accounting Pronouncements Recently Adopted

Leases

On January 1, 2019, the Company adopted ASC 842, *Leases*, under which it elected not to adjust prior comparative periods, which are reported under ASC 840. In addition, the Company elected to adopt both the practical expedient to use hindsight when determining the lease term and the package of practical expedients available under ASC 842, including:

- No re-evaluation of whether a contract is or contains a lease (embedded lease);
- Lease classification is grandfathered
- No reassessment of initial direct costs

Upon adoption of ASC 842, the Company had only one lease, the Stamford Lease (see Note 15, *Commitments and Contingencies: Leases*), which is included in operating lease right-of-use asset, or ROU asset, operating lease liability – current and operating lease liability – non-current in the Company's Condensed Balance Sheets.

In general, the Company determines if a contract, at its inception, is a lease or contains a lease based on whether the contract conveys the right to control the use of identified property, plant, or equipment (an identified asset) for a period of time in exchange for consideration. To determine whether a contract conveys the right to control the use of an identified asset for a period of time, the Company assesses whether, throughout the period of use, it has both the right to obtain substantially all of the economic benefits from use of the identified asset, and the right to direct the use of the identified asset. Both of these criteria are met by the Stamford Lease.

Under ASC 842, the Company determines the amount of the operating lease liability based on the present value of the future minimum lease payments over the remaining lease term. The amount of the operating lease ROU asset is equal to the amount of the lease liability, less accrued rent and lease incentives received from the landlord. Initial direct costs were deemed to be immaterial.

Since the Stamford Lease does not provide an implicit interest rate, the Company used an annual incremental borrowing rate of 7% based on the information available at the date of adoption for the purpose of determining the lease liability during the term of the lease.

As noted above, upon adoption of ASC 842, the Company used hindsight in determining the term of the Stamford Lease. Although the Stamford Lease is renewable for one five-year term, upon inception of the lease the renewal term was not included in the lease term since it was not reasonably certain that the Company will exercise that option. Accordingly, the lease term of the Stamford Lease was not adjusted upon adoption of ASC 842 to determine the operating lease ROU asset and operating lease liability.

The Stamford Lease contains both a lease and non-lease component which are accounted for separately. The Company allocates the consideration to the lease and the non-lease component on a relative standalone price basis. Lease expense under ASC 842 is recognized on a straight-line basis over the lease term in the Condensed Statements of Comprehensive Loss.

There was no cumulative effect adjustment as a result of the adoption of ASC 842 on January 1, 2019, which reflects the difference between the amount of lease expense under ASC 842 that would have been recognized from inception of the Stamford Lease through December 31, 2018 and the amount of rent expense actually recognized under ASC 840 during that same period.

Other Accounting Pronouncements Recently Adopted

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*, or ASU 2018-07, which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. ASU 2018-07 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. Accordingly, under ASU 2018-07, the fair value of stock options granted to nonemployees will be measured only on the grant date, the amount of which will be recognized as compensation expense over the nonemployee's service (vesting) period in the same period(s) and in the same manner as if the Company had paid cash for the goods or services instead of paying with or using share-based payment awards. On an award-by-award basis, the Company may elect to use the contractual term as the expected term when estimating the fair value of a nonemployee award to satisfy the measurement objective. Prior guidance under Subtopic 505-50 required the fair value of nonemployee stock options to be marked to market at each reporting period during the service period, which resulted in volatility of compensation expense during that period. The Company adopted ASU 2018-07 on January 1, 2019 on a modified retrospective basis and remeasured, on that date, the fair value of all outstanding unvested stock options that had been granted to nonemployees. The adoption of ASU 2018-07 did not have a material effect on its results of operations, financial position or cash flows because grants of stock options to nonemployees have been insignificant.

Accounting Pronouncements Not Yet Adopted

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606*, or ASU 2018-18, which clarifies the interaction between Topic 808 and Topic 606 by (1) clarifying that certain transactions between collaborative arrangement participants should be accounted for under Topic 606; (2) adding unit-of-account guidance in Topic 808 to align with the guidance in Topic 606; and (3) clarifying presentation guidance for transactions with a collaborative arrangement participant that are not accounted for under Topic 606. ASU 2018-18 is effective for public business entities for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted, including adoption in any interim period. The Company has determined that ASU 2018-18 will not have any effect on its financial position, results of operations or cash flows since all three of its collaboration and licensing agreements are accounted for under Topic 606 (see Note 10, *Collaboration and Licensing Agreements* and Note 11, *Revenue Recognition*).

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, or ASU 2018-13, which modifies the disclosure requirements on fair value measurements in Topic 820 to remove the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, the policy for timing of transfers between levels, and the valuation processes for Level 3 fair value measurements. ASU 2018-13 also amends Topic 820 to clarify that the measurement uncertainty disclosure is to communicate information about the uncertainty in measurement as of the reporting date. ASU 2018-13 also requires additional disclosure for changes in unrealized gains and losses for the period included in other comprehensive income for recurring Level 3 fair value measurements held at the end of the reporting period as well as the range and weighted average

(amounts in thousands, except share and per share data)

of significant unobservable inputs used to develop Level 3 fair value measurements. ASU 2018-13 is effective for all entities for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty should be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments should be applied retrospectively to all periods presented upon their effective date. Early adoption is permitted upon issuance of ASU 2018-13. The Company will adopt ASU 2018-13, as applicable, on January 1, 2020. The Company does not expect that the adoption of ASU 2018-13 will have a material effect on its results of operations, financial position or cash flows.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326), Measurement of Credit Losses on Financial Instruments*, or ASU 2016-13, which replaces the incurred loss impairment methodology in current GAAP, that delays recognition of a credit loss until it is probable that such loss has been incurred, with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 modifies the other-than-temporary impairment model for available-for-sale debt securities by requiring (1) estimating expected credit losses only when the fair value is below the amortized cost of the asset; (2) recording a credit loss without regard to the length of time a security has been in an unrealized loss position; (3) limiting the measurement of the credit loss to the difference between the security's amortized cost basis and its fair value and (4) presenting credit losses as an allowance rather than as a write-down, which will allow the Company to record reversals of credit losses in current period net income, a practice that is currently prohibited. In April 2019, codification improvements were issued to help clarify and correct certain portions of ASU 2016-13. ASU 2016-13 will be effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. As such, the Company expects to adopt ASU 2016-13 on January 1, 2020 and is currently evaluating the effect it will have on its results of operations, financial position and cash flows.

3. Available-for-Sale Marketable Securities

As of June 30, 2019 and December 31, 2018, the Company's available-for-sale marketable securities consisted of debt securities issued by the U.S. Treasury, U.S. government-sponsored entities and investment grade institutions as well as municipal bonds.

The following tables summarize the Company's available-for-sale marketable securities by major type of security as of June 30, 2019 and December 31, 2018:

As of June 30, 2019

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 12,992	$ 32	$ —	$ 13,024
U.S. government agency obligations	12,447	16	—	12,463
Corporate bonds	62,529	109	(6)	62,632
Commercial paper	23,502	14	—	23,516
Municipal bonds	5,500	—	—	5,500
Total available-for-sale marketable securities	$ 116,970	$ 171	$ (6)	$ 117,135

As of December 31, 2018

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 19,540	$ —	$ (1)	$ 19,539
U.S. government agency obligations	17,860	—	(1)	17,859
Corporate bonds	75,999	5	(94)	75,910
Commercial paper	50,413	—	(23)	50,390
Municipal bonds	4,000	—	—	4,000
Total available-for-sale marketable securities	$ 167,812	$ 5	$ (119)	$ 167,698

(amounts in thousands, except share and per share data)

All available-for-sale marketable securities are classified as Marketable securities, current or Marketable securities, non-current depending on the contractual maturity date of the individual available-for-sale security.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of June 30, 2019, the Company's marketable debt securities mature at various dates through March 2021. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows.

	As of June 30, 2019		As of December 31, 2018	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 96,712	$ 96,815	$ 146,363	146,302
One year to two years	20,258	20,320	21,449	21,396
Total	$ 116,970	$ 117,135	$ 167,812	$ 167,698

The following tables show the fair value of the Company's available-for-sale marketable securities that have unrealized losses and that are deemed to be only temporarily impaired, aggregated by investment category and length of time that the individual investments have been in a continuous unrealized loss position.

As of June 30, 2019

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Corporate bonds	$ 4,756	$ (6)	$ —	$ —	$ 4,756	$ (6)
Total	$ 4,756	$ (6)	$ —	$ —	$ 4,756	$ (6)

As of December 31, 2018

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
U.S. Treasury securities	$ 16,392	$ (1)	$ —	$ —	$ 16,392	$ (1)
U.S. government agency obligations	5,596	(1)	—	—	5,596	(1)
Corporate bonds	71,322	(94)	—	—	71,322	(94)
Commercial paper	39,445	(23)	—	—	39,445	(23)
Total	$ 132,755	$ (119)	$ —	$ —	$ 132,755	$ (119)

As of June 30, 2019 and December 31, 2018, the Company held a total of 6 out of 58 positions and 69 out of 84 positions, respectively, that were in an unrealized loss position, none of which had been in an unrealized loss position for 12 months or greater. Based on the Company's review of these securities, the Company believes that the cost basis of its available-for-sale marketable securities is recoverable and that, therefore, it had no other-than-temporary impairments on these securities as of June 30, 2019 and December 31, 2018. The Company does not intend to sell these debt securities before maturity and the Company believes it is not more likely than not that it will be required to sell these securities before the recovery of their amortized cost basis, which may be maturity.

(amounts in thousands, except share and per share data)

4. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss), or AOCI, net of tax, from unrealized gains (losses) on available-for-sale marketable securities, the Company's only component of AOCI, for the six months ended June 30, 2019 and June 30, 2018.

	Total Accumulated Other Comprehensive Income (Loss)
Balance, December 31, 2018	$ (114)
Other comprehensive income before reclassifications	279
Amount reclassified from accumulated other comprehensive income	—
Net current period other comprehensive income	279
Balance, June 30, 2019	$ 165
Balance, December 31, 2017	$ (70)
Other comprehensive loss before reclassifications	(2)
Amount reclassified from accumulated other comprehensive loss	15
Net current period other comprehensive income	13
Balance, June 30, 2018	$ (57)

The reclassifications out of AOCI and into net loss were as follows:

Component of AOCI	Three Months Ended June 30, 2019	Three Months Ended June 30, 2018	Six Months Ended June 30, 2019	Six Months Ended June 30, 2018	Affected Line Item in the Statements of Operations
Unrealized gains (losses) on available-for-sale marketable securities					
Realized gains (losses) on sale of securities	$ —	$ —	$ —	$ (15)	Other income
	—	—	—	—	Benefit from income taxes
	$ —	$ —	$ —	$ (15)	

The amounts reclassified out of AOCI into net loss were determined by specific identification.

5. Fair Value Measurements

As of June 30, 2019 and December 31, 2018, the Company’s financial instruments consisted of cash, cash equivalents, available-for-sale marketable securities, prepaid expenses, restricted cash, accounts payable and accrued liabilities. The fair values of cash, cash equivalents, prepaid expenses, restricted cash, accounts payable and accrued liabilities approximate their carrying values due to the short-term nature of these financial instruments. Available-for-sale marketable securities are reported on the Company’s Condensed Balance Sheets as Marketable Securities at their fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services, as described below.

(amounts in thousands, except share and per share data)

Current accounting guidance defines fair value, establishes a framework for measuring fair value in accordance with ASC section 820, and requires certain disclosures about fair value measurements. The valuation techniques included in the guidance are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

The Company classifies its investments in a fair value hierarchy that is intended to increase consistency and comparability in fair value measurements and related disclosures. The fair value hierarchy is divided into three levels based on the source of inputs as follows:

- Level 1 – Observable inputs – quoted prices in active markets for identical assets and liabilities.
- Level 2 – Observable inputs other than the quoted prices in active markets for identical assets and liabilities – such as quoted prices for similar instruments, quoted prices for identical or similar instruments in inactive markets, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 – Unobservable inputs – includes amounts derived from valuation models where one or more significant inputs are unobservable and require the Company to develop relevant assumptions.

Valuation Techniques - Level 2 Inputs

The Company estimates the fair values of its financial instruments categorized as level 2 in the fair value hierarchy, including U.S. Treasury securities, U.S. government agency obligations, corporate bonds, commercial paper and municipal bonds, by taking into consideration valuations obtained from third-party pricing services. The pricing services use industry standard valuation models, including both income- and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, benchmark yields, issuer credit spreads, benchmark securities, and other observable inputs. The Company obtains a single price for each financial instrument and does not adjust the prices obtained from the pricing service.

The Company validates the prices provided by its third-party pricing services by reviewing their pricing methods, obtaining market values from other pricing sources and comparing them to the share prices presented by the third-party pricing services. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by its third-party pricing services as of June 30, 2019 or December 31, 2018.

The following tables summarize the Company's financial assets measured at fair value on a recurring basis as of June 30, 2019 and December 31, 2018.

Fair value measurement as of June 30, 2019:

Financial assets Type of Instrument	Total	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Cash and cash equivalents:				
Money market funds and checking accounts	$ 18,494	$ 18,494	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	13,024	—	13,024	—
U.S. government agency obligations	12,463	—	12,463	—
Corporate bonds	62,632	—	62,632	—
Commercial paper	23,516	—	23,516	—
Municipal bonds	5,500	—	5,500	—
Restricted cash:				
Commercial money market account	769	769	—	—
Total financial assets	$ 136,398	$ 19,263	$ 117,135	$ —

(amounts in thousands, except share and per share data)

Fair value measurement as of December 31, 2018:

Financial assets Type of Instrument	Total	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Cash and cash equivalents:				
Money market funds and checking accounts	$ 15,081	$ 15,081	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	19,539	—	19,539	—
U.S. government agency obligations	17,859	—	17,859	—
Corporate bonds	75,910	—	75,910	—
Commercial paper	50,390	—	50,390	—
Municipal bonds	4,000	—	4,000	—
Restricted cash:				
Commercial money market account	769	769	—	—
Total financial assets	$ 183,548	$ 15,850	$ 167,698	$ —

There were no purchases, sales or maturities of Level 3 financial assets and no unrealized gains or losses related to Level 3 available-for-sale marketable securities for the six months ended June 30, 2019. There were no transfers of financial assets between Levels 1, 2, or 3 classifications during the six months ended June 30, 2019.

6. Restricted Cash

The Company is required to maintain a stand-by letter of credit as a security deposit under its lease for its office space in Stamford, Connecticut (refer to Note 15, *Commitments and Contingencies: Leases*). The fair value of the letter of credit approximates its contract value. The Company's bank requires the Company to maintain a restricted cash balance to serve as collateral for the letter of credit issued to the landlord by the bank. As of June 30, 2019, the restricted cash balance for the Stamford Lease was invested in a commercial money market account.

The letter of credit balance for the Stamford Lease was required to remain at $769 through May 19, 2019 and may, upon request from the Company, thereafter be reduced to $408 through the end of the lease term in November 2023. The reduction in the balance of the letter of credit for the Stamford Lease was contingent upon the Company not being in default of any provisions of that lease prior to the request for the reduction. As of June 30, 2019, the Company requested the reduction in the balance of the letter of credit and it was approved in July 2019. As of June 30, 2019 and December 31, 2018, the Company had $361 of restricted cash related to the Stamford Lease in current assets and $408 in long-term assets, respectively.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the Condensed Balance Sheets that sum to the total of the same such amounts shown in the Condensed Statements of Cash Flows.

	June 30, 2019	December 31, 2018
Cash and cash equivalents	$ 18,494	$ 15,081
Restricted cash, current assets	361	361
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 19,263	$ 15,850

(amounts in thousands, except share and per share data)

7. Prepaid expenses

As of June 30, 2019, prepaid expenses were $7,512, consisting of $6,461 of prepaid R&D clinical costs, $671 of prepaid insurance and $380 of other prepaid costs. As of December 31, 2018, prepaid expenses were $4,805, consisting of $4,377 of prepaid R&D clinical costs, $245 of prepaid insurance, and $183 of other prepaid costs.

8. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	June 30, 2019	December 31, 2018
Accounts payable	$ 2,485	$ 4,371
Accrued research projects	7,795	6,079
Accrued professional fees	527	802
Accrued compensation and benefits	1,959	2,370
Total	$ 12,766	$ 13,622

9. Stockholders' Equity

On July 29, 2019, the Company issued and sold 6,325,000 shares of its common stock in a follow-on public offering, which includes the full exercise of the underwriters' option to purchase 825,000 additional shares of common stock. The Company received net proceeds of approximately $136,446, after deducting $9,029 of underwriting discounts and commissions and estimated offering expenses payable by the Company. This offering was made pursuant to the Company's Registration Statement on Form S-3 (File No. 333-230333), or the Shelf Registration Statement, filed with the SEC on March 15, 2019 and declared effective on April 4, 2019, and a related prospectus supplement dated July 24, 2019, which was filed with the SEC on July 25, 2019 (see Note 16, *Subsequent Events*). The Shelf Registration Statement provides for aggregate offerings of up to $300,000 of common stock, preferred stock, debt securities, warrants or any combination thereof. The securities registered under the Shelf Registration Statement include unsold securities that had been registered under the Company's previous shelf registration statement (File No. 333-216657) that was declared effective on March 24, 2017.

In May 2019, as a result of the achievement of a clinical performance target, an aggregate of 74,166 restricted stock units of various executive officers vested and were settled in shares of the Company's common stock (see Note 13, *Stock-Based Compensation*).

On March 20, 2019, or the Effective Date, the Company entered into a consulting agreement with an existing stockholder. In accordance with the agreement, the stockholder will provide various consulting services to the Company in exchange for 10,195 unregistered shares of the Company's common stock. The closing price of the Company's common stock on the Effective Date was $19.37. The services to be provided by the consultant are expected to be performed during the six-month period following the Effective Date. Accordingly, the prepaid expense of $197 related to this stock issuance will be amortized on a straight-line basis as stock compensation expense within general and administrative expenses over the six-month period as services are performed. During the three and six months ended June 30, 2019, $99 of stock-based compensation expense was recognized in the Statements of Comprehensive Loss, all of which related to G&A expense.

10. Collaboration and Licensing Agreements

Vifor Fresenius Medical Care Renal Pharma Ltd.

On May 17, 2018, the Company entered into a license agreement, or the VFMCRP Agreement, with VFMCRP under which the Company granted VFMCRP an exclusive, royalty-bearing license, or the VFMCRP License, to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize CR845/difelikefalin injection, or the Licensed Product, for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients, or the Field, worldwide (excluding the United States, Japan and South Korea), or the Territory.

Upon entry into the VFMCRP Agreement, VFMCRP made a non-refundable, non-creditable $50,000 upfront payment to the Company and Vifor purchased 1,174,827 shares of the Company's common stock, or the Vifor Shares, for $20,000 at a price of $17.024 per share, which represents a premium over a pre-determined average closing price of the Company's common stock. The purchase of the Company's common stock was governed by a separate stock purchase agreement. The excess of the stock purchase price over the cost of the Vifor Shares at the closing price of the Company's common stock on the purchase date of $5,444 was added to the upfront payment for accounting purposes.

The Company is eligible to receive from VFMCRP regulatory and commercial milestone payments in the aggregate of up to $470,000, consisting of up to $30,000 in regulatory milestones and up to $440,000 in tiered commercial milestones, all of which are sales-related. The Company is also eligible to receive tiered double-digit royalty payments based on annual net sales, as defined in the VFMCRP Agreement, of CR845/difelikefalin injection in the Licensed Territories. The Company retains full commercialization rights for CR845/difelikefalin injection for the treatment of CKD-aP in the United States except in the dialysis clinics of Fresenius Medical Care North America, or FMCNA, where VFMCRP and the Company will promote CR845/difelikefalin injection under a profit-sharing arrangement (subject to the terms and conditions of the VFMCRP Agreement) based on net FMCNA clinic sales recorded by the Company.

At inception of the VFMCRP Agreement, the transaction price of $55,444 was allocated entirely to the one combined performance obligation, as described above, and was initially recorded as deferred revenue. License and milestone revenue will be recognized proportionately as the R&D services are conducted (i.e., prior to submission of an NDA).

The license also requires VFMCRP to promote and take orders in the U.S. for sale by the Company to FMC U.S. Dialysis Clinics and allows VFMCRP to grant sub-licenses, which, in certain cases, requires the Company's prior written consent. The Company retains the rights to import, distribute, promote, sell and otherwise commercialize the Licensed Product outside of the Field and outside of the Territory.

The VFMCRP Agreement terminates upon the expiration of all royalty terms with respect to the Licensed Products, which expire on a Product-by-Product and country-by-country basis, at the latest of (a) the expiration of all patent rights licensed to VFMCRP covering such Licensed Product; (b) the expiration of all regulatory and data exclusivity applicable to such Licensed Product in such country and (c) the tenth anniversary of the first commercial sale of such Product in such country.

The VFMCRP Agreement may be terminated earlier by either party for material breach that is not cured within 60 days, bankruptcy by either party and by both parties upon mutual written consent. The Company may terminate the VFMCRP Agreement if VFMCRP challenges the validity of any licensed patent rights, except if such patent challenge results from the Company's action against VFMCRP for infringement of any licensed patent in the Territory. In addition, upon the earlier of (1) the acceptance for filing of an NDA covering Licensed Product filed with the FDA (after completion of the Phase 3 program) or (2) the third anniversary of the Effective Date, the VFMCRP Agreement may be terminated by VFMCRP in its entirety or with respect to any countries within the Territory upon written notice to the Company. Such termination will be effective twelve months following the date of such notice.

If the VFMCRP Agreement terminates early for any reason stated above, VFMCRP's licenses will terminate, VFMCRP's rights to use the Company's confidential information and the Company's know-how will revert to the Company and VFMCRP will assign and transfer to the Company all right, title and interest in all regulatory applications (IND's and NDA's), regulatory approval applications and regulatory approvals in the Territory covering Licensed Product.

Maruishi Pharmaceutical Co., Ltd.

In April 2013, the Company entered into a license agreement with Maruishi, or the Maruishi Agreement, under which the Company granted Maruishi an exclusive license to develop, manufacture, and commercialize drug products containing CR845/difelikefalin for acute pain and/or uremic pruritus in Japan. Maruishi has the right to grant sub-licenses in Japan, which entitles the Company to receive sub-license fees, net of prior payments made by Maruishi to the Company. Under the Maruishi Agreement, the Company and Maruishi are required to use commercially reasonable efforts, at their own expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in the United States and Japan, respectively. In addition, the Company provided Maruishi specific clinical development services for CR845/difelikefalin used in Maruishi's field of use.

Under the terms of the Maruishi Agreement, the Company is eligible to receive milestone payments upon the achievement of defined clinical and regulatory events as well as tiered, low double-digit royalties with respect to any sales of the licensed product sold in Japan by Maruishi, if any, and share in any sub-license fees.

During the six months ended June 30, 2019, the Company recognized clinical compound revenue of $140 from the sale of clinical compound to Maruishi and as a result, the Company incurred R&D expense of $126 during the respective period. There were no clinical compound sales to Maruishi during the six months ended June 30, 2018.

Chong Kun Dang Pharmaceutical Corporation

In April 2012, the Company entered into a license agreement, or the CKDP Agreement, with Chong Kun Dang Pharmaceutical Corporation, or CKDP, in South Korea, under which the Company granted CKDP an exclusive license to develop, manufacture and commercialize drug products containing CR845/difelikefalin in South Korea. The Company and CKDP are each required to use commercially reasonable efforts, at their respective expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in the United States and South Korea, respectively. The Company identified the granting of the license as its only performance obligation under the CKDP Agreement.

Under the terms of the CKDP Agreement, the Company is eligible to receive milestone payments upon the achievement of defined clinical and regulatory events as well as tiered royalties, with percentages ranging from the high single digits to the high teens, based on net sales of products containing CR845/difelikefalin in South Korea, if any, and share in any sub-license fees.

11. Revenue Recognition

The Company currently recognizes revenue in accordance with ASC 606, as amended, for the VFMCRP, Maruishi and CKDP agreements (see Note 10, *Collaboration and Licensing Agreements*). Under each of these agreements, the Company has recognized revenue from upfront payments and, under the Maruishi Agreement and the CKDP Agreement, from clinical development milestone payments. The Company has also recognized revenue from a sub-license payment earned under the Maruishi Agreement. Under the Maruishi Agreement and the CKDP Agreement, the Company may earn additional future milestone payments upon the achievement of defined clinical events, and under the VFMCRP Agreement, the Maruishi Agreement and the CKDP Agreement upon the achievement of defined regulatory events and, under the VFMCRP Agreement and the Maruishi Agreement, from sales milestones. The Company may also recognize revenue in the future from royalties on net sales under all three agreements. In addition, the Company has recognized revenue upon the delivery of clinical compound to Maruishi in accordance with separate supply agreements.

Contract balances

As of June 30, 2019, the Company had deferred revenue, current of $26,473 and deferred revenue, non-current of $6,085 related to the performance obligations from the VFMCRP Agreement and had no balances of receivables or other assets related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of June 30, 2019. As of December 31, 2018, the Company had deferred revenue, current of $26,825 and deferred revenue, non-current of $15,184 related to the performance obligations from the VFMCRP Agreement and no balances of receivables or other assets related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of December 31, 2018.

Performance obligations

Under the VFMCRP Agreement, the Company’s performance obligations of granting a license to allow VFMCRP to commercialize CR845/difelikefalin injection worldwide, except in the United States, Japan and South Korea, which occurred at inception of the contract in May 2018, and performing R&D services by the Company to obtain sufficient clinical data which will be shared with VFMCRP to allow them to receive regulatory approval to sell CR845/difelikefalin in the licensed territory, are not distinct, and are accounted for as a single performance obligation during the period that the R&D services are rendered (see Note 10, *Collaboration and Licensing Agreements*).

The Company's distinct performance obligations under the Maruishi Agreement include transfer of the license to the Company's IP, which allowed Maruishi to develop and commercialize CR845/difelikefalin, for acute pain and uremic pruritus indications in Japan, which occurred at inception of the contract in 2013, and performance of R&D services, which occurred from 2013 to 2015, as those services were rendered. The Company agreed to conduct limited work on an oral tablet formulation of CR845/difelikefalin and to conduct Phase 1 and proof-of-concept Phase 2 clinical trials of an intravenous formulation of CR845/difelikefalin to be used to treat patients with uremic pruritus. The Company agreed to transfer the data and information from such development to Maruishi for its efforts to obtain regulatory approval in Japan. These activities are referred to as R&D services.

The Company's only performance obligation under the supply agreement with Maruishi is to deliver clinical compound to Maruishi in accordance with the receipt of purchase orders. If and when the Company enters into a supply agreement with VFMCRP, the Company's only performance obligation under this supply agreement would be to deliver CR845/difelikefalin injection to VFMCRP in accordance with the receipt of purchase orders.

Under the CKDP Agreement, the Company's only performance obligation is to transfer the license to the Company's IP related to CR845/difelikefalin, which occurred at inception of the contract in 2012.

Upon execution of the VFMCRP Agreement, the Maruishi Agreement and the CKDP Agreement, the Company received a single fixed payment from each counterparty in exchange for granting the respective licenses and performing its other obligations. In addition, each of the counterparties made an equity investment in the Company's common stock.

Transaction price allocated to the remaining performance obligations

At inception of the VFMCRP Agreement, the entire transaction price of $55,444 was allocated to the one combined performance obligation, as described above. For the three and six months ended June 30, 2019, $5,208 and $9,450, respectively, were recognized as license and milestone fees revenue based on the percentage of R&D services that were completed during the period. As of June 30, 2019, $22,886 of the $55,444 has been recognized as license and milestone fees revenue based on the percentage of R&D services that has been completed since the inception of the VFMCRP Agreement. As of June 30, 2019, there were no remaining performance obligations under either the Maruishi Agreement or the CKDP Agreement, although the Company is eligible to receive milestone payments and sales royalties in the future.

Significant judgments

In applying ASC 606, as amended, to its three contracts, the Company made the following judgments that significantly affect the timing and amount of revenue recognition:

1. Determination of the number of distinct performance obligations in a contract

The VFMCRP Agreement contains one combined performance obligation, which includes the Company's two performance obligations to grant a license to VFMCRP and conduct R&D services. Both of those performance obligations are inputs to the promise, within the context of the contract, to transfer a combined output for which VFMCRP has contracted (the ability of VFMCRP to commercialize the Licensed Product) (see Note 10, *Collaboration and Licensing Agreements*, for further discussion).

The Maruishi Agreement contains two distinct performance obligations: the granting of the license and the promise to deliver defined R&D services. Under the Maruishi Agreement, the license and the R&D services represent distinct goods or services from each other because Maruishi is able to benefit from the license on its own or together with other resources that are readily available to it (i.e., capable of being distinct). Maruishi's ability to benefit from the license without the R&D services is indicated by its ability to conduct clinical trials of CR845/difelikefalin on its own and by the provision in the Maruishi Agreement whereby if the Company suspends or discontinues its development activity, the Company will provide information regarding its development efforts up to that point so that Maruishi may continue development and commercialization of the product in Japan. Therefore, the R&D services do not significantly affect Maruishi's ability to use and benefit from the license.

In addition, the Company's promise in the Maruishi contract to transfer the license is separately identifiable from the promise to provide defined R&D services (i.e., distinct within the context of the contract) because the Company is not using the goods or services as inputs to produce or deliver the combined output or outputs specified by the customer. The combined output specified by Maruishi is its right to conduct development activities related to CR845/difelikefalin in Japan, which could result in regulatory approval in Japan. That right is derived from the Company's grant of the license. Maruishi is conducting clinical trials on its own and does not require the R&D services provided by the Company. Furthermore, the R&D services do not significantly modify or customize the license and vice versa. Finally, the license and R&D services are not highly interdependent or highly interrelated because the Company is able to fulfill its promise to transfer the initial license independently from its promise to subsequently provide the R&D services, which Maruishi can obtain on its own.

The only performance obligation in the CKDP Agreement is the granting of the license.

2. Determination of the transaction price, including whether any variable consideration is included at inception of the contract

The transaction price is the amount of consideration that the Company expects to be entitled to in exchange for transferring promised goods or services to the customer. The transaction price must be determined at inception of a contract and may include amounts of variable consideration. However, there is a constraint on inclusion of variable consideration, such as milestone payments or sales-based royalty payments, in the transaction price related to licenses of IP, if there is uncertainty at inception of the contract as to whether such consideration will be recognized in the future.

The decision as to whether or not it is probable that a significant reversal of revenue will occur in the future, depends on the likelihood and magnitude of the reversal and is highly susceptible to factors outside the entity's influence (for example, the Company cannot determine the outcome of clinical trials; the Company cannot determine if or when they or the counterparty will initiate or complete clinical trials; and the Company's ability to obtain regulatory approval is difficult). In addition, the uncertainty is not expected to be resolved for a long period of time (in the order of years) and finally, the Company has limited experience in the field.

Therefore, at inception of the VFMCRP Agreement, the Maruishi Agreement and the CKDP Agreement, milestones and sales-based royalty payments were not included in the transaction price based on the factors noted above.

Under the VFMCRP Agreement, the single combined performance obligation will be satisfied as the R&D services are rendered and the transaction price, including the upfront payment of $50,000 and the premium on the common stock purchased by VFMCRP of $5,444, will be recognized as revenue as the R&D services are performed based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation. The remaining potential consideration was considered to be variable consideration and was constrained at inception of the contract, including regulatory and sales milestones and sales royalties (see Note 10, *Collaboration and Licensing Agreements*).

All performance obligations under the Maruishi Agreement and the CKDP Agreement were satisfied by the end of 2015. In the future, any milestone event will be recognized as milestone and license fee revenue and collaboration revenue based upon the relative standalone selling prices of the two performance obligations at inception of the Maruishi Agreement, and as milestone and license fee revenue under the CKDP Agreement.

Under the Maruishi Agreement, the transaction price includes only the non-refundable and non-creditable upfront license fee of $15,337, including the premium of $337 from the sale of Company stock to Maruishi, that was paid to the Company at inception of the contract. The remaining potential consideration was considered to be variable consideration and was constrained at inception of the contract, including an aggregate of up to $10,500, which the Company is eligible to receive upon achievement of clinical development and regulatory milestones, a one-time sales milestone of one billion Yen when a certain sales level is attained; a mid-double-digit percentage of all non-royalty payments received by Maruishi from its sub-licensees, if any; and tiered royalties based on net sales of products containing CR845/difelikefalin in Japan, if any, with minimum royalty rates in the low double digits and maximum royalty rates in the low twenties.

Under the CKDP Agreement, the transaction price includes only the non-refundable and non-creditable upfront license fee of $646, including the premium of $83 from the sale of Company stock to CKDP, that was paid to the Company at inception of the contract. The remaining consideration was considered to be variable consideration and was constrained at inception of the contract, including an aggregate of up to $3,750, which the Company is eligible to earn upon achievement of clinical development and regulatory milestones. The Company is also eligible to receive a mid-double-digit percentage of all non-royalty payments received by CKDP from its sub-licensees, if any, and tiered royalties ranging from the high single digits to the high teens based on net sales of products containing CR845/difelikefalin in South Korea, if any.

3. Determination of the estimate of the standalone selling price of performance obligations

In order to recognize revenue under ASC 606, as amended, for contracts for which more than one distinct performance obligation has been identified, the Company must allocate the transaction price to the performance obligations based upon their standalone selling prices. The best evidence of standalone selling price is an observable price of a good or service when sold separately by an entity in similar circumstances to similar customers. If such evidence is not available, standalone selling price should be estimated so that the amount that is allocated to each performance obligation equals the amount that the entity expects to receive for transferring goods or services. The Company has identified more than one performance obligation only in the Maruishi Agreement. Since evidence based on observable prices is not available for the performance obligations under the Maruishi Agreement, the Company considered market conditions and entity-specific factors, including those contemplated in negotiating the agreements, as well as certain internally developed estimates.

At inception of the Maruishi Agreement, the Company determined the estimate of standalone selling price for the license performance obligation by using the adjusted market assessment approach. Under this method, the Company forecasted and analyzed CR845/difelikefalin in the Japanese market, the phase of clinical development as well as considered recent similar license arrangements within the same phase of clinical development, therapeutic area, type of agreement, etc. To estimate the standalone selling price of the R&D services, the Company forecasted its expected costs of satisfying that performance obligation and added a margin for that service.

4. Determination of the method of allocation of the transaction price to the distinct performance obligations

At inception of the Maruishi Agreement, the Company allocated the transaction price of $15,337 between the two performance obligations based on their relative standalone selling prices, determined as described above. The Company determined that the license and the R&D services had estimated standalone selling prices of $10,200 and $6,200, respectively. The resulting percentage allocations were applied to the $15,337 of total transaction price, which resulted in $9,637 being allocated to the license performance obligation, which was recognized immediately as license revenue, while $5,700 was allocated to the R&D services performance obligation. The amount allocated to the R&D services performance obligation was initially recorded as deferred revenue and was recognized as collaborative revenue as the R&D services were provided through July 2015.

Since both the VFMCRP Agreement and the CKDP Agreement each contain only one distinct performance obligation, at the inception of each of those agreements, the entire transaction price was allocated to the respective performance obligation.

5. Determination of the timing of revenue recognition for contracts

Revenue should be recognized when, or as, an entity satisfies a performance obligation by transferring a promised good or service to a customer; i.e., when the customer obtains control of the good or service. The licenses granted to both Maruishi and CKDP are being accounted for as distinct performance obligations. As discussed below, both licenses relate to functional IP for which revenue is recognized at a point in time – in the case of these two license agreements, the point in time is at inception of the contract because the customer obtained control of the license at that point.

The licenses grant Maruishi and CKDP the right to use the Company’s IP relating to CR845/difelikefalin as it existed at the point in time that the licenses were granted. That IP has significant standalone functionality as it provides the customer with the ability to perform a function or task, such as to manufacture CR845/difelikefalin and conduct clinical trials, and is considered to be functional IP.

During the license periods, the Company is continuing to develop and advance CR845/difelikefalin by conducting clinical trials. Those development efforts are for its own benefit and do not substantively change the significant standalone functionality of the licensed IP granted to Maruishi or CKDP. Therefore, the Company's ongoing development efforts do not significantly affect the IP's utility to which Maruishi or CKDP have rights. Furthermore, if the Company abandons its development efforts, Maruishi or CKDP may still continue to develop CR845/difelikefalin in their respective countries.

The R&D services performance obligation under the Maruishi Agreement represents a separate performance obligation. The R&D services were provided to Maruishi by the Company from inception of the agreement in 2013 through the third quarter of 2015, at which time the Company had fulfilled its promise related to the R&D services. Revenue related to the R&D services performance obligation was recognized as services were performed based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation.

Similarly, under the VFMCRP Agreement, revenue related to the single distinct performance obligation, which includes both granting of the license and performance of the R&D services, will be recognized as the R&D services are performed, based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation. The Company expects that the remaining amount of the transaction price that was allocated to the combined performance obligation of $32,558 at June 30, 2019 will be recognized by 2020, as the R&D services are performed, subject to certain development and regulatory uncertainties.

6. Determination of consideration as variable consideration, including factors related to inclusion in the transaction price at inception of the contract and timing of recognition as revenue.

The VFMCRP Agreement, the Maruishi Agreement and the CKDP Agreement contain potential payments related to achievement of defined milestone events and royalties upon net sales of future products, which are considered to be variable consideration because of the uncertainty of occurrence of any of those events specified in those agreements at inception of the agreements. Therefore, those potential payments were not included in the transaction price at the inception of the agreements.

Revenue related to achievement of milestone events is recognized when the Company has determined that it is probable that a milestone event will be achieved and there will not be a significant reversal of revenue in future periods. Upon probability of achievement of a milestone event, the most likely amount of variable consideration is included in the transaction price. Subsequent changes to the transaction price, after contract initiation, are allocated to the performance obligations in the contract on the same basis as at contract inception. Revenue for variable consideration is recognized in the same manner (point in time or over time) as for the performance obligations to which the payment amounts were allocated.

The Maruishi Agreement and the CKDP Agreement specify that certain development milestones will be achieved at pre-specified defined phases of a clinical trial (such as initiation or completion or other pre-specified time during a clinical trial as specified in the agreements).

During the six months ended June 30, 2019 and 2018, no milestone events were probable of occurrence or achieved.

Sublicense payments

VFMCRP's, Maruishi's and CKDP's right to grant sub-licenses is explicitly stated in their respective license agreements. The amount of any potential sub-license fees to be received by the Company, which is based on a formula, is considered to be variable consideration and is constrained from inclusion in the transaction price at inception of the contract since at that time it was probable that there would be a reversal of such revenue in the future because the Company did not know if a sublicense would be granted in the future.

(amounts in thousands, except share and per share data)

Sales-based Royalty Payments

The VFMCRP Agreement, CKDP Agreement and Maruishi Agreement each allow the Company to earn sales-based royalty payments in exchange for a license of intellectual property. In that case, the Company will recognize revenue for a sales-based royalty only when (or as) the later of the following events occurs:

a. The subsequent sale or usage occurs.

b. The performance obligation to which some or all of the sales-based royalty has been allocated has been satisfied (or partially satisfied).

Since the sale (item a, above) occurs after the license was delivered (item b, above), the sales-based royalty exception, to exclude such royalty payments from the transaction price, applies to the overall revenue stream. Therefore, sales-based royalty payments are recognized as revenue when the customer's sales occur. To date, no royalties have been earned or were otherwise due to the Company.

12. Net Loss Per Share

The Company computes basic net income (loss) per share by dividing net income (loss) by the weighted-average number of shares of common stock outstanding. Diluted net income per share includes the potential dilutive effect of common stock equivalents as if such securities were exercised during the period, when the effect is dilutive. Common stock equivalents may include outstanding stock options or restricted stock units, which are included using the treasury stock method when dilutive. For the three and six months ended June 30, 2019 and 2018, the Company excluded the effects of potentially dilutive shares that were outstanding during those respective periods from the denominator as their inclusion would be anti-dilutive due to the Company's net losses during those periods.

The denominators used in the net loss per share computations are as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Basic:				
Weighted average common shares outstanding	39,818,162	33,315,809	39,685,954	33,000,487
Diluted:				
Weighted average common shares outstanding - Basic	39,818,162	33,315,809	39,685,954	33,000,487
Common stock options*	—	—	—	—
Denominator for diluted net loss per share	39,818,162	33,315,809	39,685,954	33,000,487

* No amounts were considered as their effects would be anti-dilutive.

Basic and diluted net loss per share are computed as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Net loss	$ (22,960)	$ (17,194)	$ (44,920)	$ (33,961)
Weighted-average common shares outstanding:				
Basic and Diluted	39,818,162	33,315,809	39,685,954	33,000,487
Net loss per share, Basic and Diluted	$ (0.58)	$ (0.52)	$ (1.13)	$ (1.03)

As of June 30, 2019 and 2018, 4,705,722 and 3,871,194 stock options, respectively, were outstanding, which could potentially dilute basic earnings per share in the future, but were not included in the computation of diluted net loss per share because to do so would have been anti-dilutive. In addition, 140,834 unvested restricted stock units issued to executive officers that were outstanding at June 30, 2019 were also not included in the computation of diluted net loss per share because to do so would have been anti-dilutive. The 74,166 restricted stock units that vested and were settled in shares of common stock in May 2019 were included in the computation of basic and diluted net loss per share for the three and six months ended June 30, 2019. The 24,000 restricted stock units granted in June 2019 to the non-employee members of the Board of Directors were also not included in the computation of diluted net loss per share because to do so would have been anti-dilutive (see Note 13, *Stock-Based Compensation*).

On July 29, 2019, the Company issued and sold 6,325,000 shares of its common stock in a follow-on public offering, which includes the exercise of the underwriters' option to purchase 825,000 additional shares of its common stock (see Note 16, *Subsequent Events*).

13. Stock-Based Compensation

2014 Equity Incentive Plan

The Company's 2014 Equity Incentive Plan, or the 2014 Plan, is administered by the Company's Board of Directors or a duly authorized committee thereof, referred to as the Plan administrator. The 2014 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of equity compensation, collectively referred to as Stock Awards. Additionally, the 2014 Plan provides for the grant of performance cash awards. Incentive stock options may be granted only to employees. All other awards may be granted to employees, including officers, non-employee directors, and consultants. No incentive stock options may be granted under the 2014 Plan after the tenth anniversary of the effective date of the 2014 Plan. Stock Awards granted under the 2014 Plan vest at the rate specified by the Plan administrator. Initial grants of Stock Awards made to employees and non-employee consultants generally vest as to 25% on the first anniversary of the date of grant and the balance ratably over the next 36 months and subsequent grants vest monthly over a period of four years from the grant date. Stock options initially granted to members of the Company's Board of Directors vest over a period of three years in equal installments from the date of the grant, subject to the option holder's continued service as a Director through such date. Subsequent grants to Directors that are made automatically at Annual Meetings of Stockholders vest fully on the first anniversary of the date of grant. The Plan administrator determines the term of Stock Awards granted under the 2014 Plan up to a maximum of ten years.

The aggregate number of shares of the Company's common stock reserved for issuance under the 2014 Plan has automatically increased on January 1 of each year, beginning on January 1, 2015 and will continue to increase on January 1 of each year through and including January 1, 2024, by 3% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the Company's Board of Directors. On January 1, 2019, the aggregate number of shares of common stock that may be issued pursuant to Stock Awards under the 2014 Plan automatically increased from 4,900,481 to 6,086,907. The maximum number of shares that may be issued pursuant to the exercise of incentive stock options under the 2014 Plan is 30,000,000 shares.

Restricted Stock Units

In June 2019, the Board of Directors, upon the recommendation of the Compensation Committee, amended the Company's non-employee director compensation policy. Pursuant to the terms of the amended policy, each non-employee director was entitled to receive, at the time of the Company's 2019 Annual Meeting of Stockholders, 6,000 restricted stock units. As a result, on June 4, 2019, the date of the Company's 2019 Annual Meeting of Stockholders, an aggregate of 24,000 restricted stock units were granted to Directors under the 2014 Plan with a grant date fair value of $20.47 per share. The restricted stock units vest on the earlier of (i) June 4, 2020 and (ii) immediately prior to the Company's next Annual Meeting of Stockholders following the grant date, subject to the recipient's continued service through such date. As a result, the Company will recognize compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the three and six months ended June 30, 2019, $41 of stock compensation expense relating to the Board of Directors' restricted stock units was recognized in the Statements of Comprehensive Loss, all of which related to G&A expense. None of the 24,000 restricted stock units vested or were settled in shares of the Company's common stock as of June 30, 2019.

(amounts in thousands, except share and per share data)

In March 2019, the Compensation Committee of the Company's Board of Directors approved and granted a total of 215,000 restricted stock units to executive officers under the 2014 Plan with a grant date fair value of $16.10 per share. Vesting of the restricted stock units was contingent on the achievement of certain performance targets, subject to the recipient's continuous service through the vesting events. At the date of grant, the Company concluded that the probability of achievement of the performance targets could not be determined until they were achieved, and accordingly, the Company would recognize compensation expense associated with these awards when, and to the extent, the restricted stock units vested in accordance with achievement of the performance targets. In May 2019, performance targets relating to 74,166 restricted stock units had been achieved and thus such restricted stock units vested and the awards were settled in shares of common stock. As a result, $1,194 of stock compensation expense relating to the vesting of these restricted stock units was recognized in the Statements of Comprehensive Loss for the three and six months ended June 30, 2019, consisting of $590 relating to G&A expense and $604 relating to R&D expense.

Stock Options

Under the 2014 Plan, the Company granted 241,000 and 136,500 stock options during the three months ended June 30, 2019 and 2018, respectively, and 1,198,000 and 732,500 stock options during the six months ended June 30, 2019 and 2018, respectively. The fair values of stock options granted during the three and six months ended June 31, 2019 and 2018 were estimated as of the dates of grant using the Black-Scholes option pricing model with the following assumptions:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Risk-free interest rate	1.95% - 2.36%	2.85% - 2.94%	1.95% - 2.62%	2.51% - 2.94%
Expected volatility	73.06% - 73.78%	85.7% - 92.8%	73.06%-75.19%	85.7% - 92.8%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee options (in years)	6.25	6.25	6.25	6.25
Expected life of non-employee options (in years)	—	—	—	—

The weighted-average grant date fair value per share of options granted to employees, non-employee members of the Company's Board of Directors for their Board service and non-employee consultants during the three months ended June 30, 2019 and 2018 was $13.07 and $10.49, respectively, and during the six months ended June 30, 2019 and 2018 was $11.28 and $10.51, respectively.

Prior to January 1, 2019, the Company used the Black-Scholes option valuation model to re-measure the fair value of all outstanding options that had been granted to non-employee consultants during the vesting period of each tranche in accordance with ASC 505-50. On January 1, 2019, the Company used the Black-Scholes option valuation model to re-measure the fair value of all outstanding unvested options that had been granted to non-employee consultants in accordance with ASU 2018-07 (see Note 2, *Other Accounting Pronouncements Recently Adopted*). The range of assumptions used by the Company on January 1, 2019 and June 30, 2018 are as follows:

	January 1, 2019	June 30, 2018
Risk-free interest rate	2.59% - 2.62%	1.92% - 2.82%
Expected volatility	58.9% - 84.6%	60.4% - 96.2%
Expected dividend yield	0%	0%
Expected life of non-employee options (in years)	0.81 - 8.19	0.25 - 8.69

(amounts in thousands, except share and per share data)

During the three and six months ended June 30, 2019 and 2018, the Company recognized compensation expense relating to stock options (excluding compensation expense related to i) the issuance of common stock relating to the consulting agreement for $99 in G&A expense for the three and six months ended June 30, 2019; ii) the vesting of executives' restricted stock units for $604 in R&D expense and $590 in G&A expense for the three and six months ended June 30, 2019; and iii) compensation expense relating to the Board of Directors' restricted stock units for $41 in G&A expense for the three and six months ended June 30, 2019), as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development	$ 1,326	$ 852	$ 2,408	1,500
General and administrative	1,355	1,217	2,507	2,440
Total stock option expense	$ 2,681	$ 2,069	$ 4,915	$ 3,940

A summary of stock option award activity related to employees, non-employee members of the Company's Board of Directors and non-employee consultants as of and for the six months ended June 30, 2019 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2018	4,004,422	$ 13.34
Granted	1,198,000	16.77
Exercised	(395,997)	10.63
Forfeited	(100,703)	16.22
Outstanding, June 30, 2019	4,705,722	$ 14.39
Options exercisable, June 30, 2019	2,034,916	

The Company does not expect to realize any tax benefits from its stock option activity or the recognition of stock-based compensation expense because the Company currently has net operating losses and has a full valuation allowance against its deferred tax assets. Accordingly, no amounts related to excess tax benefits have been reported in cash flows from operations for the six months ended June 30, 2019 and 2018.

14. Income Taxes

For the three months ended June 30, 2019 and 2018, pre-tax losses were $23,195 and $17,346, respectively, and for the six months ended June 30, 2019 and 2018, pre-tax losses were $45,240 and $34,159, respectively. The Company recognized a full tax valuation allowance against its deferred tax assets as of June 30, 2019 and December 31, 2018. Upon adoption of ASU 2016-09 on January 1, 2017, the tax benefit related to the exercise of stock options is recognized as a deferred tax asset that is offset by a corresponding valuation allowance.

The benefit from income taxes of $235 and $152 for the three months ended June 30, 2019 and 2018, respectively, and $320 and $198 for the six months ended June 30, 2019 and 2018, respectively, relates to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, which permits qualified small businesses engaged in R&D activities within Connecticut to exchange their unused R&D tax credits for a cash amount equal to 65% of the value of the exchanged credits.

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act, or the Act. The Act, which is also commonly referred to as "U.S. tax reform", significantly changed U.S. corporate income tax laws by, among other provisions, reducing the maximum U.S. corporate income tax rate from 35% to 21% starting in 2018. In accordance with the reduction in U.S. corporate income tax rate during the period of enactment, the Company reduced its deferred tax assets, which were offset by a corresponding reduction to its valuation allowance. On June 30, 2019 and December 31, 2018, the Company did not have any foreign subsidiaries and the international aspects of the Act are not applicable for the respective periods.

On December 22, 2017, Staff Accounting Bulletin 118, or SAB 118, was issued by the SEC due to the complexities involved in accounting for the Act. SAB 118 requires the Company to include in its financial statements a reasonable estimate of the impact of the Act on earnings to the extent such estimate has been determined. Accordingly, the U.S. provision for income tax for 2017 was based on the reasonable estimate guidance provided by SAB 118. The Company finalized its accounting for the Act as of December 31, 2018, which resulted in insignificant adjustments.

15. Commitments and Contingencies

Leases

In December 2015, the Company entered into a lease agreement, or the Stamford Lease, for office space in Stamford, Connecticut, or the Premises, for the purposes of relocating its headquarters. The initial term of the Stamford Lease commenced in May 2016, or the Commencement Date, and ends in November 2023 and is renewable for one five-year term.

The Stamford Lease requires monthly lease payments, including rent escalations and rent holidays, during the initial lease term. The Company began to make rental payments from the Commencement Date. Prior to January 1, 2019, the Company recorded monthly rent expense on a straight-line basis from March 2016, upon taking possession of the Premises, through December 31, 2018. As of December 31, 2018, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was $864.

As of the Commencement Date, the Stamford Lease landlord had made tenant improvements of $1,094 to the leased premises. Such amount was included in Property and equipment, net and in Deferred lease obligation as of December 31, 2018. The portion of Deferred lease obligation that is related to tenant improvements was being amortized as a reduction to rent expense over the same term as rent expense. As of December 31, 2018, the balance of Deferred lease obligation related to tenant improvements was $698.

Total rent expense under the Stamford Lease was $246 and $491 for the three and six months ended June 30, 2018, respectively.

In connection with the signing of the Stamford Lease, the Company entered into a standby letter of credit agreement for $769, which serves as a security deposit for the Premises. The standby letter of credit is automatically renewed annually through November 2023. This standby letter of credit is secured with restricted cash in a money market account (refer to Note 6, *Restricted Cash*).

On January 1, 2019, the Company adopted ASC 842 (see Note 2 – *Basis of Presentation: Accounting Pronouncements Recently Adopted*). Under ASC 842, since the Company adopted the practical expedients not to re-evaluate whether a contract is or contains a lease and to maintain the lease classification under ASC 840, the Stamford Lease continues to be accounted for as an operating lease.

Upon adoption of ASC 842, the Company was required to establish an operating lease ROU asset and operating lease liability for the Stamford Lease. In establishing the ROU asset, the operating lease liability of $5,198 was reduced by lease incentives relating to tenant improvements of $698 and deferred lease obligation of $864, which were outstanding on December 31, 2018.

Under ASC 842, lease expense is recognized on a straight-line basis over the lease term. As a result, $234 of operating lease cost, or lease expense, was recognized for the three months ended June 30, 2019, consisting of $164 relating to R&D lease expense and $70 relating to G&A lease expense. For the six months ended June 30, 2019, $469 of operating lease cost was recognized, consisting of $328 relating to R&D lease expense and $141 relating to G&A lease expense.

(amounts in thousands, except share and per share data)

Other information related to the Stamford Lease was as follows:

	Three Months Ended June 30, 2019	Six Months Ended June 30, 2019
Cash paid for amounts included in the measurement of lease liability:		
Operating cash outflows relating to operating lease	$ (302)	$ (603)
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ 3,636
Remaining lease term-operating lease (years)	4.4	4.4
Discount rate - operating lease	7.0%	7.0%

Future minimum lease payments under non-cancellable operating leases, as well as a reconciliation of these undiscounted cash flows to the operating lease liability as of June 30, 2019, were as follows:

Year Ending December 31,	
2019 (Excluding the six months ended June 30, 2019)	$ 613
2020	1,239
2021	1,264
2022	1,288
2023	1,164
Total future minimum lease payments, undiscounted	5,568
Less imputed interest	(796)
Total	$ 4,772
Operating lease liability reported as of June 30, 2019:	
Operating lease liability - current	$ 923
Operating lease liability - non-current	3,849
Total	$ 4,772

Note 16. Subsequent Events

Follow-on Public Offering

In July 2019, the Company entered into an underwriting agreement with J.P. Morgan Securities LLC and Jefferies LLC, as representatives of the several underwriters named therein, relating to the issuance and sale by the Company of 6,325,000 shares of its common stock, which includes the exercise of the underwriters' option to purchase 825,000 additional shares of common stock, at a public offering price of $23.00 per share. This offering was made pursuant to the Company's Shelf Registration Statement, and a related prospectus supplement dated July 24, 2019, which was filed with the SEC on July 25, 2019.

On July 29, 2019, the Company closed the offering, including the full exercise of the underwriters' option to purchase 825,000 additional shares of common stock. The Company received net proceeds of approximately $136,446, after deducting $9,029 of underwriting discounts and commissions and estimated offering expenses payable by the Company.

Manufacturing Agreement

On July 8, 2019, the Company entered into a Master Manufacturing Services Agreement, or MSA, with Patheon UK Limited, or Patheon. The MSA governs the general terms under which Patheon, or one of its affiliates, will provide non-exclusive manufacturing services to the Company for the drug products specified by the Company from time to time. Pursuant to the MSA, the Company has agreed to order from Patheon at least a certain percentage of its commercial requirements for a product under a related Product Agreement. Each Product Agreement that the Company may enter into from time to time will be governed by the terms of the MSA, unless expressly modified in such Product Agreement.

The MSA has an initial term ending December 31, 2023, and 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 notice of its intention to terminate the MSA at least 18 months prior to the end of the then current term.

Either party may terminate the MSA or a Product Agreement upon written notice if the other party (1) has failed to remedy a material breach within a specified time or (2) is declared insolvent or bankrupt, voluntarily files a petition of bankruptcy or assigns such agreement for the benefit of creditors. The Company may terminate a Product Agreement (a) upon 90 days' prior written notice if any governmental agency takes any action that prevents the Company from selling the relevant product in the relevant territory, (b) upon six months' prior written notice if it does not intend to order manufacturing services due to a product's discontinuance in the market, or (c) upon 90 days' prior written notice if it determines that the manufacture or supply of a product likely infringes third-party rights. Patheon may terminate the MSA or a Product Agreement (i) upon six months' prior written notice if the Company assigns such agreement to an assignee that is unacceptable to Patheon for certain reasons, or (ii) upon 30 days' prior written notice if, after the first year of commercial sales, the Company forecasts zero volume for 12 months.

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

On July 8, 2019, and July 9, 2019, the Company entered into two related Product Agreements under the MSA, one with each of Patheon and Patheon Manufacturing Services LLC, or Patheon Greenville, to govern the terms and conditions of the manufacture of commercial supplies of CR845/difelikefalin injection, the Company's lead product candidate. Pursuant to the Product Agreements, Patheon and Patheon Greenville will manufacture commercial supplies of CR845/difelikefalin injection at the Monza, Italy and Greenville, North Carolina manufacturing sites, respectively, from active pharmaceutical ingredient supplied by the Company. Patheon and Patheon Greenville will be responsible for supplying the other required raw materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

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

Cautionary Note Regarding Forward-Looking Statements

This Quarterly Report on Form 10-Q contains forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," "will," or "would," and or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Quarterly Report on Form 10-Q, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

The forward-looking statements in this Quarterly Report on Form 10-Q include, among other things, statements about:

- the success and timing of our clinical trials, including our clinical trial programs for KORSUVA™ (CR845/difelikefalin) injection in chronic kidney disease associated pruritus, or CKD-aP, and Oral KORSUVA (CR845/difelikefalin) in CKD-aP, and chronic liver disease associated pruritus, or CLD-aP, and pruritus associated with atopic dermatitis, or AD, and the reporting of clinical trial results;
- the potential regulatory development pathway for KORSUVA (CR845/difelikefalin) injection in CKD-aP and CR845/difelikefalin injection in acute post-operative setting;
- our plans to develop and commercialize KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) and our other product candidates;
- the potential results of ongoing and planned preclinical studies and clinical trials and future regulatory and development milestones for our product candidates;
- the size and growth of the potential markets for pruritus management, including CKD-aP in hemodialysis and non-dialysis markets, CLD-aP and AD markets as well as post-operative care markets, and for our other product candidates and our ability to serve those markets;
- our ability to obtain and maintain regulatory approval of our product candidates, including intravenous, or I.V., and Oral CR845/difelikefalin, and the labeling under any approval we may obtain;
- the anticipated commercial launch of our lead product candidate, KORSUVA (CR845/difelikefalin) injection;
- the potential of future scheduling of KORSUVA (CR845/difelikefalin) injection by the United States Drug Enforcement Administration, or DEA, if regulatory approval is received;
- the performance of our current and future collaborators and licensees, including Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceuticals Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, as well as sub-licensees, including Kissei Pharmaceutical Co. Ltd., or Kissei, and our ability to maintain such collaborations;
- our ability to establish additional collaborations for our product candidates;
- the continued service of our key scientific or management personnel;
- our ability to establish commercialization and marketing capabilities;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any approved products;
- our ability to obtain and maintain coverage and adequate reimbursement from third-party payers for any approved products;
- our planned use of our cash and cash equivalents and marketable securities and the clinical milestones we expect to fund with such proceeds;

- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- our ability to obtain funding for our operations;
- our ability to obtain and maintain intellectual property protection for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others;
- the success of competing drugs that are or may become available; and
- the performance of third-party manufacturers and clinical research organizations.

You should refer to Part I Item 1A. “Risk Factors” of our Annual Report on Form 10-K for the year ended December 31, 2018 for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Quarterly Report on Form 10-Q will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this Quarterly Report on Form 10-Q and the documents that we reference in this Quarterly Report on Form 10-Q and have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

The following *Management's Discussion and Analysis of Financial Condition and Results of Operations* should be read in conjunction with: (i) the Condensed Financial Statements and related notes thereto which are included in this Quarterly Report on Form 10-Q; and (ii) our Annual Report on Form 10-K for the year ended December 31, 2018.

Introduction

We are a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities designed to alleviate pruritus by selectively targeting peripheral kappa opioid receptors, or KORs. We are developing a novel and proprietary class of product candidates, led by KORSUVA (CR845/difelikefalin), a first-in-class KOR agonist that targets KORs located in the peripheral nervous system, and on immune cells.

In a Phase 3 and two Phase 2 trials, KORSUVA (CR845/difelikefalin) injection (intravenous formulation) has demonstrated statistically significant reductions in itch intensity and concomitant improvement in pruritus-related quality of life measures in hemodialysis patients with moderate-to-severe CKD-aP. KORSUVA (CR845/difelikefalin) injection is currently being investigated in a global Phase 3 trial in the same patient population, i.e. hemodialysis patients with moderate-to-severe CKD-aP. We have partnered with VFMCRP, a joint venture between Vifor Pharma Group and Fresenius Medical Care, to commercialize KORSUVA (CR845/difelikefalin) injection in dialysis patients with CKD-aP worldwide, excluding the United States, Japan (Maruishi/sub-licensee Kissei), and South Korea (CKDP). We retain all rights in the United States and will promote KORSUVA (CR845/difelikefalin) injection, if approved, with VFMCRP in U.S. Fresenius Medical Care North America, or FMCNA, dialysis clinics under a profit share agreement.

CR845/difelikefalin has also demonstrated statistically significant pain reduction in clinical trials in patients with moderate-to-severe acute pain in the post-operative setting, without inducing many of the undesirable side effects typically associated with currently available opioid pain therapeutics. We retain rights to all KORSUVA/CR845 formulations and indications worldwide, excluding KORSUVA (CR845/difelikefalin) injection in dialysis patients with CKD-aP under our agreement with VFMCRP for certain ex-U.S. territories and our other license agreements for CR845/difelikefalin in Japan (Maruishi/sub-licensee Kissei) and South Korea (CKDP).

The U.S. Food and Drug Administration, or FDA, has conditionally accepted KORSUVA as the trade name for CR845/difelikefalin injection and its safety and efficacy have not been fully evaluated by any regulatory authority.

We commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our product candidates, including conducting preclinical studies and clinical trials of CR845/difelikefalin-based product candidates and raising capital. To date, we have financed our operations primarily through sales of our equity and debt securities and payments from license agreements. We have no products currently available for sale, and substantially all of our revenue to date has been revenue from license agreements, although we have received nominal amounts of revenue under research grants.

Recent Developments

Follow-on Public Offering

In July 2019, we entered into an underwriting agreement with J.P. Morgan Securities LLC and Jefferies LLC, as representatives of the several underwriters named therein, relating to the issuance and sale by us of 6,325,000 shares of our common stock, which includes the exercise of the underwriters' option to purchase 825,000 additional shares of common stock, at a public offering price of $23.00 per share. This offering was pursuant to Registration Statement on Form S-3 (File No. 333-230333), or the Shelf Registration Statement, filed with the SEC on March 15, 2019 and declared effective on April 4, 2019, and a related prospectus supplement dated July 24, 2019, which was filed with the SEC on July 25, 2019. The Shelf Registration Statement provides for aggregate offerings of up to $300.0 million of common stock, preferred stock, debt securities, warrants or any combination thereof. The securities registered under this Shelf Registration Statement include unsold securities that had been registered under our previous shelf registration statement (File No. 333-216657) that was declared effective on March 24, 2017.

On July 29, 2019, we closed the offering, including the full exercise of the underwriters' option to purchase 825,000 additional shares of common stock. We received net proceeds of approximately $136.4 million, after deducting $9.0 million of underwriting discounts and commissions and estimated offering expenses payable by us.

Manufacturing Agreement

On July 8, 2019, we entered into a Master Manufacturing Services Agreement, or MSA, with Patheon UK Limited, or Patheon. The MSA governs the general terms under which Patheon, or one of its affiliates, will provide non-exclusive manufacturing services to us for the drug products specified by us from time to time. Pursuant to the MSA, we have agreed to order from Patheon at least a certain percentage of our commercial requirements for a product under a related Product Agreement. Each Product Agreement that we may enter into from time to time will be governed by the terms of the MSA, unless expressly modified in such Product Agreement.

The MSA has an initial term ending December 31, 2023, and 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 notice of its intention to terminate the MSA at least 18 months prior to the end of the then current term.

Either party may terminate the MSA or a Product Agreement upon written notice if the other party (1) has failed to remedy a material breach within a specified time or (2) is declared insolvent or bankrupt, voluntarily files a petition of bankruptcy or assigns such agreement for the benefit of creditors. We may terminate a Product Agreement (a) upon 90 days' prior written notice if any governmental agency takes any action that prevents us from selling the relevant product in the relevant territory, (b) upon six months' prior written notice if we do not intend to order manufacturing services due to a product's discontinuance in the market, or (c) upon 90 days' prior written notice if we determine that the manufacture or supply of a product likely infringes third-party rights. Patheon may terminate the MSA or a Product Agreement (i) upon six months' prior written notice if we assign such agreement to an assignee that is unacceptable to Patheon for certain reasons, or (ii) upon 30 days' prior written notice if, after the first year of commercial sales, we forecast zero volume for 12 months.

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

On July 8, 2019, and July 9, 2019, we entered into two related Product Agreements under the MSA, one with each of Patheon and Patheon Manufacturing Services LLC, or Patheon Greenville, to govern the terms and conditions of the manufacture of commercial supplies of CR845/difelikefalin injection, our lead product candidate. Pursuant to the Product Agreements, Patheon and Patheon Greenville will manufacture commercial supplies of CR845/difelikefalin injection at the Monza, Italy and Greenville, North Carolina manufacturing sites, respectively, from active pharmaceutical ingredient supplied by us. Patheon and Patheon Greenville will be responsible for supplying the other required raw materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

Our Product Candidate

Our product candidate, CR845/difelikefalin, is a new chemical entity, which is designed to selectively stimulate kappa, rather than mu, and delta opioid receptors. CR845/difelikefalin has been designed with specific chemical characteristics to restrict its entry into the CNS and further limit its mechanism of action to KORs in the peripheral nervous system and on immune cells. Activation of kappa receptors in the CNS is known to result in some undesirable effects, including dysphoria. Since CR845/difelikefalin modulates kappa receptor signals peripherally without any significant activation of opioid receptors in the CNS, it is generally not expected to produce the CNS-related side effects of mu opioid agonists (such as addiction and respiratory depression) or centrally-active kappa opioid agonists (such as dysphoria and hallucinations). CR845/difelikefalin has been administered to more than 2,000 human subjects in Phase 1, Phase 2 and Phase 3 clinical trials as an I.V. infusion, bolus intravenous injection or oral capsule or tablet, and thus far has been observed to be generally well tolerated in multiple clinical trials.

Based on the non-clinical and clinical studies we have completed to date, we believe that CR845/difelikefalin, if approved, would be attractive to both patients and physicians as a treatment for moderate-to-severe pruritus associated with certain diseases such as CKD, CLD and dermatological conditions such as AD as well as moderate-to-severe pain due to the following attributes:

- novel, peripherally-acting, KOR agonist mechanism of action;
- evidence of efficacy in completed clinical trials of pruritus and pain;
- potential for reducing mu opioid use and opioid-related adverse events, or AEs, such as nausea and vomiting;
- potential for reduction of post-operative nausea and vomiting, or PONV;
- avoidance of mu opioid-related CNS side effects, such as respiratory depression and euphoria;
- lower potential for addiction or abuse liability;
- avoidance of interactions with other drugs because CR845/difelikefalin is not metabolized in the liver and does not interact with liver enzymes responsible for the metabolism of most commonly used classes of drugs; and
- availability in injectable form for the treatment of pruritus in CKD patients undergoing hemodialysis in the hospital and dialysis center settings as well as for pain and/or PONV treatment in the acute care setting and oral form for treatment of pruritus or chronic pain conditions in the outpatient setting.

Our current product candidate pipeline is summarized in the table below:

Program	Product Candidate	Primary Indication	Status	Commercialization Rights
Pruritus	KORSUVA (CR845/difelikefalin) Injection	Pruritus CKD - Hemodialysis	• KALM-2 (Global) Phase 3 efficacy trial ongoing • KALM-1: double blind phase completed; top-line data reported • Phase 3 safety trials ongoing • Breakthrough Therapy Designation granted by FDA in June 2017	Cara (United States); Maruishi (Japan); CKDP (South Korea); VFMCRP (Worldwide, other than United States, Japan and South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus CKD (Stage III - V)	• Phase 2 efficacy trial ongoing • Phase 2 interim assessment complete - no modifications to enrollment target	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus CLD - Primary Biliary Cholangitis	• Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus Atopic Dermatitis	• Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
Post-Op Setting	CR845/difelikefalin Injection	Acute Post-Operative Pain/PONV	• Adaptive Phase 2/3 trial completed; top-line data released	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)

KORSUVA (CR845/Difelikefalin) Injection for Treatment of Chronic Kidney Disease-Associated Pruritus (CKD-aP)

Chronic pruritus, or itch, is associated with certain conditions such as kidney disease, atopic dermatitis, liver disease and psoriasis. Based on KORSUVA (CR845/difelikefalin)'s effects on the peripheral nervous system and immune cells, which result in anti-pruritic effects in preclinical models, we believe KORSUVA (CR845/difelikefalin) has the potential to treat pruritus associated with multiple medical conditions.

CKD-aP is an intractable systemic itch condition with high prevalence for which there are no approved therapeutics in the United States or Europe.

In May 2019, we announced positive results from the double blinded phase of the first pivotal Phase 3 efficacy trial (KALM*TM*-1) of KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in patients undergoing hemodialysis. The trial met the primary and all secondary endpoints after 12 weeks of treatment. This trial was initiated in the first quarter of 2018 in the United States and has entered into a 52-week open label extension phase. In August 2018, we initiated the second pivotal Phase 3 efficacy trial, KALM-2 (with a 52-week open label extension phase) of KORSUVA (CR845/difelikefalin) injection that is expected to enroll patients in the United States and multiple countries outside the United States. In addition to these trials, we are also conducting 52-week and 12-week Phase 3 open label safety studies of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP.

In June 2017, the FDA granted breakthrough therapy designation for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe pruritus in patients with CKD undergoing hemodialysis. This regulatory decision was supported by positive results from Phase 2 clinical trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP. Breakthrough therapy designation is granted to expedite the development and review process for new therapies addressing serious or life-threatening conditions, where preliminary clinical evidence indicates that the drug candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints.

KALM-1 and KALM-2 Phase 3 Efficacy Trials of KORSUVA (CR845/Difelikefalin) Injection

In January 2018, we initiated the first Phase 3 efficacy trial (KALM-1) to support regulatory filings for the approval of KORSUVA (CR845/difelikefalin) injection. This U.S. study is a multicenter, randomized, double-blind, placebo-controlled 12-week treatment trial (with a 52-week open label extension phase) that is designed to evaluate the safety and efficacy of 0.5 mcg/kg of KORSUVA (CR845/difelikefalin) injection to be administered three times per week after dialysis in 350 hemodialysis patients with moderate-to-severe pruritus (with a pre-specified interim assessment that allowed for expansion of the study to up to 500 patients, if needed).

In May 2019, we announced positive top-line results from this trial. The study met the primary efficacy endpoint with 51% of the patients receiving 0.5 mcg/ kg of KORSUVA Injection versus 28% of patients receiving placebo achieving at least a 3-point improvement from baseline with respect to the weekly mean of the daily 24-hour worst itching intensity numeric rating scale, or NRS, score at week 12 (p= 0.000019). The study also met all secondary endpoints, including assessment of itch-related quality of life changes measured using self-assessment Skindex-10 (patients receiving KORSUVA experienced 43% improvement versus patients receiving placebo, p= 0.0004) and 5-D Itch scales (patients receiving KORSUVA experienced 35% improvement versus patients receiving placebo, p= 0.0009). In addition, 39% of patients receiving KORSUVA Injection achieved a four-point or greater improvement from baseline in the weekly mean of the daily 24-hour worst itching NRS score at week 12 versus 18% for patients receiving placebo (p= 0.000032), another key secondary endpoint. In this trial, KORSUVA (CR845/difelikefalin) injection was generally well-tolerated with a safety profile consistent with that seen in earlier trials. Overall, the incidence of adverse effects, or AEs, and serious AEs were similar across both KORSUVA (CR845/difelikefalin) Injection and placebo groups. The most common treatment emergent AEs reported in greater than 5% of patients were diarrhea (9.5% KORSUVA vs 3.7% placebo), dizziness (6.9% KORSUVA vs 1.1% placebo), vomiting (5.3% KORSUVA vs 3.2% placebo) and nasopharyngitis (3.2% KORSUVA vs 5.3% placebo).

In August 2018, we announced the dosing of the first patient in the second Phase 3 efficacy trial (KALM-2) that is similar in design and size to the KALM-1 Phase 3 trial (with a pre-specified interim assessment that allowed for expansion of the study to up to 500 patients, if needed) and will facilitate regulatory filings worldwide. This second Phase 3 trial is designed to enroll hemodialysis patients with moderate-to-severe pruritus in the United States as well as in multiple countries in Europe and Asia Pacific. Based on current enrollment projections, we expect to report top-line data from the KALM-2 Phase 3 trial in the fourth quarter of 2019.

Phase 3 Safety Trials of KORSUVA (CR845/Difelikefalin) Injection

In the second quarter of 2017, we initiated a 52-week Phase 3 safety trial that is expected to enroll up to 300 hemodialysis patients with CKD-aP, including those who have completed prior Phase 2 trials of KORSUVA (CR845/difelikefalin) injection as well as patients who have not been previously exposed to CR845/difelikefalin. This open-label trial is evaluating the long-term safety of KORSUVA (CR845/ difelikefalin) injection at the dose of 0.5mcg/kg. Currently, approximately 165 patients have completed at least six months of treatment (over 50% of these patients have completed one year of treatment).

In the second quarter of 2019, we initiated an additional open label Phase 3 safety trial of KORSUVA (CR845/difelikefalin) injection that is expected to enroll up to 400 hemodialysis patients with CKD-aP. This trial is designed to evaluate primarily safety as well as effectiveness of 0.5 mcg/kg dose of KORSUVA (CR845/difelikefalin) injection for up to 12 weeks treatment in hemodialysis patients with CKD-aP.

The design and dose selection for our Phase 3 trials are based on results of the previously completed Phase 2 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP in consultation with the FDA as part of our End of Phase 2 meeting with the FDA that was held in 2017.

Phase 2/3 Adaptive Design Trial of KORSUVA (CR845/Difelikefalin) Injection in Dialysis Patients

In June 2016, we initiated a two-part Phase 2/3 adaptive design trial of KORSUVA (CR845/difelikefalin) injection in dialysis patients suffering from moderate-to-severe pruritus. In March 2017, we announced top-line data from the Phase 2 trial, which was a randomized, double-blind, placebo-controlled trial of three doses of intravenous KORSUVA (CR845/difelikefalin) injection (0.5 mcg/kg, 1.0 mcg/kg and 1.5 mcg/kg) administered three times per week after dialysis over an eight-week treatment period in 174 patients with moderate-to-severe pruritus.

The primary endpoint of this trial was the change from baseline of the mean worst itching score for week eight measured on a patient reported 24-hour worst itching intensity 11-point NRS scale. Patients receiving KORSUVA (CR845/difelikefalin) injection experienced a 68% greater reduction from baseline in worst itch scores than those receiving placebo ($p<0.0019$). The secondary endpoints of this trial focused on itch-related quality of life measures including the Skindex-10 scale, 5-D itch scale, and sleep disturbance subscale. In addition to reduction of pruritus, patients experienced substantial improvement in multiple itch-related quality of life (Skindex-10, 5-D Itch scale) measures and sleep over two months of treatment. Additionally, in a post-hoc analysis, (1) 64% of the patients treated at the 0.5 mcg/kg dose experienced at least a 3-point improvement from baseline with respect to the weekly mean NRS score versus 29% of patients on placebo ($p<0.01$), and (2) 51% of the patients treated at the 0.5 mcg/kg dose experienced at least a 4-point improvement from baseline with respect to the weekly mean NRS score versus 24% of patients on placebo ($p<0.05$).

Overall, KORSUVA (CR845/difelikefalin) was observed to be generally well tolerated over the eight-week treatment period and the unblinded Drug Safety Monitoring Board did not raise any safety concerns during the course of the trial. The most common treatment-emergent adverse events were somnolence, headache, dizziness, mental status changes, nausea and diarrhea, generally in line with what has been observed in previous clinical studies of KORSUVA (CR845/difelikefalin). The Phase 3 part of this study has been replaced by the KALM-1 Phase 3 trial.

Oral KORSUVA (CR845/Difelikefalin) for Treatment of Chronic Kidney Disease-Associated Pruritus (CKD-aP)

In July 2018, we announced the dosing of the first patients in a Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in stage III - V (moderate-to-severe) CKD patients. The Phase 2, multicenter, randomized, double-blind, placebo-controlled 12-week trial is designed to evaluate the safety and efficacy of three tablet strengths (0.25 mg, 0.5 mg and 1 mg, once daily administration) of Oral KORSUVA versus placebo in approximately 240 stage III-V (moderate to severe) CKD patients with moderate-to-severe pruritus, with a pre-specified interim assessment that allows for expansion of the study to up to 480 patients, if needed. The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour worst itch NRS score at Week 12 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of Week 12, as assessed by the total Skindex-10 and 5-D itch scores, as well as the proportion of patients achieving an improvement from baseline ≥3 points with respect to the weekly mean of the daily 24-hour worst itch NRS score at week 12.

In July 2019, we announced that, based on the recommendation of the Independent Data Monitoring Committee, or IDMC, the ongoing Phase 2 trial will continue as planned with no changes to the original enrollment target of 240 patients. The IDMC's recommendation was based on the results of a pre-specified interim conditional power assessment conducted after approximately 50% of the targeted patient number completed the designated 12-week treatment period. We also announced that the target enrollment has been reached and we expect to report the top-line results in the fourth quarter of 2019.

The dosing of the above Phase 2 trial was informed by the results of our Phase 1 trial of Oral KORSUVA (CR845/difelikefalin) in patients with Stage III - V CKD. Data from the Phase 1 trials were used to assess the PK and safety of different tablet strengths of Oral KORSUVA (CR845/difelikefalin) (0.25 mg, 0.5 mg and 1.0 mg), dosed daily over a one-week treatment period in patients with moderate and severe renal impairment. The exposure levels achieved with Oral KORSUVA tablets were approximately equivalent to the exposure level achieved with 0.5 mcg/kg dose of I.V. KORSUVA that exhibited statistically significant and clinically meaningful reduction in itch intensity in hemodialysis patients with moderate to severe CKD-aP in a previous Phase 2 trial.

Oral KORSUVA (CR845/Difelikefalin) for Treatment of Chronic Liver Disease-Associated Pruritus

Pruritus is a common and irritating symptom in patients with chronic liver disease, or CLD, especially those with chronic cholestatic disease. Severe pruritus can have debilitating effects and can lead to a significant reduction in a patient's quality of life. Although the pathogenesis of CLD-aP remains poorly understood, it is likely multifactorial including evidence for an imbalance in the endogenous opioid system driven by higher mu receptor activation (pruritic) versus kappa receptor activation (antipruritic). Consequently, the use of selective kappa-opioid receptor agonists has been suggested for the treatment of pruritus in patients with CLD.

In June 2019, we announced the initiation of a Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in patients with hepatic impairment due to primary biliary cholangitis, or PBC. Pruritus is a common symptom with a prevalence of up to 70% in patients with PBC. The Phase 2 multicenter, randomized, double-blind, placebo-controlled 16-week trial is designed to evaluate the safety and efficacy of 1 mg tablet of Oral KORSUVA (CR845/difelikefalin) taken twice daily or BID versus placebo in approximately 60 patients with PBC and moderate-to-severe pruritus. The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour worst itching NRS score at Week 16 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of Week 16 as assessed by the Skindex-10 and 5-D itch scales, as well as the assessment of proportion of patients achieving an improvement from baseline of ≥3 points with respect to the weekly mean of the daily 24-hour worst itching NRS score at week 16.

The dose of 1 mg BID in the Phase 2 trial is based on comparison to the exposure levels achieved with 0.5 mcg/kg dose of I.V. KORSUVA (CR845/difelikefalin) that exhibited statistically significant and clinically meaningful reduction in itch intensity in hemodialysis patients with moderate-to-severe pruritus in the Phase 2 and 3 trials.

In the fourth quarter of 2017, we submitted an investigational new drug application, or IND, to the FDA for Oral KORSUVA (CR845/difelikefalin) for the symptomatic relief of CLD-aP and initiated a Phase 1 safety and PK clinical trial of Oral KORSUVA (CR845/difelikefalin) in patients with CLD in the first quarter of 2018. The open-label study was designed to evaluate the safety and PK profile of repeated doses of Oral KORSUVA (CR845/difelikefalin) taken twice daily in up to 60 patients with CLD and up to 12 matched healthy control subjects. Oral KORSUVA was evaluated over an eight-day treatment period in patients with CLD based on their Child-Pugh classification (i.e., Class A, B and C). The study is now complete. The PK parameters were dose-proportional in patients with mild-to-moderate CLD and Oral KORSUVA (CR845/difelikefalin) was generally well tolerated with no unexpected safety signals reported.

Oral KORSUVA (CR845/difelikefalin) for Treatment of Moderate-to-Severe Pruritus Associated with Atopic Dermatitis (AD)

Atopic dermatitis, or AD, is a chronic, pruritic inflammatory dermatosis that affects up to 25% of children and 2-5% of adults. Chronic pruritus is one of the defining features of AD. The itch is so common in AD that AD is often described as the itch that rashes. The point prevalence of chronic pruritus ranges between 87 to 100% in AD. Both quality of life and psychosocial well-being are known to negatively correlate with itch severity. The associated psychosocial morbidity of this distressing symptom includes sleep disruption, depression, agitation, anxiety, altered eating habits, reduced self-esteem and difficulty concentrating.

The cause of AD is multifactorial, including genetic predisposition, impaired skin barrier, environmental triggers and immune dysregulation. The sensation of itch in AD is similarly complex. Chronic itch in AD is mediated by a complex interplay between keratinocytes, cutaneous nerve fibers, pruritogenic molecules and the peripheral and central nervous system. An imbalance in the epidermal opioid system has also been described as potentially playing a role in the modulation of pruritus in AD.

In July 2019, we initiated a Phase 2 randomized, double-blind, placebo-controlled trial that is designed to evaluate the efficacy and safety of Oral KORSUVA (CR845/difelikefalin) for moderate-to-severe pruritus in approximately 240 adult subjects with AD. Subjects will be randomized to three tablet strengths of Oral KORSUVA: 0.25 mg, 0.5 mg and 1 mg BID versus placebo for 12 weeks followed by a 4-week active extension phase. The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour itch NRS score at Week 12 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of Week 12 as assessed by the total Skindex-10 and 5-D itch scales, and itch related Sleep Quality Assessment. Safety endpoints used to evaluate the overall safety and tolerability of Oral KORSUVA (CR845/difelikefalin) will also be included.

Intravenous CR845/Difelikefalin for Treatment of Acute Postoperative Pain

We have also investigated CR845/difelikefalin for the treatment of pain in an acute care setting. CR845/difelikefalin is designed to provide pain relief without stimulating mu opioid receptors and therefore potentially without mu opioid-related side effects, such as nausea, vomiting, respiratory depression and euphoria.

Phase 2/3 Efficacy and Safety Trial of CR845/Difelikefalin Injection in Patients Undergoing Abdominal Surgery

In June 2018, we reported positive top-line date from the adaptive Phase 2/3 study of CR845/difelikefalin in patients undergoing abdominal surgery. This trial was initiated in September 2015 and was designed as a multi-center, randomized, double-blind, placebo-controlled, parallel-group adaptive design trial with repeated doses of CR845/difelikefalin injection or placebo administered both prior to and following abdominal surgery. The trial protocol initially included three dose levels of CR845/difelikefalin injection (1.0 mcg/kg, 2.0 mcg/kg and 5.0 mcg/kg versus placebo) that was subsequently modified in June 2016 to test two doses of I.V. CR845/difelikefalin (1.0 mcg/kg and 0.5 mcg/kg) versus placebo, based on a safety review by us, the trial's IDMC, and the FDA, of unblinded safety data from the first 90 patients dosed. The safety review was conducted in response to a clinical hold that the FDA placed on the trial in February 2016 and removed in April 2016 following the safety review. The clinical hold was based on a pre-specified stopping rule related to elevated serum sodium levels of greater than 150 mmol/L that was included in the clinical trial protocol. The trial enrolled 444 patients undergoing abdominal surgery, composed of 228 patients who underwent ventral hernia surgery and 216 patients who completed a hysterectomy procedure. The primary endpoint was pain relief as measured by Area Under the Curve, or AUC, of the NRS pain intensity scores collected over the first 24-hour period after the baseline dose (0 hour) post-surgery for all combined surgeries. The secondary endpoints included incidence of vomiting, improvement in impact scores of PONV, reduction in use of rescue analgesic medication, as well as patient global assessment at 24 hours post baseline dose after surgery.

- CR845 injection achieved statistical significance for the primary endpoint of pain relief over 24 hours (AUC 0-24) post-surgery with the 1.0 mcg/kg dose versus placebo (p=0.032). The 0.5 mcg/kg dose did not achieve statistical significance over the 0-24 hour period (p=0.076). In addition, improvement in pain AUC was statistically significant for both the 0.5 and 1.0 mcg/kg doses over 0 to 6 hours (p=0.041, p=0.001) and 0 to 12 hours (p=0.035, p=0.004) periods and also statistically significant for the 1.0 mcg/kg dose over the 0 to 18-hour period (p=0.013) post-surgery.
- At 6 and 24 hours after baseline dose post-surgery, there were statistically significant improvements in PONV impact scores with both doses of CR845 injection compared to placebo: 0.5 mcg/kg (6 hrs.: p=0.0072, 24 hrs.: p<0.006) and 1.0 mcg/kg (6 hrs.: p<0.0001, 24 hrs.: p<0.0001).
- There were statistically significant differences between placebo and both doses of CR845 with respect to the total use of anti-emetic medication over the first 24 hours post-surgery (0.5 mcg/kg: p=0.0003; 1.0 mcg/kg: p< 0.0001).
- There was a 73% reduction in the incidence of patient-reported vomiting in the group receiving the 1.0 mcg/kg dose versus placebo (p=0.029). Although the 0.5 mcg/kg also showed reduction in vomiting, it did not reach statistical significance. Both doses of CR845 exhibited numerical trends toward reduced use of rescue analgesic medication compared to placebo, but did not achieve statistical significance.
- There was no significant effect, compared to placebo, on patient's global assessment of medication for either dose of CR845 over the 24-hour period.

Common adverse effects reported in the placebo and both CR845 groups were generally low and similar in incidence, and included nausea, constipation, vomiting, flatulence, headache and dyspepsia.

The next steps for the acute post-operative program will be determined after we have completed detailed analysis of the data and consulted with the FDA.

Human Abuse Liability Trial of CR845/Difelikefalin Injection

In the fourth quarter of 2014, we successfully completed a Human Abuse Liability, or HAL, trial of CR845/difelikefalin injection. The results from this HAL trial indicate that I.V. CR845/difelikefalin (5 mcg/kg or 15 mcg/kg) demonstrates statistically significant lower "drug liking" scores as measured by VAS Emax (p <0.0001) when compared to I.V. pentazocine (0.5 mg/kg), an approved Schedule I.V. opioid receptor agonist. I.V. CR845 also demonstrated highly statistically significant lower "feeling high," "overall liking," and "take drug again" scores (p <0.0001) as compared to pentazocine. Additionally, CR845/difelikefalin injection showed no "drug liking" dose response as both doses of CR845/difelikefalin injection exhibited similar responses and were not different from placebo injection. Those scores represent standard subjective measures recommended by the FDA to assess a drug's abuse liability. We believe that the totality of the results from the HAL trial are supportive of the potential for CR845/difelikefalin to be the first non-scheduled or low (Schedule V) scheduled peripheral kappa opioid for acute pain or pruritus.

Respiratory Safety Phase 1 Trial of CR845/Difelikefalin Injection

In April 2017, we announced summary results from our quantitative Phase 1 trial evaluating respiratory safety of CR845/difelikefalin injection. Respiratory depression remains the most life-threatening side effect of traditional, centrally acting, opioid analgesics, the most commonly used drug class for current treatment of postoperative pain in the United States. The Phase 1 trial was a randomized, double-blind, placebo-controlled, three-way crossover trial of two doses of CR845/difelikefalin injection versus placebo on three measures of respiratory drive in 15 healthy volunteers. Each subject was randomized to one of three treatment sequences and was administered I.V. bolus placebo, I.V. CR845/difelikefalin (1.0 mcg/kg) and I.V. CR845/difelikefalin (5.0 mcg/kg) on sequential 24-hour periods, with I.V. CR845/difelikefalin (5.0 mcg/kg) representing a projected five-fold supra-therapeutic dose. After each administration, and continuing through four hours post-dosing, end-tidal CO_2, or $ETCO_2$, oxygen saturation, or SpO_2, and respiratory rate were continuously monitored. The primary safety endpoints were: a >10 mmHg sustained ($\geq$30 seconds duration) increase in $ETCO_2$ above baseline or to >50 mmHg, and a sustained reduction in SpO_2 to <92%.

There were no statistically significant differences in any respiratory measures observed between groups throughout the four-hour observation period post-dosing and no individual subject met the threshold for a respiratory safety event. Additionally, all treatment-emergent adverse events were previously reported with CR845/difelikefalin administration and were mild, resolving without intervention.

Components of Operating Results

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. Substantially all of our revenue recognized to date has consisted of upfront payments under license agreements with VFMCRP, Maruishi and CKDP, and milestone and sub-license payments under license agreements with CKDP and Maruishi for CR845/difelikefalin, some or all of which was deferred upon receipt, as well as license agreements for CR665, our first-generation drug program for which development efforts have ceased and clinical compound sales from certain license agreements. To date, we have earned a total of $5.3 million in clinical development or regulatory milestone payments, sub-license fees under our Maruishi and CKDP collaborations, net of contractual foreign currency adjustments and South Korean withholding taxes, and clinical compound sales from certain license agreements. We have not yet received any milestone payments under the VFMCRP Agreement or royalties under any of our collaborations.

Research and Development (R&D)

Our R&D expenses relate primarily to the development of CR845/difelikefalin. R&D expenses consist of expenses incurred in performing R&D activities, including compensation and benefits for full-time R&D employees, clinical trial and related clinical manufacturing expenses, third-party formulation expenses, fees paid to contract research organizations, or CROs, and other consultants, stock-based compensation for R&D employees and consultants and other outside expenses. Our R&D expenses also included expenses related to preclinical activities for our earlier stage programs in prior periods and may include such expenses in the future.

R&D costs are expensed as incurred. Non-refundable advance payments for goods or services to be received in the future for use in R&D activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Most of our R&D costs have been external costs, which we track on a program-by program basis. Our internal R&D costs are primarily compensation expenses for our full-time R&D employees. We do not track internal R&D costs on a program-by-program basis.

R&D 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. Based on our current development plans, we presently expect that our R&D expenses for 2019 will increase over those for 2018. However, it is difficult to determine with certainty the duration and completion costs of our current or future nonclinical programs and clinical trials of our product candidates, or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors including, but not limited to:

- per patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trial is conducted;
- the length of time required to enroll eligible patients;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profile of the product candidate.

In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each product candidate, as well as an assessment of each product candidate's commercial potential.

General and Administrative

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, legal, business development and human resources functions. Other costs include facility costs not otherwise included in R&D expenses, legal fees, insurance costs, investor relations costs, patent costs and fees for accounting and consulting services.

We anticipate that our general and administrative expenses for 2019 will generally approximate those for 2018 to support our continued R&D activities and potential commercialization of our product candidates. These expenses will likely include costs related to the hiring of additional personnel, fees to outside consultants, lawyers, accountants and investor relations firms. In addition, if I.V. CR845/difelikefalin, Oral CR845/difelikefalin or any future product candidate obtains regulatory approval for marketing, we expect to incur expenses associated with building a sales and marketing team.

Other Income

Other income consists of interest and dividend income earned on our cash, cash equivalents, marketable securities and restricted cash, realized gains and losses on the sale of marketable securities and property and equipment as well as accretion of discounts/amortization of premiums on purchases of marketable securities.

Benefit from Income Taxes

The benefit from income taxes relates to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, which permits qualified small businesses engaged in R&D activities within Connecticut to exchange their unused R&D tax credits for a cash amount equal to 65% of the value of the exchanged credits.

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2019 and 2018

Revenue

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
License and milestone fees revenue	$ 5,208	$ 2,874	81%	$ 9,450	$ 2,874	229%
Clinical compound revenue	—	—	N/A	140	—	100%
Total revenue	$ 5,208	$ 2,874	81%	$ 9,590	$ 2,874	234%

License and milestone fees revenue

License and milestone fees revenue for the three and six months ended June 30, 2019 was $5.2 million and $9.5 million, respectively. License and milestone fees revenue for the three and six months ended June 30, 2018 was $2.9 million. License and milestone fees revenue for the three and six months ended June 30, 2019 and June 30, 2018 was related to license fees earned by us during the respective periods in connection with the VFMCRP Agreement (see Note 10 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

Clinical compound revenue

Clinical compound revenue for the six months ended June 30, 2019 was $140 thousand which was related to the sale of clinical compound to Maruishi. There was no clinical compound revenue for the three months ended June 30, 2019 and the three and six months ended June 30, 2018.

Research and Development Expense

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 17,542	$ 12,739	38%	$ 35,283	$ 22,087	60%
Consultant services in support of clinical trials	1,122	914	23%	2,380	1,456	63%
Stock-based compensation	1,929	852	126%	3,011	1,500	101%
Depreciation and amortization	27	94	-71%	55	199	-72%
Other R&D operating expenses	3,736	2,403	55%	7,235	5,187	39%
Total R&D expense	$ 24,356	$ 17,002	43%	$ 47,964	$ 30,429	58%

For the three months ended June 30, 2019 compared to the three months ended June 30, 2018, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $9.5 million, mainly from activities related to the Phase 3 (12-week) safety study in hemodialysis patients with CKD-aP, the two Phase 3 efficacy trials of I.V. KORSUVA (CR845/difelikefalin) in CKD patients undergoing hemodialysis, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients, the Phase 2 efficacy trial for pruritus associated with AD and costs related to a supportive Phase 1 study. Those costs were partially offset by a decrease of $2.6 million, mainly from the Phase 3 long-term (52-week) safety study of I.V. KORSUVA (CR845/difelikefalin) in hemodialysis patients with CKD-aP and costs associated with certain Phase 1 studies. There was also a decrease of $1.7 million in drug manufacturing costs. The increase in stock-based compensation expense was primarily the result of additional stock option grants to R&D employees as well as the vesting of restricted stock units granted to R&D executive officers. The increase in other R&D operating expenses was primarily the result of an increase in payroll and related costs associated with R&D personnel.

For the six months ended June 30, 2019 compared to the six months ended June 30, 2018, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $22.4 million, mainly from activities related to the Phase 3 (12-week) safety study in hemodialysis patients with CKD-aP, the two Phase 3 efficacy trials of I.V. KORSUVA (CR845/difelikefalin) in CKD patients undergoing hemodialysis, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients, the Phase 2 efficacy trial for CLD-aP, the Phase 2 efficacy trial for pruritus associated with AD and costs related to a supportive Phase 1 study. Those costs were partially offset by a decrease of $6.5 million, mainly from the Phase 2/3 I.V. CR845/difelikefalin adaptive clinical trial in post-operative pain and costs associated with certain Phase 1 studies. There was also a decrease of $1.4 million in drug manufacturing costs. The increase in stock-based compensation expense was primarily the result of additional stock option grants to R&D employees as well as the vesting of restricted stock units granted to R&D executive officers. The increase in other R&D operating expenses was primarily the result of an increase in payroll and related costs associated with R&D personnel.

The following table summarizes our R&D expenses by programs for the three and six months ended June 30, 2019 and 2018:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
I.V. CR845 - Pruritus	$ 13,298	$ 8,187	62%	$ 27,188	$ 11,858	129%
I.V. CR845 - Pain	160	699	-77%	359	3,968	-91%
Oral CR845 - Pruritus	5,195	3,317	57%	10,094	5,563	81%
Oral CR845 - Pain	12	1,450	-99%	22	2,153	-99%
Internal research and development expenses	5,691	3,349	70%	10,301	6,887	50%
Total research and development expenses	$ 24,356	$ 17,002	43%	$ 47,964	$ 30,429	58%

General and Administrative Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 903	$ 889	2%	$ 1,832	$ 1,482	24%
Stock-based compensation	2,085	1,217	71%	3,238	2,440	33%
Depreciation and amortization	22	20	12%	44	40	12%
Other G&A operating expenses	1,984	1,559	27%	3,788	3,420	11%
Total G&A expense	$ 4,994	$ 3,685	36%	$ 8,902	$ 7,382	21%

For the three months ended June 30, 2019 compared to the three months ended June 30, 2018, the increase in stock-based compensation expense was primarily the result of additional stock option grants to G&A employees as well as the vesting of restricted stock units granted to G&A executive officers. The increase in other G&A operating expenses was primarily the result of increases in payroll and related costs associated with G&A personnel and increases in franchise taxes. Professional fees and public/investor relations expenses remained consistent between the respective periods.

For the six months ended June 30, 2019 compared to the six months ended June 30, 2018, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs, legal fees and accounting fees. The increase in stock-based compensation expense was primarily the result of additional stock option grants to G&A employees as well as the vesting of restricted stock units granted to G&A executive officers. The increase in other G&A operating expenses was primarily the result of increases in payroll and related costs associated with G&A personnel and increases in franchise taxes.

Other Income

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other Income	$ 947	$ 467	103%	$ 2,036	$ 778	162%

During the three months ended June 30, 2019 compared to the three months ended June 30, 2018, the increase in other income was due to an increase in interest and accretion income resulting from a higher average balance of our portfolio of investments in the 2019 period.

During the six months ended June 30, 2019 compared to the six months ended June 30, 2018, the increase in other income was due to an increase in interest and accretion income resulting from a higher average balance of our portfolio of investments in the 2019 period.

Benefit from Income Taxes

For the three months ended June 30, 2019 and 2018, pre-tax losses were $23.2 million and $17.3 million, respectively, and we recognized a benefit from income taxes of $235 thousand and $152 thousand, respectively. For the six months ended June 30, 2019 and 2018, pre-tax losses were $45.2 million and $34.2 million, respectively, and we recognized a benefit from income taxes of $320 thousand and $198 thousand, respectively.

The benefit from income taxes relates to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, as discussed above. We recognized a full valuation allowance against deferred tax assets at June 30, 2019 and December 31, 2018.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception and through June 30, 2019, we have raised an aggregate of approximately $486.6 million to fund our operations, including (1) net proceeds of $309.8 million from the sale of shares of our common stock in four public offerings, including our initial public offering; (2) proceeds of $73.3 million from the sale of shares of our convertible preferred stock and from debt financings prior to our initial public offering; (3) payments of $88.9 million under our license agreements, primarily with VFMCRP, Maruishi, CKDP and an earlier product candidate for which development efforts ceased in 2007; and (4) net proceeds of $14.6 million from the purchase of our common stock in relation to the license agreement with VFMCRP (see Note 10 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

In order to fund our future operations, including our planned clinical trials, we filed the Shelf Registration Statement, which provides for aggregate offerings of up to $300.0 million of common stock, preferred stock, debt securities, warrants or any combination thereof. The securities registered under the Shelf Registration Statement include unsold securities that had been registered under our previous shelf registration statement (File No. 333-216657) that was declared effective on March 24, 2017. We believe that our Shelf Registration Statement provides us with the flexibility to raise additional capital to finance our operations as needed.

In July 18 2018, we entered into an underwriting agreement with Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, as representatives of the several underwriters named therein, relating to the issuance and sale by us of up to 5,175,000 shares of our common stock, including 675,000 shares of common stock the underwriters had the option to purchase, at a public offering price of $19.00 per share. This offering was made by pursuant to our Registration Statement on Form S-3 (File No. 333-216657), filed with the SEC on March 13, 2017 and declared effective on March 24, 2017, and a related prospectus dated March 24, 2017 and a prospectus supplement dated July 18, 2018, which was filed with the SEC on July 20, 2018.

On July 23, 2018, we closed the offering, including the full exercise of the underwriters' option to purchase 675,000 additional shares of common stock. We received net proceeds of approximately $92.1 million, after deducting $6.3 million relating to underwriting discounts and commissions and offering expenses.

In July 2019, we entered into an underwriting agreement with J.P. Morgan Securities, LLC and Jefferies LLC, as representatives of the several underwriters named therein, relating to the issuance and sale by us of 6,325,000 shares of our common stock, which includes the exercise of the underwriters' option to purchase 825,000 additional shares of common stock, at a public offering price of $23.00 per share. This offering was made by pursuant to our Shelf Registration Statement, and a related prospectus supplement dated July 24, 2019, which was filed with the SEC on July 25, 2019.

On July 29, 2019, we closed the offering, including the full exercise of the underwriters' option to purchase 825,000 additional shares of common stock. We received net proceeds of approximately $136.4 million, after deducting $9.0 million of underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this most recent underwritten offering, along with our existing cash and cash equivalents and marketable securities, to fund our clinical and research development activities, including the submission of a new drug application to the U.S. FDA for KORSUVA (CR845/difelikefalin) injection for the treatment of pruritus associated with CKD in hemodialysis patients and subsequent pre-commercialization activities, and the advancement of our clinical programs for Oral KORSUVA, including completion of Phase 2 trials for the treatment of pruritus in patients with CKD (Stage III-V), patients with CLD and patients with AD, as well as for working capital and other general corporate purposes.

We may offer additional securities under our Shelf Registration Statement from time to time in response to market conditions or other circumstances if we believe such a plan of financing is in the best interests of our stockholders.

As of June 30, 2019, we had $135.6 million in unrestricted cash and cash equivalents and available-for-sale marketable securities, which does not include the net proceeds from our July 2019 follow-on public offering described above. We believe our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient to fund our currently anticipated operating expenses and capital expenditures into the second half of 2021, without giving effect to any potential milestone payments we may receive under our licensing and collaboration agreements with VFMCRP, Maruishi and CKDP. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs.

Under the VFMCRP Agreement, we are eligible to receive regulatory and commercial milestone payments in the aggregate of up to $470 million, consisting of up to $30 million in regulatory milestones and up to $440 million in tiered commercial milestones, all of which are sales-related. We are also eligible to receive tiered double-digit royalty payments based on annual net sales, as defined in the VFMCRP Agreement, of CR845/difelikefalin injection in the Licensed Territories.

Under the Maruishi Agreement, we are also potentially eligible to earn up to an aggregate of $6.0 million in clinical development milestones and $4.5 million in regulatory milestones, before any foreign exchange adjustment, as well as tiered royalties, with percentages ranging from the low double digits to the low twenties, based on net sales of products containing CR845/difelikefalin in Japan, if any, and share in any sub-license fees. As of June 30, 2019, we have received milestone payments of $2.5 million before contractual foreign currency exchange adjustments.

Under the CKDP Agreement, we are potentially eligible to earn up to an aggregate of $2.3 million in clinical development milestones and $1.5 million in regulatory milestones, before South Korean withholding tax, as well as tiered royalties with percentages ranging from the high single digits to the high teens, based on net sales of products containing CR845/difelikefalin in South Korea, if any, and share in any sub-license fees. As of June 30, 2019, we have received milestone payments of $1.5 million before South Korean withholding tax.

The next potential milestone that could result in us receiving payment under the CKDP Agreement will be for a clinical development milestone related to the Phase 3 trial of CR845/difelikefalin in pruritus. When achieved, this milestone will result in a payment of $750 thousand, before South Korean withholding tax, being due to us. As of June 30, 2019, we determined that this milestone event has not occurred. We will continue to monitor this milestone event in future periods.

Our ability to earn these payments and their timing is dependent upon the outcome of I.V. and Oral CR845/difelikefalin development activities and, potentially, commercialization. However, our receipt of any further such amounts is uncertain at this time and we may never receive any more of these amounts.

Funding Requirements

Our primary uses of capital have been, and we expect will continue to be, compensation and related expenses, third-party clinical R&D services and clinical costs. In the past, we have also previously used capital for laboratory and related supplies.

Since inception, we have incurred significant operating and net losses. Our net losses were $23.0 million and $17.2 million for the three months ended June 30, 2019 and 2018, respectively, and $44.9 million and $34.0 million for the six months ended June 30, 2019 and 2018, respectively. As of June 30, 2019, we had an accumulated deficit of $339.3 million. We expect to continue to incur significant expenses and operating and net losses in the near future. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials, the receipt of additional milestone payments, if any, under our licensing and collaborations with VFMCRP, Maruishi and CKDP, the receipt of payments under any future collaborations and/or licensing agreements we may enter into, and our expenditures on other R&D activities.

We anticipate that our expenses will increase as we:

- continue the development of KORSUVA (CR845/difelikefalin) injection for CKD-aP in dialysis patients;
- continue the development of Oral KORSUVA (CR845/difelikefalin) for CKD-aP and other diseases associated with pruritus, such as CLD-aP and AD;
- explore the potential to further develop I.V. CR845/difelikefalin in the post-operative setting;
- conduct R&D of any potential future product candidates;
- seek regulatory approvals for I.V. CR845/difelikefalin and any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our global intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development and potential future commercialization efforts.

The successful development of any of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of I.V. CR845/difelikefalin, Oral CR845/difelikefalin or our other current and future programs. We are also unable to predict when, if ever, we will generate any further material net cash inflows from CR845/difelikefalin. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- achieving meaningful penetration in the markets which we seek to serve; and
- obtaining adequate coverage or reimbursement by third parties, such as commercial payers and government healthcare programs, including Medicare and Medicaid.

A change in the outcome of any of these variables with respect to the development of I.V. CR845/difelikefalin, Oral CR845/difelikefalin or any of our future product candidates would significantly change the costs and timing associated with the development of that product candidate.

Because our product candidates are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the total amounts necessary to successfully complete the development and commercialization of all our product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements, including our existing licensing and collaboration agreements with VFMCRP, Maruishi and CKDP.

We will require additional capital beyond our current balances of cash and cash equivalents and available-for-sale marketable securities and anticipated amounts as described above, and this additional capital may not be available when needed, on reasonable terms, or at all. In particular, because we do not have sufficient financial resources to meet all of our development objectives, especially the completion of our planned development of I.V. and Oral CR845/difelikefalin for the treatment of pruritus, we will need to raise additional capital. If we are not able to do so, we could be required to postpone, scale back or eliminate some, or all, of these objectives. To the extent that we raise additional capital through the future sale of equity or convertible debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on timing expectations and projected costs for our current clinical development plans, which include completing our Phase 3 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients suffering from moderate-to-severe CKD-aP to enable the submission of a new drug application, conducting supportive Phase 1 trials and Phase 2 trials of Oral KORSUVA (CR845/difelikefalin) in patients with pruritus associated with CKD, CLD and AD, we expect that our existing cash and cash equivalents and available-for-sale marketable securities, including the $136.4 million of net proceeds that we received in July 2019 in our recent public offering, will be sufficient for us to fund our currently anticipated operating expenses and capital expenditures into the second half of 2021, without giving effect to any potential milestone payments we may receive under our collaboration agreements with VFMCRP, Maruishi and CKDP. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs. Because the process of testing product candidates in clinical trials is costly and the timing of progress in these trials is uncertain, it is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we presently expect.

The Tax Cuts and Jobs Act of 2017

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act, or the Act. The Act, which is also commonly referred to as “U.S. tax reform”, significantly changed U.S. corporate income tax laws by, among other provisions, reducing the maximum U.S. corporate income tax rate from 35% to 21% starting in 2018. In accordance with the reduction in U.S. corporate income tax rate during the period of enactment, we reduced our deferred tax assets, which were offset by a corresponding reduction to our valuation allowance. On June 30, 2019 and December 31, 2018, we did not have any foreign subsidiaries and the international aspects of the Act are not applicable for the respective periods.

On December 22, 2017, Staff Accounting Bulletin 118, or SAB 118, was issued by the SEC due to the complexities involved in accounting for the Act. SAB 118 requires us to include in our financial statements a reasonable estimate of the impact of the Act on earnings to the extent such estimate has been determined. Accordingly, our U.S. provision for income tax for 2017 was based on the reasonable estimate guidance provided by SAB 118. We finalized the accounting for the Act as of December 31, 2018, which resulted in insignificant adjustments.

Cash Flows

The following is a summary of the net cash flows provided by (used in) our operating, investing and financing activities for the six months ended June 30, 2019 and 2018:

	Six Months Ended June 30,	
	2019	2018
	Dollar amounts in thousands	
Net cash (used in) provided by operating activities	$ (52,422)	$ 22,552
Net cash provided by (used in) investing activities	51,627	(30,442)
Net cash provided by financing activities	4,208	16,304
Net increase in cash, cash equivalents and restricted cash	$ 3,413	$ 8,414

Net cash (used in) provided by operating activities

Net cash used in operating activities for the six months ended June 30, 2019 consisted primarily of a net loss of $44.9 million, a $3.9 million cash outflow from net changes in operating assets and liabilities and a $3.6 million cash outflow from net non-cash charges. The net change in operating assets and liabilities primarily consisted of a cash outflow of $2.6 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs, a cash outflow of $0.9 million from a decrease in accounts payable and accrued expenses, and a cash outflow of $0.4 million from operating lease liability relating to lease payments made for the Stamford Lease as a result of our adoption of ASC 842: *Leases*. Net non-cash charges primarily consisted of a decrease of $9.5 million in deferred revenue associated with our VFMCRP Agreement and $0.8 million related to accretion of available-for-sale securities, partially offset by stock-based compensation expense of $6.2 million.

Net cash provided by operating activities for the six months ended June 30, 2018 consisted primarily of a $56.2 million cash inflow from net non-cash charges and a $0.4 million inflow from net changes in operating assets and liabilities, partially offset by a net loss of $34.0 million. Net non-cash charges primarily consisted of an increase in deferred revenue of $52.6 million related to the VFMCRP Agreement and stock-based compensation expense of $3.9 million. The net change in operating assets and liabilities primarily consisted of a cash inflow of $4.0 million from an increase in accounts payable and accrued expenses, partially offset by a cash outflow of $4.0 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs.

Net cash provided by (used in) investing activities

Net cash provided by investing activities was $51.6 million for the six months ended June 30, 2019, which primarily included cash inflows of $122.9 million from maturities of available-for-sale marketable securities, partially offset by cash outflows of $71.2 million for the purchase of available-for-sale marketable securities.

Net cash used in investing activities was $30.4 million for the six months ended June 30, 2018, which primarily included cash outflows of $98.3 million for the purchase of available-for-sale marketable securities, partially offset by cash inflows of $56.7 million from maturities of available-for-sale marketable securities and $11.1 million from the sale of available-for-sale marketable securities.

Net cash provided by financing activities

Net cash provided by financing activities for the six months ended June 30, 2019 consisted of proceeds of $4.2 million received from the exercise of stock options.

Net cash provided by financing activities for the six months ended June 30, 2018 consisted of proceeds of $14.6 million from the sale of our common stock relating to the VFMCRP Agreement and $1.7 million received from the exercise of stock options.

Significant Contractual Obligations and Commitments

Contractual obligations and commitments as of June 30, 2019 consisted of an operating lease obligation in connection with our operating facility in Stamford, Connecticut. See Note 15 of Notes to Condensed Financial Statements, *Commitments and Contingencies: Leases*, in this Quarterly Report on Form 10-Q.

Recent Accounting Pronouncements

Please refer to Note 2 of Notes to Condensed Financial Statements, *Basis of Presentation*, in this Quarterly Report on Form 10-Q.

Off-Balance Sheet Arrangements

We did not have during the periods presented in our condensed financial statements included in this report, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

Discussion of Critical Accounting Policies

The preparation of financial statements in conformity with GAAP requires us to use judgment in making certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities and the reported amounts of revenues and expenses in our condensed financial statements and accompanying notes. Critical accounting policies are those that are most important to the portrayal of our financial condition and results of operations and require difficult, subjective and complex judgments by management in order to make estimates about the effect of matters that are inherently uncertain. During the six months ended June 30, 2019, there were no significant changes to our critical accounting policies from those described in our Annual Report on Form 10-K for the year ended December 31, 2018.

Item 3. ***Quantitative and Qualitative Disclosures About Market Risk.***

Interest Rate Risk

As of June 30, 2019, we invested a majority of our cash reserves in a variety of available-for-sale marketable securities, including investment-grade debt instruments, principally corporate notes, commercial paper, municipal bonds and direct obligations of the U.S. government and U.S. government-sponsored entities, and in cash equivalents. See Note 3 of Notes to Condensed Financial Statements, *Available-for-Sale Marketable Securities*, in this Quarterly Report on Form 10-Q for details about our available-for-sale marketable securities.

As of June 30, 2019, we had invested $117.1 million of our cash reserves in such marketable securities. Those marketable securities include $117.1 million of investment grade debt instruments with a yield of approximately 2.68% and maturities through March 2021. As of December 31, 2018, we had invested $167.7 million of our cash reserves in such marketable securities. Those marketable securities included $167.7 million of investment grade debt instruments with a yield of approximately 2.64% and maturities through November 2020.

We maintain an investment portfolio in accordance with our investment policy, which includes guidelines on acceptable investment securities, minimum credit quality, maturity parameters, and concentration and diversification. The primary objectives of our investment policy are to preserve principal, maintain proper liquidity and meet our operating needs. Our investments are subject to interest rate risk and will decrease in value if market interest rates increase. However, due to the conservative nature of our investments and relatively short duration, interest rate risk is mitigated.

Duration is a sensitivity measure that can be used to approximate the change in the fair value of a security that will result from a change in interest rates. Applying the duration model, a hypothetical 1% increase in interest rates as of June 30, 2019 and December 31, 2018, would have resulted in immaterial decreases in the fair values of our portfolio of marketable securities at those dates. We do not currently use interest rate derivative instruments to manage exposure to interest rate changes.

Credit Quality Risk

Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Nonetheless, deterioration of the credit quality of an investment security subsequent to purchase may subject us to the risk of not being able to recover the full principal value of the security.

Item 4. ***Controls and Procedures.***

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of June 30, 2019. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2019, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC, and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosures.

Changes in Internal Control Over Financial Reporting

Beginning January 1, 2019, we implemented ASC 842, *Leases*. Although the new leasing standard did not have a material impact on our results of operations or cash flows, it did have a material impact on our financial position due to the recording of an operating lease right-of-use asset and operating lease liability beginning on January 1, 2019. As a result, we did implement changes to our processes related to leases and the control activities within them during the six months ended June 30, 2019. These included ongoing contract review requirements and gathering of information provided for disclosures, as well as other requirements as necessary per the new lease guidance.

There was no other change in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended June 30, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Controls and Procedures

Management, including our Chief Executive Officer and Chief Financial Officer, recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost benefit relationship of possible controls and procedures. Because of the inherent limitations in all control systems, no evaluation of controls and procedures can provide absolute assurance that all control issues and instances of fraud, if any, within Cara Therapeutics, Inc. have been detected.

PART II

OTHER INFORMATION

Item 1. ***Legal Proceedings***

From time to time, we may become subject to arbitration, litigation or claims arising in the ordinary course of business. We are not currently a party to any arbitration or legal proceeding that, if determined adversely to us, would have a material adverse effect on our business, operating results or financial condition. The results of any future claims or proceedings cannot be predicted with certainty, and regardless of the outcome, litigation can have an adverse impact on us because of defense and litigation costs, diversion of management resources, and other factors.

Item 1A. ***Risk Factors.***

Please refer to *Item 1A. Risk Factors* in our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 12, 2019, for a description of certain significant risks and uncertainties to which our business, operations and financial condition are subject. During the six months ended June 30, 2019, we did not identify any additional risk factors or any material changes to the risk factors discussed in the Annual Report on Form 10-K for the year ended December 31, 2018.

Item 2. ***Unregistered Sales of Equity Securities and Use of Proceeds.***

None.

Item 3. ***Defaults upon Senior Securities.***

None.

Item 4. ***Mine Safety Disclosures.***

Not applicable.

Item 5. ***Other Information.***

None.

Item 6. ***Exhibits.***

Exhibit No.	Description of Exhibit
3.1	Amended and Restated Certificate of Incorporation (1)
3.2	Amended and Restated Bylaws (2)
10.1 †	Amended and Restated Non-Employee Director Compensation Policy.
10.2 †#	Master Manufacturing Services Agreement between the Registrant and Patheon UK Limited and related Product Agreements.
31.1 †	Certification of Chief Executive Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
31.2 †	Certification of Chief Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
32.1 †*	Certifications of Chief Executive Officer and Chief Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101 †	Interactive Data File
101.CAL †	XBRL Taxonomy Extension Calculation Linkbase.
101.INS †	XBRL Instance Document.
101.LAB †	XBRL Taxonomy Extension Label Linkbase.
101.PRE †	XBRL Taxonomy Extension Presentation Linkbase.
101.SCH †	XBRL Taxonomy Extension Schema Linkbase.
101.DEF †	XBRL Definition Linkbase Document.

(1) Filed as exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-36279) filed with the Securities and Exchange Commission on February 7, 2014 and incorporated herein by reference.

(2) Filed as exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-36279) filed with the Securities and Exchange Commission on February 7, 2014 and incorporated herein by reference.

† Filed herewith.

* These certifications are being furnished solely to accompany this quarterly report pursuant to 18 U.S.C. Section 1350 and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Portions of this exhibit (indicated by asterisks) have been omitted because the Registrant has determined they are not material and would likely cause competitive harm to the Registrant if publicly disclosed.

SIGNATURES

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.

CARA THERAPEUTICS, INC.

Date: August 7, 2019

By /s/ DEREK CHALMERS
Derek Chalmers, Ph.D., D.Sc.
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: August 7, 2019

By /s/ MANI MOHINDRU
Mani Mohindru, Ph.D.
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 10.1

CARA THERAPEUTICS, INC.
AMENDED AND RESTATED
NON-EMPLOYEE DIRECTOR COMPENSATION POLICY

Equity:

- Initial option grant upon joining the board: 35,000 shares
- Annual equity awards granted on the date of each annual meeting of stockholders (for directors continuing as directors following the annual meeting):
    - Option: 9,000 shares
    - Restricted stock units: 6,000 shares

The initial option grant will vest over three years in equal annual installments, subject to the director's continued service as a director through each such vesting date.

Each annual equity award will vest on the earlier of (1) the one year anniversary of the date of grant and (2) immediately prior to the next annual meeting of stockholders following the date of grant, in each case, subject to the director's continued service as a director through such date.

Cash Comp:

- Annual board retainer fee - $40,000
- Chairman (if any) fee (including annual board retainer fee) - $75,000
- Audit Committee
    - Chairman fee (including member fee) - $20,000
    - Member fee - $10,000
- Compensation Committee
    - Chairman fee (including member fee) - $15,000
    - Member fee - $7,500
- Nominating and Corporate Governance Committee
    - Chairman fee (including member fee) - $8,000
    - Member fee - $4,000

These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on the board of directors or applicable committee.

Reimbursement of Expenses:

The Company will reimburse non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings.

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE CARA THERAPEUTICS, INC. HAS DETERMINED THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO CARA THERAPEUTICS, INC. IF PUBLICLY DISCLOSED.

Master Manufacturing Services Agreement

Effective Date: June 27, 2019

PARTIES

PATHEON UK LIMITED
a company existing under the laws of England and Wales, with its registered office at Kingfisher Drive, Covingham, Swindon, SN3 5BZ ("**Patheon**"),

- and -

CARA THERAPEUTICS INC.
a corporation existing under the laws Delaware with its principal place of business at 4 Stamford Plaza, 107 Elm Street, 9th Floor, Stamford, Connecticut 06902, United States ("**Client**").

Table of Contents

With effect from the date stated at the start of this Agreement (the “**Effective Date**”), the Parties have agreed to the following terms:

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 that is agreeable to Client, may perform Manufacturing Services for Client or any Affiliate of Client. This master form of agreement is intended to allow the Parties, or any of their Affiliates, to contract for the manufacture of one or more Products through Patheon’s global network of manufacturing sites by entering into specific Product Agreements without having to re-negotiate the general terms and conditions that apply.

1.2 Product Agreements.

This Agreement is structured so that Product Agreements may be entered into by the parties (or their Affiliates) for the manufacture of one or more Products at any Patheon manufacturing site agreeable to Client. Each Product Agreement will be governed by and will incorporate by reference the terms and conditions of this Agreement, and in the case of any conflict between the terms of a Product Agreement and this Agreement, the terms of this Agreement shall control, except to the extent that the applicable Product Agreement specifically and expressly provides to the contrary, as to the specific conflicting terms in that Product Agreement that are to control. Unless otherwise agreed by the Parties, each Product Agreement will be substantially in the general form, and contain the information referred to, in Appendix 1.

1.3 Definitions.

The following capitalized terms will have the respective meanings set out below, and grammatical variations of these terms will have corresponding meanings:

"**Affiliate**" means, with respect to a particular Party, a business entity that, directly or indirectly, controls, is controlled by, or is under common control with such Party;

For this definition, the term "control" means (with correlative meanings for the terms “controlled by” and “under common control with”) that the applicable entity has the lawful right and actual ability to determine (by ownership of shares or otherwise) the election of the majority of directors (or equivalent managers) of the applicable Party, or otherwise has the actual ability (by contract or otherwise) to control and direct the business affairs of such Party;

"**Annual Volume**" means, for the purpose of the Price for a particular Product, Patheon's assumed minimum volume of Product to be manufactured in any Year as set out in the "Annual Volume Forecast" section of Schedule A of the applicable Product Agreement for such Product;

"**API**" means the active pharmaceutical material as listed in the applicable Product Agreement (references to "Active Materials" or "Active Pharmaceutical Ingredient" in documents forming part of this Agreement or of a Product Agreement will mean "API");

"**API Credit Value**" means the value of the API for certain purposes of this Agreement, as set out in the applicable Product Agreement;

"**Applicable Laws**" means: (i) for Patheon, the Laws of the jurisdiction where the Manufacturing Site is located; and (ii) for Client and the Products, the Laws of all jurisdictions where the Products are manufactured, distributed, and marketed as these are agreed by the parties in the applicable Product 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, with competent jurisdiction over a Party, the Manufacturing Services, or the relevant Product (or its use);

"**Business Day**" means a day other than a Saturday, Sunday or a day that is a statutory holiday in Patheon's resident jurisdiction, Client's resident jurisdiction, or the jurisdiction where the applicable Manufacturing Site is located;

"**Capital Equipment Agreement**" means the separate agreement that the Parties may enter into that addresses the rights and responsibilities of the Parties regarding capital equipment and facility modifications that may be required to perform the Manufacturing Services under a particular Product Agreement;

"**Certificate of Analysis**" means, with respect to Product ordered Client and delivered by Patheon hereunder, a document signed by an authorized employee of the Patheon Quality organization stating and confirming that the Product to which such document refers has been manufactured in accordance with the Processing Instructions, and cGMPs.

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

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

(b) Commission Directive (EU) 2017/1572 (art. 2); and

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

together with current final industry-accepted Health Canada, 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 generated, made, discovered, created, in-licensed or derived (b) by Client at any time prior to or during the term of this Agreement, or (b) by Patheon while performing any Manufacturing Services, which Intellectual Property is specific to, or dependent upon, a Product or the manufacture or use thereof;

“**Client-Supplied Components**” means those Components supplied or to be supplied to Patheon by or on behalf of Client as identified in Schedule A of a Product Agreement, for use by Patheon for performing the Manufacturing Services under such Product Agreement;

"**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 Product under a particular Product Agreement in accordance with the applicable Processing Instructions, other than the API;

“**Confidential Information**” has the meaning specified in Section 11.1;

“**DEA**” means the Drug Enforcement Administration of the United States Department of Justice;

“**Deficient Product**” has the meaning specified in Section 6.1(b)(i);

“**Disclosing Party**” has the meaning specified in Section 11.1;

"**EMA**" means the European Medicines Agency;

"**FDA**" means the United States Food and Drug Administration;

"**Firm Order**" has the meaning specified in Section 5.1(d);

"**Health Canada**" means the department of the Canadian Government known as Health Canada and includes, among other relevant branches, the Therapeutic Products Directorate and the Health Products and Food Branch Inspectorate;

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

"**Intellectual Property**" means all legal rights in intellectual property, including all rights granted by or inherent in patents, patent applications, trademarks, trademark applications, trade-names, copyrights, industrial designs, trade secrets, and proprietary and confidential Inventions;

"**Invention**" means any innovation, improvement, development, discovery, computer program, device, trade secret, know-how, method, 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, and all information comprising any of the foregoing;

"**Inventory**" means all inventories of Components and work-in-process produced or held by or on behalf of Patheon (or its applicable Affiliate) for the manufacture of the applicable Product;

"**Knowledge**" means, with respect to a particular statement herein, that to the actual knowledge of the executive officers of Client or Patheon, as applicable, such officers are not aware of any facts or information that make such statement materially untrue.

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

"**Local Currency**" has the meaning specified in Appendix 4;

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

"**Manufacturing Services**" means, as to a particular Product, the manufacturing, quality control, quality assurance, stability testing, packaging, and related services for the manufacture of such Product, as set out in the relevant Product Agreement, for the manufacture and supply to Client of such Product;

"**Manufacturing Site**" means the facility identified in a Product Agreement where the Manufacturing Services for the applicable Product will be performed;

"**Minimum Order Quantity**" means, for each manufacturing campaign ordered by Client under a particular Product Agreement, the minimum number of units or batches of the relevant Product that Client must purchase under such campaign, as set out in Schedule A of such Product Agreement;

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

"**Patheon Competitor**" means a business entity that derives greater than 50% of its revenues from performing contract pharmaceutical or biopharmaceutical manufacturing services for clinical development or commercial use;

"**Patheon Intellectual Property**" means Intellectual Property generated, made, discovered, created, in-licensed or derived by Patheon or its Affiliates 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, the Product or its manufacture or use, which may include Inventions and Intellectual Property that apply generally to manufacturing processes or the formulation or development of drug products or drug delivery systems that are unrelated to the specific requirements or manufacture of a Product;

“**Price**” means, with respect to a particular Product, the fees to be charged by Patheon for:

(a) performing the Manufacturing Services for such Product;

(b) the cost of the applicable Components (other than Client-Supplied Components); and

(c) any separate cost items and other fees applicable to the manufacture and supply of the Product under the applicable Product Agreement;

all as set out in Schedule A of the applicable Product Agreement;

"**Processing Instructions**" means, for a particular Product, the set of documents relating to such Product as agreed by the Parties in writing to be the “processing instructions” for the manufacture and supply of such Product under the applicable Product Agreement, which shall include:

(a) quality control testing methods for the API and Components for such Product;

(b) all manufacturing instructions, directions, standard operating procedures and processes for the manufacture, quality control and assurance, and packaging of such Product;

(c) any storage requirements for such API and Components;

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

(e) the finished Product quality control testing methods, packaging instructions and shipping requirements for the Product, and the form of Certificate of Analysis for the Product;

"**Product**" means the pharmaceutical product listed in Schedule A of a particular Product Agreement;

“**Product Warranty**” has the meaning set forth in Section 9.4.

“**Product Agreement**” means an agreement entered into between Patheon and Client (or their applicable Affiliates) substantially in the form set out in Appendix 1, under which Patheon will perform Manufacturing Services for a particular Product;

“**Product Claims**” has the meaning specified in Section 6.1(b)(i);

"**Quality Agreement**" means a separate agreement between the Parties that sets out the quality assurance standards and related obligations applicable to the performance of Manufacturing Services;

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

“**Recipient**” has the meaning specified in Section 11.1;

“**Regulatory Approval**” has the meaning specified in Section 7.5(a);

"**Regulatory Authority**" means the FDA, EMA, and Health Canada and any other foreign regulatory agencies with the legal authority to grant marketing approvals for pharmaceutical or biopharmaceutical products, including the Products, in the applicable country or jurisdiction in the Territory;

“**Release Date**” means, in relation to a particular batch of Product manufactured under a particular Product Agreement, the scheduled date by which the Product will be released by Patheon’s quality department (by confirmation or certification) as agreed in the Quality Agreement and made available for shipment, and as confirmed by Patheon in a Firm Order;

“**Representatives**” means, as to a Party, all the directors, officers, employees, legal advisers, agents, consultants, subcontractors (excluding the other Party and its Affiliates), service partners, professional advisors, or legal representatives of such Party or its Affiliate;

“**Rolling Forecast**” has the meaning specified in Section 5.1(b);

"**Technical Dispute**" has the meaning specified in Appendix 2;

"**Territory**" means, as to a particular Product, the geographic area described in the relevant Product Agreement where such Product manufactured by Patheon will be distributed by or on behalf of Client or its Affiliate or licensees or distributors;

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

"**VAT**" has the meaning specified in Section 13.14; and

"**Year**" means, with respect to this Agreement or a particular Product Agreement: (a) in the first year of this Agreement or such Product Agreement, the time from the effective date of the applicable agreement up to and including December 31 of the same calendar year, and (b) after that will mean a calendar year.

1.4 Interpretation.

The division of this Agreement into Sections, Subsections, Appendices and Schedules, 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 or Schedule refers to the specified Section, Appendix or Schedule to this Agreement. In this Agreement, the term "**this Agreement**" and similar expressions refer to this Agreement as a whole and not to any particular part, Section, Appendix or Schedule of this Agreement. Except as otherwise expressly stated or unless the context otherwise requires, all references to the singular will include the plural and vice versa. The term “including” or “includes” shall not be interpreted to limit the scope or breadth of the provisions preceding such term and shall be deemed to mean “including without limitation”.

2. Patheon's Manufacturing Services

2.1 Manufacturing Services.

Patheon will perform the Manufacturing Services as set out in the relevant Product Agreement for the Price and in accordance with the terms and conditions of this Agreement, such Product Agreement and the Quality Agreement. Subject to the preceding sentence, Patheon will convert API and Components into Product, and provide supportive Manufacturing Services such as quality assurance (for example quality controls, analytical testing, and stability programs), primary and secondary packaging, and any other related Manufacturing Services as agreed between the parties under the relevant Product Agreement. Patheon (and its applicable Affiliates) will perform all Manufacturing Services in accordance with all Applicable Laws.

For each Product for which the Parties (or their respective Affiliates) have entered into a Product Agreement, and unless otherwise expressly agreed in a Product Agreement, and except as otherwise provided in this Agreement, Patheon will be a non-exclusive manufacturer during the term of the applicable Product Agreement of the Products offered for sale by Client or its Affiliates, provided that, Client agrees to order and purchase from Patheon, and Patheon agrees to manufacture and supply hereunder, [***] of Client’s requirements for Products for commercial sale in the United States (as provided in Client’s rolling forecasts); *provided further that*, for clarity, the foregoing does not apply to manufacture of any API or Components.

Except as otherwise provided in the Product Agreement covering manufacture of particular Product for Client, for each Product that is covered by a Product Agreement during the term of this Agreement, Patheon shall maintain, commencing on the date that is twelve months after the launch of commercial sales of such Product in the Territory for such Product (or at such later date as agreed in writing, as to a particular Product), at least two separate and distinct manufacturing sites that are fully qualified and able to perform the Manufacturing Services set forth herein (“Manufacturing Redundancy”). The details of the allocation of the manufacturing services between such sites, for a Product, shall be as agreed reasonably by the Parties at the time of qualification. In the event Patheon fails to maintain, for a consecutive period of [***] in any twelve month period, the required Manufacturing Redundancy for a

particular Product covered by a Product Agreement, then Client shall no longer be required to use Patheon as the manufacturer of at least [***] of Client's requirements for such Product under the relevant Product Agreement.

2.2 Subcontracting.

Patheon may subcontract the Manufacturing Services under a particular Product Agreement to one or more of its Affiliates, as agreed in writing in advance by Client (such agreement not to be unreasonably withheld) pursuant to the applicable Product Agreement. In the case of such subcontracting, such Affiliate shall be deemed to be bound by Patheon's obligations under this Agreement, the Quality Agreement and the applicable Product Agreement, Patheon will remain liable to Client for any breach of this Agreement, the Quality Agreement or such Product Agreement by, or the negligence or recklessness of, by its Affiliates in the course of performing: (i) subcontracted Manufacturing Services under a Product Agreement; or (ii) obligations under the Quality Agreement. Patheon may also arrange for non-Affiliate subcontractors to perform specific services arising under any Product Agreement with the consent of Client ("**Third Party Subcontractors**"). Patheon also may subcontract to a Third Party Subcontractor certain Manufacturing Services under a particular Product Agreement, as agreed in writing in advance by Client pursuant to the applicable Product Agreement. Patheon will be liable to Client for any failure by any Third Party Subcontractor to perform any part of the subcontracted services in compliance with the obligations under this Agreement, the Quality Agreement, or the relevant Product Agreement, or the breach, negligence or recklessness of the Third Party Subcontractor in performing such services. But Patheon's liability for Third Party Subcontractors will remain subject to all limitations on Patheon's liability as set out in this Agreement. Patheon will have no liability arising from the performance of services by Third Party Subcontractors: (i) that are initially chosen by Client and required by Client to be used by Patheon; or (ii) that are suppliers or service providers not validated and utilized by Patheon prior to the date of this Agreement.

3. Client's Obligations

3.1 Payment.

In consideration for Manufacturing Services actually performed and Product supplied to Client in accordance with the terms of this Agreement and the applicable Product Agreement, Client will pay Patheon the applicable Price in accordance with Sections 4 and 5. All cost items that are not included in the Price (as and to the extent specified in the applicable Product Agreement) are subject to additional fees to be paid by Client as provided in such Product Agreement.

3.2 Processing Instructions.

Before the start of commercial manufacturing of Product under this Agreement and the applicable Product Agreement, Client will provide to Patheon a copy of the Processing Instructions for such Product manufacturing, which must be accompanied by the applicable specifications for the API, the applicable Components and the finished Product (if applicable, precisely matching the applicable specifications approved by the applicable Regulatory Authority). If the Processing Instructions or accompanying documents provided by Client are subsequently amended by or on behalf of Client, or no longer reflect those currently approved by the Regulatory Authority, then Client will give Patheon a copy of the revised Processing Instructions documents (if applicable, precisely matching the revised specifications approved by the applicable Regulatory Authority). All such Processing Instructions shall be deemed accepted by Patheon on the date received, *unless* Patheon provides to Client, within [***] of such receipt, with reasonable written objections (a "PI Objection") to particular document(s) or instructions in such Processing Instructions and provides in such PI Objection the detailed reasons for why such document(s) or instructions are improper and not acceptable to Patheon. If, as to particular Processing Instructions provided by Client, Patheon timely provides a PI Objection to such Processing Instructions, then the Parties shall meet as soon as practicable thereafter and work reasonably and in good faith to agree as soon as practicable on mutually agreeable modifications to such Processing Instructions (which must comply with all Applicable Laws). If the Parties cannot agree on such modifications, such that the Processing Instructions (as modified) are mutually agreed and acceptable to the Parties, within [***] of the date such PI Objection is received, then such issue shall be a "Dispute" under the provisions of Appendix 2, and the Parties will proceed under the "Negotiations" paragraph of Appendix 2. If such Dispute is not resolved by the Senior Officers under the terms of such paragraph, then: (a) if Client reasonably believes that the Processing Instructions that are the subject of the PI Objection in such Dispute are reasonably required (either by the Applicable Laws or regulations in the applicable Territory, or due to other legitimate, material business concerns), then Client may terminate the applicable Product Agreement on [***] prior written notice (in which case section 8.3 shall apply), unless agreement can be reached in such 90 day period; or (b) as to all other such Disputes, the Parties shall proceed to seek to resolve such dispute pursuant to the other terms of Appendix 2. Upon acceptance (or deemed acceptance) of Processing Instructions (including all accompanying documents), as such Processing Instructions may be modified by the Parties (if applicable) according to the foregoing, Patheon will give Client a signed and dated receipt indicating Patheon's acceptance of such Processing Instructions. At Patheon's reasonable request, Client will provide evidence of the executed original documents comprising the Processing Instructions submitted by or on behalf of Client to the applicable Regulatory Authority.

3.3 API and Components.

(a) With respect to Patheon's manufacture of a particular Product, Client will, at its sole cost and expense, use reasonable efforts to deliver the API and any Client-Supplied Components for such Product to the applicable Manufacturing Site, such delivery to be effected DDP (Incoterms 2010). Client's obligation will include obtaining the release of the API and any Client-Supplied Components from the applicable customs agency and Regulatory Authority. Unless otherwise agreed in writing, Client or Client's designated broker will be the "**Importer**" or "**Importer of Record**" (or equivalent, as understood under Applicable Laws) for such API

and Client-Supplied Components to the extent imported to the Manufacturing Site, and Client is responsible for compliance with Applicable Laws (and the cost of compliance) relating to that role as the importer. For API or Client-Supplied Components which may be subject to import or export to or from the United States, Client agrees that its vendors and carriers will comply with applicable requirements of the U.S. Customs and Border Protection Service and the Customs Trade Partnership Against Terrorism.

(b) Unless otherwise agreed in writing between the Parties, the API and any Client-Supplied Components shall be delivered by the Client to the Manufacturing Site at least [***] before the scheduled manufacture start date for Product covered by a Firm Order in sufficient quantity to enable Patheon to manufacture the agreed quantities of Product, and if such delivery is not timely made, then Patheon is not obligated to initiate such manufacture campaign (but will use reasonable efforts to do so, if the applicable API and any Client-Supplied Components are delivered by Client at time that allows Patheon to commence such manufacturing at the scheduled date) until a revised date, such date to be agreed by the parties, both acting reasonably and in good faith, such date to be as soon as practicable after such delivery by Client, taking into account Patheon's other business commitments. Patheon reserves the right to refuse to store any quantity of API materially in excess of the amount necessary for the particular Manufacturing Services covered by a Firm Order, at its sole discretion at any time. If Client does not deliver the API or Client-Supplied Components within the agreed time period and, making commercially reasonable efforts, Patheon is unable to manufacture Product on the scheduled date because of the delay in such delivery, the delivery date for the Products under such Firm Order will be considered a postponement of the Release Date by Client to a new Release Date based on the revised manufacturing initiation date agreed to by the Parties as referred to above, and Section 5.1(e) will apply. Patheon will reschedule manufacture under a replacement purchase order at Client's request subject to Patheon's manufacturing slot availability at the time of the request.

(c) Patheon will control the unloading of API and Client-Supplied Components arriving at the Manufacturing Site, and Client will comply and ensure that its carrier complies with all related reasonable unloading directions of Patheon. The API and Client-Supplied Components will be held by Patheon on behalf of Client as set out in this Agreement. The API and Client-Supplied Components will at all times remain the property of Client. Any API and Client-Supplied Components received by Patheon will only be used by Patheon to perform the applicable Manufacturing Services.

(d) Client will ensure that: (i) all delivered API meets the specifications for that API as set forth in the applicable Processing Instructions; and (ii) all shipments of API to Patheon are accompanied by the required documentation as specified in the applicable Quality Agreement.

(e) If Client asks Patheon to qualify an additional supplier for the API or any Component, the Parties must agree on the scope of work to be performed by Patheon and the additional fees to be paid by Client for such work performed. For any such API or Component, this work at a minimum will include: (i) laboratory testing to confirm the API or Component meets existing

specifications therefor as set forth in the applicable Processing Instructions; (ii) manufacture of an experimental batch of Product using such API or Component that will be placed on three 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).

(f) Patheon will promptly advise Client if it encounters API or Component supply problems, including delays and/or delivery of non-conforming API or Components from a Client designated additional supplier. In such event, the Parties will cooperate to reduce or eliminate any supply problems from these additional suppliers. If supply problems persist, Patheon may suspend the Manufacturing Services affected by the problems until it is satisfied that the Client has resolved the problems with its supplier or appointed an alternative supplier. Client will certify (according to typical industry standards) all Client designated additional suppliers 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 supplier on behalf of Client, it will do so for an additional fee agreed to and payable by Client.

3.4 Packaging and Artwork.

Client will be responsible for the cost of artwork development and approval of all artwork. Client will be responsible for changes to labels, product inserts, and other packaging for the Products, including obtaining all required approvals. Client will be responsible for the cost of labelling obsolescence as contemplated in Section 5.2. Patheon's name will not appear on the label or anywhere else on the Products unless: (i) required by any Applicable Laws; or (ii) Patheon consents in writing to the use of its name. At least [***] prior to the Release Date of Product for which new or modified artwork is required, Client will provide at no cost to Patheon and in accordance with the applicable specifications, final camera ready artwork for all packaging Components to be used in the manufacture of the Product. Client will be responsible for all costs associated with complying with any and all regulatory requirements for the labelling and tracking of the manufactured Product, including product serialisation, product data transfer and anti-counterfeiting requirements in the Territory.

4. Price and Price Adjustments

4.1 First Year Pricing.

The Price for each particular Product will be listed in Schedule A of the applicable Product Agreement, and a Price may be adjusted under this Section 4.

4.2 Annual Price Adjustments.

[***]

4.3 Price Adjustments at any Time.

The Prices may be adjusted by Patheon at any time upon written notice to Client as follows:

(a) Extraordinary Increases in Component Costs. If the cost of a Component increases cumulatively by at least [***] as a result of market factors, then Patheon will be entitled to adjust the Price proportionately (to account solely for that actual increase in price of the Component) and as otherwise agreed in the Product Agreement. The revised Price will become effective with the first use of the higher cost Component in the manufacture of the Product. For a Price adjustment under this Section 4.3(a), Patheon will deliver to Client a revised Schedule A to the Product Agreement. In the event Patheon invokes the increase contemplated in this Section 4.3(a), Patheon shall review such Component costs every six months and in the event the price of such Component decreases by [***], Patheon shall reduce the price proportionately (to account solely for the actual decrease in price of the Component). In any case, Patheon shall provide Client the basis for the Price adjustment, which shall include the current and increased costs and inventory of existing Component available.

(b) Changes. The scope of the Manufacturing Services is set by the agreed Processing Instructions, the Regulatory Approvals, the Quality Agreement and any assumptions, inclusions, exclusions and other parameters set out in the applicable Product Agreement. Changes to the scope of the Manufacturing Services and related changes to the Price must be agreed in writing by the Parties (using a "**Change of Scope**" agreement, or similar, setting out the agreed activities and costs of implementation) and are subject to the change control provisions of the Quality Agreement. Where Patheon requests a change to the Manufacturing Services, the change will be implemented following appropriate regulatory approvals and upon written approval of Client, which Client will not unreasonably withhold, condition or delay.

5. Purchasing Product

5.1 Orders and Forecasts.

(a) Long Term Forecast. [***] If, for a particular Product, Patheon foresees any capacity constraint affecting any portion of any Long Term Forecast submitted by Client for such Product, it will notify Client of the details of such capacity constraint, within [***] after Client's submission of such Long Term Forecast, and promptly thereafter the Parties will meet and discuss reasonably and in good faith such capacity issue and shall agree in writing on a revised Long Term Forecast within Patheon's expected capacity, and for clarity, Client will be free to contract with alternative sources of supply for the manufacture of amounts of such Product in excess of such revised Long Term Forecast (or, absent such agreement on a revised Long Term Forecast, in excess of the amount Patheon asserts in such notification it has capacity to manufacture).

(b) Rolling Forecast. Before each Product Agreement is executed, Client will give Patheon a written forecast of the volume of the Product covered by such Product Agreement that Client expects to order in each of the next [***] (a "**Rolling Forecast**" for such Product). The Rolling Forecast must be reasonably consistent with the applicable time period in the most recent Long Term Forecast for such Product. Client will provide an updated Rolling Forecast: (i) on or before the tenth day of each month; and (ii) if at any time it determines that the total forecast volumes estimated in the most recent Rolling Forecast have changed by [***]. Each updated Rolling Forecast supersedes all previous Rolling Forecasts for the applicable Product.

(c) Orders. On or before the tenth day of each month, Client will issue a new purchase order for the amount of Product required by Client. Each purchase order must meet the Minimum Order Quantity for the applicable month and specify the purchase order number, quantities by Product type, and requested release dates for the Product (which must occur at least [***] after the first day of the next month; each a "**Release Date**").

(d) Acceptance of Purchase Orders. To the extent that a purchase order covers amounts of Product that are no more than [***] of the amount that is forecast to be ordered in the most recent Rolling Forecast for such month (and provided that Client shall use good faith efforts to provide Rolling Forecasts that are accurate so that it does not need to exceed the forecast in its submitted purchase orders, except on exceptional bases), Patheon must accept the purchase order by sending an acknowledgement to Client, including the confirmed Release Dates. Subject to Section 5.1(f), if Patheon fails to acknowledge receipt of a purchase order within [***], the purchase order will be considered accepted by Patheon. An "exceptional basis" means no more than twice a year for the purposes of this section. Client may submit purchase order in excess of such [***] limitation, but Patheon need not accept the amount of such purchase order that is in excess of such [***] limitation, but will use reasonable efforts to do so if it has the capacity to meet such excess order. An accepted purchase order will be binding on the Parties (a "**Firm Order**"), except that either Party may request to change any Release Date beyond [***] after the first day of the next month. The Parties will negotiate reasonably and in good faith and seek to agree on any requested alternative release date, *provided that* neither Party may unreasonably reject an alternative release date requested under this Section 5.1(d), but, if the Parties cannot agree, the original Release Date specified in the Firm Order confirmed by Patheon will apply.

(e) Cancellation or Postponement. Patheon will determine the manufacturing schedule of all Product covered by Firm Orders, which manufacturing schedule must allow Patheon to meet the Release Dates applicable to such Firm Orders. If Client cancels or reduces a Firm Order, or wishes to postpone the applicable Release Date (subject to Section 5.1(d)), Client will remain liable to pay Patheon [***] of the Price for the Firm Order.

(f) Capacity Reservation. In advance of each Year of a Product Agreement, Patheon will use the Rolling Forecast for such Product to reserve its manufacturing capacity in that Year for Product as follows:

(i) for the first Year, by reference to the first Rolling Forecast;

(ii) for the second Year: (1) if the Effective Date of the Product Agreement occurs after July 1, by reference to the first Rolling Forecast; and (2) otherwise, by reference to the Rolling Forecast applicable at July 1 of the previous Year;

(iii) for each subsequent Year, by reference to the Rolling Forecast applicable at July 1 of the previous Year,

with the applicable Rolling Forecast (as determined above) for a particular Year being the "**Yearly Forecast Volume**" for such Product for that Year.

At the end of each Year, if the aggregate actual volume of Product ordered by Client with a confirmed Release Date within the Year, taking into account any Product paid for but not ordered, ("**Actual Yearly Volume**") is less than [***], then Patheon may invoice and Client will pay Patheon [***].

If the quantity of Product requested by Client in a Year (in purchase orders received by Patheon) exceeds [***] of the Yearly Forecast Volume for that Year, Patheon will use commercially reasonable efforts to supply the additional Product volumes (i.e., in excess of such [***] limitation) ordered; however, Patheon will not be considered to have accepted any purchase order to the extent such purchase order is for additional Product volumes above such [***] of the Yearly Forecast Volume for such Product without written confirmation of such acceptance.

(g) Failure to Deliver Ordered Product. Patheon shall promptly notify Client if Patheon reasonably anticipates that it will be unable to meet a scheduled Release Date for a Firm Order. If Patheon does not deliver any amount of Product ordered by Client under a Firm Order by the specified Release Date for such order (a "Supply Problem"), then (i) on written request by Client, Patheon will as soon as possible provide Client with the cause of such delay of delivery and Patheon's best estimate for the date that Patheon will be able to deliver to Client the Product that has not been delivered; and (ii) Patheon shall use diligent good faith efforts to deliver such undelivered Product as soon as possible, and (iii) Client may obtain supply of such undelivered amount of Product from another supplier, and if Client determines that it will be able to obtain such supply from another supplier and it gives Patheon written notice of same prior to Patheon commencing manufacture of such undelivered Product, then Client can cancel the Firm Order with regards to the amount of Product that was not timely supplied by Patheon, but otherwise Client shall not be able to cancel such Purchase Order. If (x) a Supply Problem for a particular Product occurs, and (y) such Supply Problem involves Patheon's failure to supply on a timely basis at least [***] of the amount of such Product ordered under the applicable Firm Order, and (z) Patheon has not fully cured such Supply Problem, by delivering to Client the full amounts of such Product, by the date that is [***] after the specified Release Date under such Firm Order, then (1) the Parties shall meet as soon as possible and discuss reasonably and in good faith appropriate modifications; and (2) Client shall thereafter be free to purchase any or all of its needs or requirements for Product from other supplier(s) for sale in the applicable Territory until such time as the cause of the failure to supply has been fixed.

(h) Controlled Substance Quota Requirements (if applicable). Client will give Patheon the information set out below for obtaining any required DEA or equivalent agency quotas ("**Quota**") needed to perform the Manufacturing Services. Patheon will be responsible for routine management of Quota information in accordance with Applicable Laws. The Parties

will cooperate to communicate the information and to assist each other in Regulatory Authority information requirements related to the Product as follows: (i) by April 1 of each Year for the applicable Product, Client will provide to Patheon the next Year's annual Quota requirements for the Product; (ii) by August 1 of each Year, Client will provide to Patheon any changes to the next Year's Quota requirements; (iii) Client will pro-actively communicate any changes to the Quota requirements for the then-current Year in sufficient time to allow Patheon to file and finalize Regulatory Authority filings supporting the changes; (iv) upon Patheon receiving the necessary forecast information from Client in order to request additional Quota, Patheon will submit to the applicable Regulatory Authority, on a timely basis, all filings necessary to obtain Quotas for API and will use commercially reasonable efforts to secure sufficient Quota from the applicable Regulatory Authority so as to achieve Release Dates for Product as set out in applicable purchase orders and forecasts submitted to Patheon by Client or its designee; and (v) Patheon will not be responsible for any Regulatory Authority's refusal or failure to grant sufficient Quota for reasons beyond the reasonable control of Patheon (including where Client fails to provide the required information in accordance with this Section 5.1(h)).

5.2 Obsolete Stock.

(a) Client understands and acknowledges that, with respect to each Product, Patheon will rely on Client's purchase orders, the Firm Orders, and the most recent applicable Long Term Forecast and Rolling Forecast in ordering the Components (other than Client-Supplied Components) required to meet anticipated Firm Orders. Patheon shall use good faith, reasonable efforts purchase the Components in sufficient volumes, and reasonably in advance of the expected use of the Component (taking into account lead times), to meet the production requirements for Products covered by anticipated (in accordance with the applicable Rolling Forecasts) Firm Orders or to meet the production requirements of any longer period agreed to by the Parties. Patheon shall use good faith, reasonable efforts to purchase all such Components at the lowest price reasonably obtainable.

(b) Client will reimburse Patheon for the cost of Components ordered or purchased by Patheon specifically in order to manufacture Products ordered under Firm Orders in accordance with Section (a) above that (i) are not used in the Manufacturing Services within six months after the forecasted month for which the purchases have been made (provided that Patheon has used good faith, reasonable efforts to avoid purchasing excess amounts of such Components), or (ii) have expired or are rendered obsolete due to Client changes in any forecast, Processing Instructions, GMP, artwork or Applicable Laws during the period (collectively, "**Obsolete Stock**"). This reimbursement will include [***]. If any non-expired Components are used in Products subsequently manufactured for Client or in third party products manufactured by Patheon, Client will receive credit for any costs of those Components previously paid to Patheon by Client. Patheon shall use good faith, reasonable efforts to minimize the creation of Obsolete Stock.

5.3 Storage.

If: (i) Client does not take possession or arrange for the destruction of Obsolete Stock within [***] of receipt of written notice from Patheon identifying the Obsolete Stock; (ii) any equipment (other than existing Patheon equipment) is stored at the Manufacturing Site at any time prior to its use in the Manufacturing Services; or (iii) Product is not collected by Client within [***] of the Release Date notified by Patheon, Client will pay Patheon [***] after that for storing such Obsolete Stock, unused equipment or Product. Storage fees for Obsolete Stock or Product which contain controlled substances or require refrigeration will be charged at [***]. Storage fees are subject to a one pallet minimum charge per month. Patheon may ship Product held by it longer than [***] to Client at Client's expense on [***] written notice to Client. If Patheon is unable to store any material due to capacity constraints, Patheon may use an Affiliate or third party storage provider to store (outside the Manufacturing Site) any material under this Agreement. After the limited storage periods stated above, Client will assume all risk of loss or damage to materials and Client will be responsible for having appropriate insurance coverage in place for this risk.

5.4 Invoices and Payment.

For shipments to Client of Product ordered by Client hereunder, Patheon will issue invoices to Client on or after the Release Date of the Product. Otherwise, Patheon will issue invoices for Manufacturing Services on completion or as agreed in the applicable Product Agreement. Patheon will also submit to Client, with each shipment of Products, a duplicate copy of the invoice covering the shipment. Invoices will be sent by email to the email address given by Client to Patheon in writing. 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 the undisputed amounts in all invoices within [***] of the date of the invoice. If any portion of an invoice is disputed, 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 1.0% per month (or such lesser amount as required by Laws). If Client is more than [***] late in paying undisputed amounts on an invoice, and such past due amount is material, Patheon may, on giving [***] notice to Client, suspend all Manufacturing Services until all such undisputed past due invoices have been paid in full. Patheon will have no liability to Client if this suspension results in delayed performance of any Manufacturing Services or cancellation or rescheduling of any manufacturing slots.

5.5 Delivery and Shipping.

Delivery of Products ordered by Client hereunder will be made EXW (Incoterms 2010) from Patheon's Manufacturing Site for such Product, unless otherwise agreed in a Product Agreement. Subject to Section 8.3, 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. Each delivery of Product shall be accompanied by a signed Certificate of Analysis for the batch of Product delivered, as well as any other documents required by the relevant Product Agreement and/or Quality Agreement ("**Delivery Documents**"). Client will notify Patheon in writing within [***] of receipt of such Delivery Documents if Client has identified a compliance issue that

will prevent shipment. Subject to Client's acceptance of the Delivery Documents as set forth above, if Client does not collect, or arrange for the collection, of Product within one month after Client has received written notice from Patheon that it has been released for shipment by Patheon, Client will assume all risk of loss or damage to the released Product, and Patheon may, in accordance with Client's instructions and as agent for Client, at Client's risk, arrange for shipping (to Client or any third party nominated by Client) of such Product, 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 activity under this Agreement.

5.6 Sale. Client agrees that it will not sell (itself or through a third party) Product supplied by Patheon hereunder in any market where Client (or its Affiliate or sublicensee or third party seller) does not have the permits or regulatory approvals (or registrations) required to sell such Product in such market.

6. Product Claims and Recalls

6.1 Product Claims.

(a) Rejection. Client may reject any manufactured Product that it reasonably considers (by reference to the results of the agreed release testing) to be defective based on documentation provided by Patheon or Client's own inspection or testing of delivered Product.

(b) Product Claims.

(i) Client may claim a remedy (a "**Product Claim**") for any portion of any batch of Product that does not comply with the Product Warranty or for which Patheon did not perform the Manufacturing Services in accordance with the then-current Processing Instructions, cGMPs, or Applicable Laws ("**Deficient Product**"). Client will inspect Product manufactured by Patheon, or batch documentation provided by Patheon, promptly after receipt and will give Patheon written notice of all Product Claims within [***] after receipt or, in the case of any defects not reasonably susceptible to discovery upon receipt by such inspection process, within [***] after discovery by Client, but not after the expiration date of the Product. If Client does not provide a Product Claim within the applicable 30 day period, then the Product will be considered to have been accepted by Client on the 31st day of such period. Except as set forth in Section 10.3, Patheon will have no liability for any deficiency for which Client has not sent such notice within the applicable 30 day period.

(ii) This Section 6 and Sections 10.2 and 10.3 sets out the only liabilities of Patheon for Deficient Products. Patheon will provide a remedy for Product Claims as specified in Section 10.2, but Patheon will have no obligation for any particular Product Claim for Deficient Product to the extent that such Deficient Product was caused to be defective: (i) solely due to deficiencies in the Processing Instructions; (ii) by safety or efficacy issues of the Product that are either (1) not caused by failure of Patheon to perform

Manufacturing Services in accordance with the agreed Processing Instructions, cGMPs or Applicable Laws, or (2) not due to manufacturing defects that result from Patheon's (or its Affiliate's) negligence or other fault; (iii) due to a defect in the API or an incorporated Component that was not reasonably discoverable by Patheon using the test methods set out in the Processing Instructions; (iv) by actions of Client or third parties occurring after the Product is delivered by Patheon; (v) resulting from packaging design or labelling defects or omissions for which Patheon has no responsibility; (vi) by an unascertainable reason in the case where Patheon performed the Manufacturing Services for the Product in accordance with the Processing Instructions, cGMPs, and Applicable Laws; or (vii) due to any breach by Client of its obligations under this Agreement. If after a full investigation as set out in the Quality Agreement and this Section 6.1(b)(ii), it is determined that particular Product, which is believed by Client to be Deficient Product, was manufactured by Patheon in accordance with the then-current Processing Instructions, cGMPs, and Applicable Law, and, if it was delivered, such Product complied with the Product Warranty at the time of delivery by Patheon to Client (or its carrier) hereunder, then Client will pay Patheon the Price for such Product Patheon's only liability for API loss or damage is set out in Appendix 3.

(c) Determination of Deficiency. Upon receipt of a Product Claim, Patheon will have [***] to advise Client by notice in writing whether it disagrees with the contents of the Product Claim. If the Parties do not agree within [***] after Patheon's notice to Client as to whether any Product identified in the Product Claim was Deficient Product, the Parties will investigate the matter in accordance with the Quality Agreement. If, after joint testing or investigation has been performed, the Parties still cannot agree on whether the Product is Deficient Product, then the provisions of Appendix 2 will apply and, after the required negotiation, the dispute will be handled as a Technical Dispute.

(d) Shortages and Price Disputes. Claims for shortages in the amount of Product shipped by Patheon or a Price dispute will be dealt with by reasonable agreement of the Parties. Any claim for a shortage or a Price dispute will be considered waived by Client if it has not been presented within [***] of the date of the relevant invoice.

6.2 Product Recalls and Returns.

(a) Records and Notice. Each of the Parties will maintain records necessary to permit a Recall of any Product delivered to Client or customers of Client. Each Party will promptly notify the other of any information which might affect the marketability, safety or effectiveness of the Product or which might result in the Recall or seizure of the Product in accordance with the Quality Agreement. Upon receiving this notice or upon this discovery, the Parties will discuss in good faith the appropriate steps and whether it is appropriate to stop making any further shipments of such Product in its possession or control, until a decision has been made by Client 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 solely by Client. "**Recall**" will mean any action: (i) by (or on behalf of) Client or

its Affiliate or licensee to recover title to or possession of quantities of the Product sold or shipped to third parties (including, without limitation, the voluntary withdrawal of Product from the market); or (ii) by any Regulatory Authority to detain or destroy any of the Product.

(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 the restrictions on the use of any Product, then Patheon will co-operate in all such actions and efforts as reasonably required by Client, having regard to all Applicable Laws.

(c) Recalled Product. To the extent that a Recall results from, or arises from Deficient Product, Patheon will be responsible for the reasonable documented out-of-pocket expenses of conducting the Recall and will use its commercially reasonable efforts to replace (at its sole cost) the Deficient Product with replacement Products as per Section 10. In all other circumstances, Recalls, returns, or other corrective actions will be made at Client's cost and expense. Patheon's only liability for API loss is set out in Appendix 3.

6.3 Disposition of Defective or Deficient Products.

Client will not dispose of any damaged, defective, returned, or Deficient Products for which it intends to assert a Product Claim against Patheon without Patheon's prior written authorization to do so, such authorization not to be unreasonably withheld. Patheon may instruct Client to return the Deficient Products to Patheon. Patheon will bear all costs of return, disposition and/or destruction of any Deficient Products that Patheon agrees are Deficient Product, or that is determined (as above) to be Deficient Product. In all other circumstances, Client will bear the cost of return and disposition, including all applicable fees for Manufacturing Services related to such Deficient Product. Patheon will pay for Client's reasonable and actual third party storage fees (as documented) of all agreed (or determined to be) Deficient Products until such time as Patheon instructs Client to return or dispose of the Deficient Product.

7. Co-operation and Regulatory Affairs

7.1 Governance.

Each Party will promptly after execution of this Agreement appoint one of its employees to be a relationship manager responsible for liaison between the Parties for the day to day interactions under this Agreement and the Product Agreements. The relationship managers will meet (which may be by telephone or video conference) on a frequency agreed between the Parties to review the current status of the business relationship and manage any issues that have arisen.

7.2 Governmental Agencies.

Subject to any restrictions in the Quality Agreement, and expect as otherwise provided below in this Section 7.2, Client shall have the sole right to communicate with any Regulatory Authority responsible for granting Regulatory Approval for the Products and any other relevant Authority regarding the Products. If, in the opinion of Patheon's counsel, Patheon must make a communication to such a Regulatory Authority regarding the manufacture of Product because such communication is necessary to comply with the terms of this Agreement or the requirements of the Authority or Applicable Laws, then Patheon must, subject to the timing requirements for such communications set out in Applicable Laws (which will take precedence), at least [***] prior to making any such communication, give notice to Client of such necessary communication and the reasons it is believed to be necessary, and in such case the Parties will consult with each other immediately in relation to such proposed regulatory communications relating to the Product, and Patheon shall not make such communication except with Client's prior written approval, not to be unreasonably withheld. The Parties also will cooperate with each other regarding communications with Regulatory Authorities in accordance with the Quality Agreement.

7.3 Records.

Patheon will keep complete and accurate records of the manufacture, testing, and shipping of the Products, and retain samples of the Products as are necessary to comply with manufacturing regulatory requirements applicable to Patheon, Applicable Laws, cGMP and the Quality Agreement. Copies of the records and samples will be retained as and for the period specified in the Quality Agreement. 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 30 days of receipt of notice from Patheon.

7.4 Audits and Inspections.

(a) Subject to the limits agreed in the Quality Agreement, 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, all as needed to permit Client to verify that the Manufacturing Services are being performed in accordance with the Process Instructions, the terms of this Agreement and the applicable Product Agreement, cGMPs, and Applicable Laws. If Client wishes to audit Patheon beyond the agreed limits, except where the audit is required due to Patheon's material breach, Client will pay to Patheon a fee of [***]. Under no circumstances will: (a) Client have a right of access to Patheon's financial records; or (b) any Patheon Competitor be permitted access to the Manufacturing Site.

(b) Patheon shall notify Client within the period specified in the Quality Agreement after it receives notice from a Regulatory Authority of an audit or inspection involving the Product, any component thereof, or any portion of Patheon's facility used or likely to be used in connection with the activities of Patheon to be conducted under this Agreement and, to the extent reasonably practicable, shall allow Client to be present at the Manufacturing Facility to support Patheon during the audit or inspection, but not to participate. The responsibility for

conducting the audit or inspection rests with Patheon. In each such case, whether or not Client was present at the Manufacturing Facility such audit or inspection, Patheon shall provide to Client copies of any resulting document of action (e.g., FDA Form 483 inspection observation report, regulatory letters, etc.) resulting from such audits or inspections, which pertains to the Product, any component thereof, or any portion of Patheon's facility used or likely to be used in connection with the activities of Patheon to be conducted under this Agreement, within the period specified in the Quality Agreement after receipt. Should either Patheon or Client receive any such document of action, it shall so notify the other within the period specified in the Quality Agreement after receipt and shall provide to the other an opportunity to the extent feasible under the circumstances, to provide input to any response to any such document of action.

7.5 Regulatory Filings.

(a) Regulatory Authority Documentation. Patheon will reasonably cooperate with Client in its interactions with Regulatory Authorities for Products, and provide all reasonable assistance for such interactions and for the preparation of applications for Regulatory Approvals of Product as requested by Client, which will be subject to reasonable fees being reasonably agreed between the Parties. Client will use reasonable efforts to provide copies of all relevant documents (i.e., relevant to Patheon's Manufacturing Services hereunder) included in applications to Regulatory Authority for approval for the commercial manufacture, distribution and sale of the Products ("**Regulatory Approval**") to Patheon on reasonable request as required under the Quality Agreement. Patheon will review and verify the accuracy of these documents in accordance with the Quality Agreement. Client is not entitled to submit, in applications for Regulatory Approvals, documents that referring to Patheon or its Affiliates or the Services until the relevant documents are approved by Patheon.

(b) Deficiencies. If Patheon reasonably determines that any Product regulatory information relating to manufacture of Product given by Client is inaccurate or deficient in any manner that may cause Patheon material regulatory or legal risk (the "**Regulatory Deficiencies**"), Patheon will notify Client in writing of the Regulatory Deficiencies and will provide all information regarding why it believes the information is inaccurate or deficient and creates risk for Patheon. In such event, the parties will work together to have the Regulatory Deficiencies resolved prior to the date of filing of the relevant regulatory approval application and in any event before any Product pre-approval inspection of the applicable Manufacturing Site or before the Product is placed on the market if a pre-approval inspection is not performed.

(c) Inspection by Regulatory Authorities. If Client does not give Patheon the documents reasonably requested under this Section 7.5 or the Quality Agreement within the time specified and if Patheon reasonably believes that Patheon's standing with a Regulatory Authority may be materially jeopardized due to such not having access to such documents, then Patheon may, in its sole discretion, delay or postpone any inspection by the Regulatory Authority of the applicable Manufacturing Site with respect to such Product until Patheon has reviewed the requested documents and is reasonably satisfied with their contents.

(d) Pharmacovigilance. Client will be responsible, at its expense, for all pharmacovigilance obligations for the Products in accordance with Applicable Laws and the monitoring and management of post-marketing complaints and queries at its cost (including, without limitation, the cost of assistance required of Patheon under the Quality Agreement). Unless required by Applicable Law, neither Party will be obliged to exchange with the other Party any information or data which it compiles in carrying out pharmacovigilance obligations or activities.

(e) No Patheon Responsibility. Except as otherwise agreed in the Quality Agreement, Patheon will not assume any responsibility for: (a) the submission, accuracy or cost of any application for Regulatory Approval or related documentation (or the success of those applications); (b) any activity that is required by Applicable Laws for Regulatory Approval (including pharmacovigilance and complaints handling, and preparation and submission of any regular quality or other update); or (c) any dealings with the relevant Regulatory Authority on behalf of Client 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 or a Product Agreement. Patheon will be not be obliged to undertake these activities or to pay for the fees or costs until the Parties reach agreement on scope and fees for Patheon's assistance, except as otherwise provided in the Quality Agreement (including required inspections by Regulatory Authorities of the Manufacturing Sites).

7.6 Release.

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 relating to the Manufacturing Services. Nothing in this Agreement will remove or limit the authority of the relevant quality function (as specified by the Quality Agreement) to determine whether the Products are to be released for sale or distribution.

7.7 Withdrawal on Completion.

No later than [***] following completion or permanent cessation of the Manufacturing Services at the applicable Manufacturing Site, Client will: (a) ensure that any regulatory filings relating to the Product are withdrawn or amended to remove all references to the Manufacturing Site and, as applicable, Patheon and/or its Affiliates and their facilities (except in an historic context); and (b) provide to Patheon written confirmation of its compliance with this Section 7.7. If this time is not sufficient to meet the requirements of certain Regulatory Authorities, despite Client's commercially reasonable efforts, then Patheon may agree to extend the period based on the written reassurances of Client.

8. Term and Termination

8.1 Initial Term.

This Agreement will become effective as of the Effective Date and will continue until December 31 of the fifth Year of the Agreement (the "**Initial Term**"), unless terminated earlier by one of the Parties as provided below in this Article 8. This Agreement will automatically renew after the Initial Term (and as the term may be extended pursuant to this sentence) for successive terms of two Years each if there is a Product Agreement then in effect, unless either Party gives written notice to the other Party of its intention to terminate this Agreement at least 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. Each Product Agreement will have an initial term from the Effective Date of the Product Agreement until December 31 of the Year agreed to by the parties in the Product Agreement (each, an "**Initial Product Term**"). Product Agreements will automatically renew after the Initial Product Term (as such term is extended hereunder) 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 18 months prior to the end of the then current term.

8.2 Termination for Cause.

(a) If a Party materially breaches this Agreement, or a Product Agreement, then the other Party may terminate this Agreement or the Product Agreement upon written notice where the other Party has failed to remedy such material breach of this Agreement or the Product Agreement within 60 days (the "**Remediation Period**") following receipt of a written notice of the breach from the aggrieved Party that expressly states that it is a notice under this Section 8.2(a) and which provides specific details on the nature of the alleged breach (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 120 days following the expiry of the Remediation Period (where the breach has not been remedied during such period) and if the termination right is not exercised during this 120 day period then the aggrieved party will be considered to have waived the right to terminate solely with respect to the breach described in the Breach Notice. The right to terminate a Product Agreement under this Section 8.2(a) does not extend to any other Product Agreements where there has been no material breach of those other Product Agreements and is in addition to any other rights and remedies the aggrieved Party may have under this Agreement and/or at law or equity.

(b) A Party may immediately terminate this Agreement or a Product Agreement upon written 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 or insolvency is filed in any court of competent jurisdiction by the other Party and such petition is not dismissed within 90 days thereafter; or (iii) this Agreement or a Product Agreement is assigned by the other party for the benefit of creditors.

(c) Client may remove one or more countries or jurisdictions from the definition of Territory in a Product Agreement upon 90 days' prior written notice if any Authority takes any action, or raises any objection, that on its terms permanently prevents Client from selling the Product in that or those countries or jurisdictions in the Territory.

(d) Client may terminate a Product Agreement upon six months' prior written notice if it intends to no longer order Manufacturing Services for a Product due to the Product's discontinuance in the market.

(e) Patheon may terminate this Agreement or any Product Agreement upon six months' prior written notice if Client assigns under Section 13.4 any of its rights under this Agreement or a Product Agreement to an assignee that: (i) is a Patheon Competitor, or (ii) does not have a market capitalization (at the time of the assignment) of at least $500 million.

(f) If, after the first full year of commercial sales of the Product, Client forecasts zero volume for twelve successive months during the term of a Product Agreement after obtaining Regulatory Approval of the Product in the U.S. or the EU, then Patheon may terminate the Product Agreement by providing 30 days prior written notice to Client. Within that period, Client may either: (i) withdraw the zero forecast and re-submit a reasonable volume forecast, after which the termination notice will be null and void; or (ii) negotiate other terms and conditions on which the Product Agreement will remain in effect.

(g) Client may terminate a Product Agreement upon 90 day's prior written notice if it determines that the manufacture or supply of Product under such Product Agreement, or the sale of such Product, more likely than not infringes Third Party Rights, provided that, (i) prior to issuing such termination notice, Client must provide its material evidence of the risk of infringement to Patheon; and (ii) Client must actually permanently withdraw the applicable Product from the relevant market in the Territory because of the risk of infringement, *except that* if Client subsequently determines to recommence sales of such Product in such market (e.g., because it obtains a license under the applicable Third Party rights, or determines that the risk of infringement is actually low), then Client shall cause such Product Agreement to be reinstated on written notice, and in such case the Parties shall negotiate and re-execute such Product Agreement (provided that Patheon has at that time sufficient manufacturing capacity to perform its obligations under the Product Agreement). If Patheon reasonably believes that the manufacture or sale to Client of Product under a Product Agreement likely infringes Third Party Rights, then Patheon may provide Client written notice of such believe, which notice shall include all material evidence of such infringement in Patheon's (or its Affiliate's or attorney's) control or awareness. The Parties will meet promptly after any such Patheon notice and shall discuss, reasonably and in good faith, the infringement risk and any appropriate actions to be taken. If (w) the Parties do not agree on an acceptable resolution to such infringement risk, and (x) such infringement risk is *not* based solely on manufacturing steps used by Patheon that are not specified by the Processing Instructions, (y) Patheon reasonably demonstrates that the risk of infringement by the manufacture or supply by Patheon of the Product is significant, and (z) Client does not obtain a license (or other resolution) to the infringement risk, then Patheon may terminate such Product Agreement upon 60 day's prior written notice.

8.3 Obligations on Termination.

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

(a) Client will take delivery of and pay for all undelivered Products that are manufactured and packaged in accordance with this Agreement under a Firm Order for such Product, at the Price in effect at the time the Firm Order was placed;

(b) Client will purchase all Inventory that was purchased (or will be purchased under existing unfulfilled orders for Components), maintained or produced by Patheon solely and specifically in contemplation of filling Firm Orders submitted by Client prior to notice of termination or expiration (as applicable) or in accordance with Section 5.2, at Patheon's actual cost (including all costs incurred by Patheon for the purchase, handling, and processing of the Inventory). If Patheon uses non-expired Components in the manufacture of third party products, Client will receive a credit for the cost of such Components to the extent paid by Client. Patheon shall use good faith, reasonable efforts minimize creation of Obsolete Stock.

(c) Client, at its own expense, will remove from the Manufacturing Site, within [***] following the completion, termination, or expiration of the Product Agreement, all unused API and Client-Supplied Components, all applicable Inventory (whether current or obsolete), supplies, undelivered Product, chattels, equipment or other moveable property owned by Client, related to the Agreement and located at the Manufacturing Site or that is otherwise under Patheon's care and control ("**Client Property**"). If Client does not remove such Client Property within the 30 day period, Client will pay Patheon [***] for any of Client Property that contains controlled substances, requires refrigeration or other special storage requirements) after that for storing Client Property and will assume any third party storage charges invoiced to Patheon regarding Client Property (which Patheon may incur at its discretion). Patheon may ship Client Property to Client or to an external warehouse at Client's risk and expense. Patheon will invoice Client for these storage charges as set out in Section 5.3 of this Agreement. If Client fails to remove Client Property within [***] following the completion, termination, or expiration of the Product Agreement, Client will assume all risk of loss or damage to the stored Client Property and it will be Client's responsibility to have appropriate insurance coverage in place for this risk. If Client asks Patheon to destroy any Client Property, Client will be responsible for the cost of destruction; and

(d) any termination or expiration of this Agreement or a Product Agreement will not affect any prior outstanding obligations or payments due nor will it prejudice any other remedies that either of the Parties may have under this Agreement or a Product Agreement or any related Capital Equipment Agreement for breaches obligations occurring prior to the termination. 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 Sections 5.1(e), 5.1(f), 5.4, 5.5, 8.3, 10, 11, 12, 13.14, 13.15 and 13.16, all of which survive any termination or expiration, as well as any other provisions that are by implication or otherwise intended to

survive any termination or expiration. Where Patheon has agreed to provide stability services beyond the final supply of Product, the relevant provisions of this Agreement will survive for the agreed duration of those stability services.

8.4 Technology Transfer.

Following expiration or termination of a Product Agreement for any reason, or if Client elects to utilize a second manufacturer as provided in Section 2.1, or in the event of a failure to supply pursuant to Section 5.1(g), or at Client's request within twelve months before the end of the term of the Product Agreement, Patheon will provide all reasonable assistance to transfer to Client (or its designated contract manufacturer) the actual manufacturing process, know-how and analytical testing methodology for the applicable Product (a "**Technology Transfer**") as reasonably needed for use by Client (or its contract manufacturer) to manufacture the Product. Patheon will also disclose to Client any Patheon Intellectual Property that is reasonably required to manufacture the Product. Patheon will, upon request of Client, prepare a written proposal to perform the Technology Transfer. Client will pay the agreed fees for the Technology Transfer performed by Patheon, which must be no more than a commercially reasonable compensation for the work involved.

9. Representations and Warranties

9.1 Authority.

Each Party 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 under this Agreement.

9.2 Client Warranties.

(a) Non-Infringement. Client represents and warrants to Patheon as of the Effective Date that:

(i) the Processing Instructions (including the specifications therein) for each Product are its or its Affiliate's property and that Client may lawfully disclose the Processing Instructions to Patheon for use in accordance with this Agreement;

(ii) any Client Intellectual Property used by Patheon in performing the Manufacturing Services (A) is Client's or its Affiliate's unencumbered property (including as licensed to Client), (B) may be lawfully used as directed by Client and agreed in this Agreement, and (C) to the Knowledge of Client, the use of such Client Intellectual Property by Patheon to perform the requested Manufacturing Services does not infringe and will not infringe any Third Party Rights;

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

(iv) there are no actions or other legal proceedings by a Third Party against Client or its Affiliates that concerns the infringement of Third Party Rights based upon manufacture or use of Product or the practice any of the Processing Instructions (including the specifications therein), or the manufacture or use of any of the API or Client-Supplied Components, or the sale, use, or other disposition of any Product made in accordance with the Processing Instructions.

(b) Quality and Compliance. Client represents and warrants as of the Effective Date that:

(i) To the Knowledge of Client, the Processing Instructions (including the specifications therein) for all Products conform to all Applicable Laws;

(ii) To the Knowledge of Client, the Products, if labelled and manufactured in accordance with the Processing Instructions and in compliance with applicable cGMPs and Applicable Laws, and if complying with the Product Warranty at the time of delivery: (i) may be lawfully sold and distributed in every jurisdiction in which Client markets the Products,; and

(iii) on receipt by Patheon, the API, will conform to the specifications for the API that Client has given to Patheon and will be adequately contained, packaged, and labelled in accordance with Applicable Laws and will conform to the affirmations of fact on the container.

9.3 Patheon Warranties.

Patheon represents, and warrants to Client that:

(a) it will perform the Manufacturing Services in accordance with the terms of this Agreement, the Quality Agreement and the applicable Product Agreement, the Processing Instructions, cGMPs, and Applicable Laws;

(b) as of the Effective Date any Patheon Intellectual Property used by Patheon to perform the Manufacturing Services (i) is Patheon's or its Affiliate's unencumbered property, (ii) may be lawfully used by Patheon, and (iii) to its Knowledge, does not infringe and will not infringe any Third Party Rights;

(c) 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

(d) 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 Product Warranty. Patheon hereby represents and warrants that, on delivery, each Product: (a) will have been manufactured in accordance with the Processing Instructions, cGMPs, and Applicable Laws; (b) will conform to the Product specification in the Processing Instructions; and (c) will not be adulterated as such term is defined in Applicable Laws (the "Product Warranty "). .

9.5 Permits.

(a) Client will be solely responsible for obtaining or maintaining, on a timely basis, any permits or other regulatory approvals for the Products, Processing Instructions or specifications, including, without limitation, all marketing and post-marketing approvals, and any specific approvals referred to in the Quality Agreement.

(b) Patheon will maintain at all relevant times when performing the Manufacturing Services all required governmental permits, licenses, approval, and authorities.

9.6 No Warranty.

OTHER THAN THE WARRANTIES OF PATHEON EXPRESSLY SET OUT IN THIS AGREEMENT, PATHEON MAKES NO OTHER WARRANTY OR CONDITION OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, INCLUDING ANY GENERAL WARRANTY OR CONDITION OF FITNESS FOR A PARTICULAR PURPOSE OR MERCHANTABILITY FOR THE PRODUCTS OR ANY GENERAL WARRANTY OF NON-INFRINGEMENT.

OTHER THAN THE WARRANTIES OF CLIENT EXPRESSLY SET OUT IN THIS AGREEMENT, CLIENT MAKES NO OTHER WARRANTY OR CONDITION OF ANY KIND, EITHER EXPRESSED OR IMPLIED, BY FACT OR LAW, INCLUDING ANY GENERAL WARRANTY OR CONDITION OF FITNESS FOR A PARTICULAR PURPOSE, OR ANY WARRANTY OF MERCHANTABILITY FOR THE PRODUCTS.

10. Liability and Remedies

10.1 Consequential and Other Damages.

Under no circumstances whatsoever will either Party be liable to the other Party, whether in contract, tort, negligence, indemnity, breach of statutory duty, or otherwise, for: (i) any (direct or indirect) damages or penalty caused by delay, loss of profits, of anticipated savings, of business, of goodwill, or of use of the Product or costs of any substitute services; or (ii) any reliance damages, including 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 consequential, indirect, punitive or special damages incurred by the other party, or (iv) for any other liability, damages, costs, penalty, or expense of any kind of an indirect or consequential nature regardless of any notice of the possibility of these damages.

10.2 Deficient Product Remedies; Limitations.

(a) Remedies for Deficient Product. If Client makes a Product Claim under Section 6.1 and the Parties agree or it is otherwise determined that the applicable Product (batch or part thereof) is Deficient Product, or the Product is determined to be Deficient Product under Section 6.1(b)(ii), Patheon will promptly, at Client's election, either:

(i) replace the Product conforming to the Product Warranty and other obligations of this Agreement, as soon as reasonably practicable and at Patheon's cost (after which Patheon may invoice for the replacement unless Client has paid for the original Deficient Product), if Patheon is able to manufacture the replacement Product at the Manufacturing Site and contingent upon the receipt from Client of all API and Client-Supplied Components required for the manufacture of the replacement Product; or

(ii) refund 100% of the Price paid for the Deficient Product (by credit or offset against other amounts due to Patheon under the Product Agreement, as elected by Client).

Except for the indemnity set out in Section 10.3 and any claim for expenses related to a Recall under Section 6.2(c), the remedies described in Section 6.2 and this Section 10.2 will be Client's sole remedy in contract, tort, negligence, equity or otherwise, for Deficient Product.

The remedy under this Section 10.2, if applicable (including in the case of Recall), will apply only to the extent that the affected Deficient Product is unsold and returned, destroyed or otherwise disposed of by Client in accordance with this Agreement, or if sold, is demonstrated by reasonable means to be Deficient Product.

(b) API. Except as expressly set out in Appendix 3, under no circumstances whatsoever will Patheon be liable to Client in contract, tort, negligence, indemnity, breach of statutory duty, or otherwise for any loss or damage to the API. Patheon's maximum aggregate liability for loss of or damage to the API will not exceed [***].

(c) Maximum Liability. In any Year, in addition to the specific remedies under Section 10.2(a) for Deficient Product (which are not limited by this subsection (c)), Patheon's maximum aggregate liability to Client under or in connection with this Agreement or any Product Agreement (however arising, including contract, tort, negligence, indemnity, breach of statutory duty, losses of API, or otherwise) will not exceed on a per Product basis [***] of revenues (being payments of the Price) received by Patheon for that Product under the applicable Product Agreement during the previous Year (or, in the case of the first Year, the expected revenue for that Product if the agreed Yearly Forecast Volumes were ordered).

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

10.3 Patheon Indemnity.

(a) Patheon agrees to defend and indemnify Client and its Affiliates, and their respective officers, agents and employees (the "Client Indemnitees"), against all losses, damages, costs, judgments and liability ("Losses") suffered by a Client Indemnitee resulting from any claims, demands, subpoenas, and legal actions ("Claims") by a Third Party against any Client Indemnitee for personal injury or property damage to the extent that the injury or damage is the result of (i) a failure by Patheon (or its Affiliate or contractor) to perform the Manufacturing Services in accordance with the Processing Instructions, cGMPs, and/or Applicable Laws, or other fault of Patheon (or its Affiliate) that causes Product to breach the Product Warranty at delivery; or (ii) a breach by Patheon (or its Affiliate or contractor) of this Agreement or the applicable Product Agreement (including breach of the Product Warranty; and except to the extent that the Losses and/or Claims are due to the negligence or wrongful act(s) of Client, its officers, employees, or Affiliates.

(b) If a Third Party Claim against a Client Indemnitee occurs for which Client intends to seek indemnity under the above subsection (a), Client will: (i) promptly notify Patheon of the Claim; (ii) use commercially reasonable efforts to mitigate the effects of the Claim; (iii) reasonably cooperate with Patheon in the defense of the Claim; and (iv) permit, at Patheon's option, Patheon to control the defense and settlement of the Claim, all at Patheon's cost and expense, provided that if Patheon does not defend such Claim using reasonable efforts and on a timely basis, Client may defend the Claim, at Patheon's expense.

10.4 Client Indemnity.

(a) Client agrees to defend and indemnify Patheon and its Affiliates, and their respective officers, agents and employees (the "Patheon Indemnitees") against all Losses of a Patheon Indemnity resulting from any Claim by a Third Party against a Patheon Indemnity to the extent that such Claim or Loss is the result of: (i) any claim of infringement of any Third Party Rights by (1) the Products or (2) the manufacture of the Product by a proprietary process disclosed by Client or by Patheon's use of Client's Intellectual Property to perform the Manufacturing Services, or any portion of them, or (ii) any claim of personal injury or property damage caused by sale or use of Product, *excluding* any Loss or Claim to the extent that the injury or damage or Claim or Losses arises from Deficient Product; and except to the extent that the Losses and/or Claims are due to the breach of this Agreement or a Product Agreement by, or negligence or wrongful act(s) of, Patheon, its officers, employees, contractors, or Affiliates.

(b) If a Third Party Claim against a Patheon Indemnitee occurs for which Patheon intends to seem indemnity under the above subsection (a), Patheon will: (i) promptly notify Client of the claim; (ii) use commercially reasonable efforts to mitigate the effects of the Claim; (iii) reasonably cooperate with Client in the defense of the Claim; and (iv) permit, at Client's option, Client to control the defense and settlement of the Claim, all at Client's cost and expense, provided that if Client does not defend such Claim using reasonable efforts and on a timely basis, Patheon may defend the Claim, at Patheon's expense.

10.5 Reasonable Allocation of Risk.

This Agreement (including, without limitation, this Section 10) is reasonable and creates a reasonable allocation of risk for the relative profits the Parties each expect to derive from its activities on 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 will hold the marketing approval for the Products, Client requires Patheon to manufacture and label the Products strictly in accordance with the Processing Instructions, and Client, not Patheon, is best positioned to inform and advise potential users about the circumstances and manner of use of the Products. Thus, Patheon shall bear risks based solely on its manufacturing obligations (and breaches thereof or negligence with respect thereto), subject to the liability limitations and exclusions set out in this Agreement.

10.6 Validation Batches.

Where Products are manufactured by Patheon (or any of its Affiliates) under a separate pharmaceutical development or technology transfer agreement (the "**Development Agreement**") and then released by Patheon for commercial sale or distribution by Client, the performance of the applicable pharmaceutical development or technology transfer services including the manufacture of the Product will be governed by the terms of the Development Agreement and will not be subject to the terms and conditions of this Agreement. The terms of this Agreement and the applicable Product Agreement will apply to any Product after quality release by Patheon.

11. Confidentiality

11.1 Confidential Information.

"**Confidential Information**" means, with respect to a particular Party (the "Disclosing Party", as to such information), any information disclosed by the Disclosing Party to the Recipient (whether disclosed in oral, written, electronic or visual form) that is non-public, confidential or proprietary, which may include information relating to the Disclosing Party's patent and trademark applications, process designs, process models, products, manufacturing methods, drawings, plans, designs, data, databases and extracts therefrom, formulae, methods, know-how and other Intellectual Property, its clients and its clients' 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 Recipient's Representatives containing Confidential Information of the Disclosing Party will be considered Confidential Information of the Disclosing Party, and all Client Intellectual Property will be considered the Confidential Information of Client. All Patheon Intellectual Property will be considered the Confidential Information of Patheon. Samples or materials provided under this Agreement as well as any and all information derived from the approved analysis of the samples or materials will also constitute Confidential Information. A Party's rights and obligations under this Section 11 will apply to any Confidential Information that is disclosed by or received by that Party's Representatives. For the purposes of this Section 11, a Party receiving Confidential Information of the other Party under this Agreement (including through its Representatives) is

a “**Recipient**” as to such information, and a Party disclosing Confidential Information under this Agreement (including through its Representatives) is the “**Disclosing Party**” as to such information. The existence, parties to, and terms of this Agreement or of any Product Agreement will be considered Confidential Information of each Party.

11.2 Use of Confidential Information.

The Recipient will use the Confidential Information of the Disclosing Party solely for the purpose of exercising its rights and meeting its obligations under this Agreement, and will not use such Confidential Information for any other purpose. The Recipient will keep the Confidential Information of the Disclosing Party strictly confidential and will not disclose such Confidential Information in any manner whatsoever, in whole or in part, other than as otherwise permitted in this Agreement, or 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 by using all reasonable precautions to prevent the unauthorized disclosure, dissemination or use of the Confidential Information, which precautions will not be less than those exercised by Recipient for its own confidential or proprietary Confidential Information of a similar nature.

11.3 Exclusions.

A Recipient’s obligations of confidentiality, non-disclosure and non-use in this Section 11 will not apply to particular Confidential Information of the other Party to the extent that such Confidential 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, if 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 for 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 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 are covered by exceptions in this Section 11.3, unless the combination itself is covered by any of those exceptions.

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.

11.5 Permitted Disclosure.

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* the Recipient will advise the Disclosing Party reasonably in advance of the disclosure and limit the required disclosure to the extent practicable and permissible by the order, law, regulation or stock exchange rule and any other applicable law, will reasonably cooperate with the Disclosing Party, if required, in seeking an appropriate protective order or other remedy, and will otherwise continue to perform its obligations of confidentiality set out in this Agreement. If any public disclosure is required by law, the Parties will consult concerning the form of announcement prior to the public disclosure being made.

11.6 Marking.

The Disclosing Party will use reasonable efforts to summarize in writing the content of any oral disclosure or other non-tangible disclosure of Confidential Information within [***] 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, summaries, compilations, analyses or other notes derived from the Confidential Information except for one copy which may be maintained by the Recipient in its archival records solely for use in complying with the terms of this Article 11. The retained copy will remain subject to all confidentiality provisions contained in this Agreement. Client will not unreasonably require the return of Confidential Information that is necessary or useful to perform the Manufacturing Services.

11.8 Remedies.

Each of the Parties acknowledges that monetary damages may not be sufficient to remedy a breach by a Party of this Section 11 and agrees that the non-breaching Party will be entitled to seek specific performance, injunctive and/or other equitable relief to prevent breaches of this Section 11 and to specifically enforce Section 11 in addition to any other remedies available at law or in equity. These remedies will not be the exclusive remedies for breach of this Section 11 but will be in addition to any and all other remedies available at law or in equity.

12. Intellectual Property

12.1 Inventions.

(a) For the term of this Agreement, Client grants to Patheon a non-exclusive, paid-up, royalty-free, non-transferable license under applicable Client's Intellectual Property that Patheon must use in order to perform the Manufacturing Services, solely to perform the Manufacturing Services for Client under Product Agreements, and for no other purpose.

(b) All Client Intellectual Property will be the exclusive property of Client. Patheon shall disclose to Client and hereby assigns to Client the entire rights, title and interest in and to all Client Intellectual Property created, made, discovered or obtained by Patheon or its Affiliate under this Agreement or a Product Agreement.

(c) All Patheon Intellectual Property will be the exclusive property of Patheon. Unless Patheon identifies in advance any specific Patheon Intellectual Property that will be subject to a separate licensing agreement between the Parties, Patheon grants to Client a non-exclusive, perpetual, paid-up, royalty-free, transferable license of the Patheon Intellectual Property used by Patheon in the manufacture of the Product for use in relation to manufacturing that Product only.

(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) Either Party will give the other party written notice, as promptly as practicable, of all Inventions which can reasonably be considered to be improvements or other modifications of the Products, processes or technology owned or otherwise controlled by the party.

12.2 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. Miscellaneous

13.1 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 three years after that. This insurance will have policy limits of not less than: (i) EURO 5,000,000/USD 5,000,000 for each occurrence for personal injury or property damage liability; and (ii) EURO 5,000,000/USD 5,000,000 in the aggregate per annum for product and completed operations liability. If reasonably 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. The insurance certificate will further provide for a minimum of [***] written notice to the insured of a cancellation of, or material change in, the insurance. If a party is unable to maintain the insurance policies required under this Agreement through no fault of its own, then the party will without delay 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.

13.2 Independent Contractors.

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

13.3 No Waiver.

Neither party's failure to require the other party to comply with any provision of this Agreement or any Product Agreement will be considered a waiver of the provision or any other provision of this Agreement or any Product Agreement, with the exception of Sections 6.1 and 8.2 of this Agreement.

13.4 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, this consent not to be unreasonably withheld.

(b) Client may assign this Agreement or any Product Agreement or any of its associated rights or obligations without approval from Patheon, provided that this assignment right shall not disable in any way Patheon's rights under Section 8.2(e). Client will give Patheon prior written notice of any assignment, and any such assignee will covenant in writing with Patheon to be bound by the applicable assigned terms of this Agreement or the Product Agreement in the stead of Client. Prior to any such assignment, Client may inquire of Patheon whether Patheon believes that the proposed assignee is a Patheon Competitor, or

a party with less than $500 million in market capitalization, (such that Patheon would have termination rights in Section 8.2(e)), and Patheon shall answer such inquiry truthfully (according to its knowledge at the time) and in writing within [***] of such inquiry, and if such inquiry answer is in the negative, such answer shall be binding on Patheon. Where necessary, Client shall assist Patheon by providing reasonable, non-privileged information in its possession regarding the assignee to enable Patheon to form this belief. If Client makes a partial assignment (i.e., assigns only certain of its rights and/or obligations under the Agreement or a Product Agreement), then Patheon may conduct a cost review of the impact of the assignment on the manufacturing costs for the assigned Products, and if Patheon determines that such costs actually will increase based on such assignment, Patheon may terminate this Agreement or any Product Agreement or any assigned part of them, on 12 months' prior written notice to Client and the assignee, if good faith discussions between the Parties do not lead to agreement on amended Manufacturing Service fees to reflect such actual increase in costs, within a reasonable time after such Patheon determination.Client will reimburse Patheon for any costs incurred by Patheon in connection with the partial assignment including any expenses incurred by Patheon for any due diligence audits in connection with the partial assignment.

(c) Despite the preceding provisions of this Section 13.4, 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, but the assignee must provide a written commitment to the non-assigning Party whereby the assignee agrees to be bound by the obligations of this Agreement owed to the non-assigning Party.

13.5 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, cyber-attacks, 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, regulation, or enforcement decision of any government entity (a "**Force Majeure Event**"). A party claiming a right to excused performance under this Section 13.5 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.

13.6 Additional Products and Services.

Additional Products may be added to, or existing Products deleted from, any Product Agreement by amendment to the Product Agreement including its Schedules as applicable. If Client requests services other than those expressly set out in this Agreement or in any Product Agreement (such as

qualification of a new packaging configuration or shipping studies, or validation of alternative batch sizes), or any cost items that are specifically excluded from the Price, Patheon will provide a 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 agreed in writing by the parties.

13.7 Notices.

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

If to Client:

CARA THERAPEUTICS INC.
4 Stamford Plaza, 107 Elm Street, 9th Floor,
Stamford, Connecticut 06902, United States
Attention: Frederique Menzaghi, Senior VP, Research and Development
Email address: [***]
Mandatory copy to: Scott Terrillion, General Counsel, Secretary & Chief Compliance Officer
Email address: [***]

If to Patheon:

Patheon UK Limited
Kingfisher Drive
Covingham
Swindon
SN3 5BZ
United Kingdom
Attention: Legal Director
Email address: [***]

or to any other addresses or email addresses given to the other party in accordance with the terms of this Section 13.7. Notices or written communications made or given by personal delivery, or email will be considered 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 (supported by reasonable written evidence), whichever is sooner.

13.8 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.

13.9 Entire Agreement.

This Agreement, together with its Appendices, the applicable Product Agreement, Capital Equipment Agreement (if any) and the Quality Agreement, constitutes the full, complete, final and integrated agreement between the parties relating to the subject matter of the Agreement and supersedes all previous written or oral negotiations, commitments, representations, agreements, transactions, or understandings concerning the subject matter of this Agreement. The basis of the parties' agreement is set out expressly and they have not been induced by or relied on any statement or representation that is not set out in this Agreement. 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, Product Agreement, and the Quality Agreement (except that the Quality Agreement will prevail in relation to quality matters) as further described in Section 1.2.

13.10 Other Terms.

No terms, provisions or conditions of any purchase order or other business form or written authorization used by the parties 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 a party 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.

13.11 No Third Party Benefit or Right.

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 (except that Patheon Affiliates acting as subcontractors under this Agreement may enforce Sections 10.1 and 10.2). The rights of the parties to terminate, rescind or agree any variation, waiver or settlement under this Agreement are not subject to the consent of any other person.

13.12 Execution in Counterparts.

This Agreement and any Product Agreement may be executed in two or more counterparts, by original or electronic (including "pdf") signature, each of which will be considered an original, but all of which together will constitute one and the same instrument.

13.13 Use of Name.

Neither party may use the other party's name, trademarks or logo or any variations of them, alone or with any other word or words, without the prior written consent of the other party. Despite this, Client agrees that Patheon may include Client's name and logo in customer lists or related marketing and promotional material for the purpose of identifying users of Patheon's Manufacturing Services.

13.14 Taxes.

(a) VAT.

[[Any payment due to Patheon under this Agreement in consideration for the provision of Manufacturing Services to Client by Patheon is exclusive of value added taxes ("**VAT**"), turnover taxes, sales taxes or similar taxes, including any related interest and penalties (together referred to as "**Transaction Tax**"). If any Transaction Tax is payable on a Manufacturing Service supplied by Patheon to Client under this Agreement, this Transaction Tax will be added to the invoice amount and will be for the account of (and reimbursable to Patheon by) Client.

If any Transaction Tax on the supplies by Patheon is payable by Client under a reverse charge or withholding procedure (i.e., shifting of liability, accounting or payment requirement to recipient of supplies), Client will ensure that Patheon will not effectively be held liable for this Transaction Tax by the relevant taxing authorities or other parties.

Where applicable, Patheon will use its reasonable commercial efforts to ensure that its invoices to Client are issued in a way to meet the requirements for deduction of input VAT by Client, if Client is permitted by law to do so.

Each Party will provide the other with reasonable assistance to enable the recovery, as permitted by Applicable Laws, of Transaction Tax resulting from payments made under this Agreement, this recovery to be for the benefit of the Party bearing the Transaction Tax.

If Patheon is acting as Client's buying agent, Patheon will always charge to Client the Transaction Tax in the relevant territory in addition to the amount paid by Patheon to supplier.

For the avoidance of doubt, reference to the Manufacturing Services in this Section also includes any element (or the entirety) of the Manufacturing Services characterized as a supply of goods by Patheon, its subcontractors or any tax authority for Transaction Tax purposes.

(b) Duties. Client will bear the cost of all duties, levies, tariffs and similar charges (and any related interest and penalties) (together "**Duties**") however designated, arising from the performance of the Manufacturing Services by Patheon, including (without limitation) those imposed as a result of the shipping of materials (including drug substance, materials, components and finished Product) to, from or between Patheon site(s). If these Duties are incurred by Patheon, then Patheon will be entitled to invoice Client for these Duties at the time that they are incurred.

(c) Withholding Tax.

Where any sum due to be paid to Patheon hereunder is subject to any withholding or similar tax, Client will pay the withholding or similar tax to the appropriate Government Authority without deduction from or offset of the amount then due to Patheon. The Parties agree to cooperate with one another and use reasonable efforts to reduce or eliminate or enable the recovery of any tax withholding or similar obligations in respect of royalties, milestone payments, and other payments made by Client to Patheon under this Agreement.

Patheon will provide Client any tax forms that may be reasonably necessary in order for Client not to withhold tax or to withhold tax at a reduced rate under an applicable bilateral income tax treaty.

Each Party will provide the other with reasonable assistance to enable the recovery, as permitted by Applicable Laws, of withholding taxes, or similar obligations resulting from payments made under this Agreement, this recovery to be for the benefit of the Party bearing the withholding tax.

(d) No Offset. Any Transaction Tax, Duty, Withholding Tax or other tax that Client pays, or is required to pay, but which Client believes should properly be paid by Patheon under this Agreement may not be offset against sums due by Client to Patheon whether due under this Agreement or otherwise.

13.15 Governing Law and Jurisdiction.

This Agreement and any Product Agreement, and any related contractual or non-contractual causes of action, disputes and claims, will be governed by and construed in accordance with the laws of State of New York, USA, and irrevocably subject to the exclusive jurisdiction of the courts of the State of New York, USA. The UN Convention on Contracts for the International Sale of Goods will not apply to this Agreement.

13.16 Dispute Resolution.

All disputes that arise under or in connection with this Agreement will be resolved in accordance with Appendix 2.

[Signature page to follow]

This Agreement is signed by the authorized representatives of the parties on the dates shown below and will take effect from the Effective Date.

PATHEON UK LIMITED		CARA THERAPEUTICS INC.	
By:	/s/ A. Robinson	By:	/s/ Derek Chalmers
Name:	A. Robinson	Name:	Derek Chalmers
Title:	Director	Title:	CEO
Date:	08 July 2019	Date:	June 27, 2019

APPENDIX 1 – Form of Product Agreement

Product Agreement for [INSERT PRODUCT NAME]

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated [INSERT DATE] between [PATHEON ENTITY] and [CLIENT ENTITY] (the "**Master Agreement**"), and is entered into between [PATHEON ENTITY], a corporation existing under the laws of [England] [or applicable founding jurisdiction for Patheon entity], having a principal place of business at [Kingfisher Drive, Covingham, Swindon, SN3 5BZ, England] ("**Patheon**") and [CLIENT ENTITY] [insert Client name, legal entity, founding jurisdiction and address] ("**Client**"). For the purpose of this Product Agreement, references in the Master Agreement to "Patheon" and "Client" mean the entities defined respectively as Patheon and Client in this Product Agreement.

The terms and conditions of the Master Agreement are incorporated into this Product Agreement except to the extent this Product Agreement expressly modifies specific provisions in the Master 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.

Initial Product Term: will be from the Effective Date until December 31, 20[ ]

Manufacturing Site: The Manufacturing Services will be performed at the following Manufacturing Site(s): [ ]

Notices: (if different to Section 13.7 of the Master Agreement): [insert contact details]

API Name: [insert API name]

API Credit Value: Client's actual cost for API not to exceed [ ] per kilogram. API value to be provided by Client and supported by such reasonable evidence as Patheon requests.

Local Currency: [insert currency]

Billing Currency: [insert currency]

Initial Exchange Rate: [1.00 Local Currency] to [1.00 Billing Currency]

Inflation Index: [if different from the Master Agreement]

Governing Law: [if different from the Master Agreement]]

Modifications to the Master Agreement (if any): [insert here]

Schedule A – Commercial Supply Pricing Proposal: Description of the Manufacturing Services and related terms of this Product Agreement, which may include: Product Features and Assumptions, Key Assumptions to be Finalized, Annual Volume Forecasts, Pricing Tables, Costs Included in Price, Costs Not Included in Price, Equipment Requirements (if applicable), Manufacturing Parameters, Packaging Parameters, Testing Conditions, Supply Chain.

In case of conflict between Schedule A and the other parts of this APPENDIX 1, those other parts will prevail.

This Agreement is signed by the authorized representatives of the parties on the dates shown below and will take effect from the later of those dates (the "**Effective Date**").

[PATHEON ENTITY]		**[CLIENT ENTITY]**	
By:	_____	By:	_____
Name:	_____	Name:	_____
Title:	_____	Title:	_____
Date:	_____	Date:	_____

Schedule A – Commercial Supply Pricing Proposal

[Insert Commercial Supply Pricing Proposal]

[End of Product Agreement]

APPENDIX 2 – Dispute Resolution

Negotiation

If any dispute or issue between the Parties arises under or out of this Agreement or any Product Agreement (a "Dispute"), the Parties will first try to resolve the Dispute amicably by good faith, reasonable discussions. In the case of any Dispute, either Party may send a notice of the Dispute to the other, and each Party will appoint, within [***] from receipt of the notice, an appropriate single representative having full power and authority to discuss and seek to resolve the Dispute. Such representatives will meet promptly and as necessary in order to resolve the Dispute. If the representatives are unable to resolve the Dispute within one month from their appointment (which resolution will be reflected in a written document signed by authorized senior representatives of each Party), or if a Party fails to appoint a representative as required above, then: (a) for Technical Disputes, the expert determination procedure (as set forth below) may be started by either Party; and for all other Disputes, either Party will refer the Dispute immediately to the Chief Operating Officer or equivalent (or another senior manager as he/she may designate) ("**Senior Officers**") who will meet and discuss reasonably and in good Faith as necessary to try to resolve the Dispute amicably.

Mediation

If, as to an unresolved Dispute that has been referred to the Senior Officers as provided in the above paragraph, the Senior Officers do not resolve the Dispute within [***] of that referral, the Parties may (on written agreement of each Party) l attempt in good faith to settle the Dispute promptly by confidential mediation under the then current CPR Mediation Procedure, before resorting to litigation. If the Parties agree, such mediation procedure shall be initiated prior to the expiration of the applicable negotiation periods. The mediator will be chosen with the assistance of CPR (and CPR's choice will be accepted by the parties in the absence of conflict or bias), unless the parties agree a specific mediator in writing within [***] of the referral to mediation. The mediation will take place in New York, New York and the language of the mediation will be English. Unless otherwise agreed, the parties will select a mediator from the CPR Panels of Distinguished Neutrals. If one Party does not agree to participate in such settlement negotiations using such mediation procedure, then either Party may initiate litigation in an applicable court with jurisdiction to resolve the Dispute in accordance with Section 13.15.

Except where proceedings are required for the purpose of an interim injunction or other interim equitable relief or to preserve a parties legal position pending the outcome of negotiation or mediation, neither Party may commence any court proceedings in relation to a Dispute until the required discussions under "Negotiation" paragraph above has concluded without resolving that Dispute or the other Party fails to participate in those discussions. Where a Party decides not to take part in mediation under this Appendix 2, it will send written notice of that decision to the other Party.

Technical Disputes

If a Dispute arises 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, including conformance of Product to applicable specifications (a "**Technical Dispute**"), the Parties will use all reasonable efforts to resolve the Dispute by amicable negotiations as provided in the "Negotiation" paragraph above. If the Parties are unable to resolve a Technical Dispute by such negotiations, by the end of the applicable time periods, then the Technical Dispute will, at the written request of either Party, be referred for determination to a an expert in the following manner:

(a) Appointment of Expert. Within [***] after the written request, the Parties will together agree on and appoint a single expert who (i) has significant experience and expertise in the subject matter of the Technical Dispute and in the operation of manufacturing agreements similar to this Agreement; and (ii) is neutral and has no relations or affiliation with either Party or its Affiliates. As a condition of any expert's appointment, the Parties will ensure that the expert discloses any actual or potential conflicts of interest promptly as they arise. If the parties fail to agree the appointment within that period, then either party may request that a neutral from the International Institute of Conflict Prevention and Resolution appoints a suitable expert (and both parties will accept that appointment in the absence of evident conflict or bias).

(b) Procedure. The expert shall establish a reasonable schedule for briefing on the technical dispute at issue, and shall provide each Party reasonable briefing on such issue(s) and for providing any needed testimony before the expert. The Parties will require the expert to provide an opinion on each referred issue (with reasonably detailed reasoning) within [***] after the conclusion of all such briefing and testimony (or as otherwise agreed by the Parties with the expert). Each party will give to the expert all the evidence and information within their respective possession or control relating to the technical issue as the expert may reasonably request, which they will disclose promptly and in any event within [***] of a written request from the expert to do so. At all times the parties will co-operate in good faith and seek to narrow and limit the issues to be determined.

(c) Final and Binding. The determination of the expert will, except for fraud or manifest error or where an unapproved conflict of interest is discovered, be final and binding upon the parties with respect to the referred Technical Dispute.

(d) Costs. Each party will bear its own costs for any matter referred to an expert under this Appendix 2 and, in the absence of express agreement to the contrary, the costs and expenses of the expert will be shared equally by the parties.

APPENDIX 3 – API Yield Calculation

Actual Annual Yield

Reconciliation: For each Year, Patheon will prepare an annual reconciliation of API including the calculation of the Actual Annual Yield as set forth below.

"**Actual Annual Yield**" means the percentage of the Quantity Dispensed that was converted to Products for the Product at the Manufacturing Site in that Year and is calculated as follows:

$$Actual\ Annual\ Yield\ (\%) = \frac{Quantity\ Converted}{Quantity\ Dispensed} \times 100.$$

"Quantity Dispensed" means the API received and dispensed in commercial manufacturing of Products, calculated as follows:

The total quantity of API that complies with the specifications and is received at the Manufacturing Site during the Year added to the inventory of API that complies with the specifications held at the start of the Year, minus the inventory of API that complies with the specifications held at the end of the Year.

The Quantity Dispensed includes API lost in the warehouse prior to and during dispensing but excludes (i) API retained by Patheon as samples; (ii) API contained in Product retained as samples; (iii) API used in testing (if applicable); (iv) API contained in Product that is rejected for specific market related requirements such as visual inspection of the Product that is not part of normal processing and (v) API received or dispensed in technical transfer activities or development activities, including without limitation, any regulatory, stability, validation or test batches manufactured during the applicable period.

"Quantity Converted" means the total amount of API contained in the Products manufactured with the Quantity Dispensed (including any additional Products supplied as a replacement remedy), released for delivery, and not rejected as Deficient Product in accordance with Section 6.1**.** The quantity of API contained in Deficient Product will be included in the Quantity Dispensed but not in the Quantity Converted.

Target Yield and Credit Calculation

[***]

Shortfall Credit. 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 [***] after the end of each Year.

Surplus Credit. If there is a Surplus for a Product in a Year, then Patheon will be entitled to apply the amount of the Surplus as a credit against any Shortfall for that Product which may occur in the next Year. If there is no Shortfall in the next Year the Surplus credit will expire.

Each credit under this paragraph will be summarized in an annual reconciliation report. Upon expiration or termination of a Product Agreement, any remaining Shortfall credit amount owing under this paragraph will be paid to Client.

Limits on API Liability

A Shortfall caused by rejected Deficient Product (including in the case of Recall) will only result in a Shortfall Credit to the extent the affected Product is unsold and returned, destroyed or otherwise disposed of by Client in accordance with the terms of this Agreement.

Any payable reimbursement (within the maximum liability limits) for lost API will be made at the API Credit Value.

APPENDIX 4 – Price Adjustments

Price Adjustment Calculation Due To Inflation

Refer to Section 4.2(a)

Definitions:

"**Inflation Index**" means the overall harmonised Index of Consumer Prices (HICP) published by the European Central Bank (www.ecb.europa.eu/stats/prices/hicp/html/index.en.html) for Manufacturing Sites in Europe, and the Producer Price Index pcu32541235412 for Pharmaceutical Preparation Manufacturing (PPI) published by the United States Department of Labor, Bureau of Labor Statistics (hyperlink) for Manufacturing Sites in North America.

"**Inflation Percentage**" means the average of the monthly annual percentage changes in the Inflation Index from September of the preceding Year to August of the then current Year. For example, at the end of 2019 the new Inflation Percentage would be calculated as follows (figures are for illustration only):

From: Month - Year	**To: Month - Year**	**Annual Percentage Change**
September - 2017	September - 2018	0.7 %
October - 2017	October - 2018	1.1 %
November - 2017	November - 2018	1.0 %
December - 2017	December - 2018	0.8 %
January - 2018	January - 2019	0.8 %
February - 2018	February - 2019	1.1 %
March - 2018	March - 2019	1.1 %
April - 2018	April - 2019	1.5 %
May - 2018	May - 2019	1.7 %
June - 2018	June - 2019	1.4 %
July - 2018	July - 2019	1.2 %
August - 2018	August - 2019	1.1 %
Inflation Percentage		**1.13%**

Calculation:

$$New\ Price = Current\ Price + (Current\ Price \times Inflation\ Percentage)$$

Price Adjustment Calculation Due To Currency Fluctuation

Refer to Section **Error! Reference source not found.**

Definitions:

"**Billing Currency**" means the currency in which the Manufacturing Services will be invoiced and paid as specified in the Product Agreement.

"**Local Currency**" means the currency that is used in the country where the Manufacturing Site is located as specified in the Product Agreement.

"**Initial Exchange Rate**" means the initial exchange rate set out in the Product Agreement to convert one unit of the Patheon Manufacturing Site Local Currency into the Billing Currency for the first Year of the Product Agreement.

"**Current Year Exchange Rate**" means the exchange rate calculated as of the current Year of the Product Agreement (starting from the second year), and is calculated as the average interbank exchange rate for conversion of one unit of the Patheon Manufacturing Site Local Currency into the Billing Currency during the period (September 1st of the preceding year to August 31th of the current year) as published by OANDA.com under the heading "Average Exchange Rates" at www.oanda.com/currency/average.

"**Preceding Year Exchange Rate**" means the exchange rate calculated in the previous Year to the then current Year of the Product Agreement.

Calculation:

$$New\ Price = \frac{Current\ Price\ (after\ inflation)}{\substack{Preceding\ Year\ Exchange\ Rate \\ or\ Initial\ Exchange\ Rate\ (second\ Year\ only)}} \times Current\ Year\ Exchange\ Rate$$

For example:

Billing Currency	USD
Local Currency	EURO
Current Price (after inflation)	1.50 USD
Preceding Year Exchange Rate	1.2 (1 EURO to 1.2 USD)
Current Year Exchange Rate	1.1 (1 EURO to 1.1 USD)
New Price	$= \frac{1.50\ USD}{1.2} \times 1.1$ $= 1.375\ USD$

Product Agreement for CR 845 Sterile Liquid Vials

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated June 27, 2019 between Patheon UK Limited and Cara Therapeutics Inc (the "**Master Agreement**"), and is entered into on 28 June 2019 (the "**Effective Date**") between Patheon Manufacturing Services LLC, a corporation existing under the laws of Delaware, having a principal place of business at 5900 Martin Luther King Jr. Highway, Greenville, NC 27834, USA ("**Patheon**") and Cara Therapeutics Inc a company existing under the laws of Delaware with its principal place of business at 4 Stamford Plaza, 107 Elm Street, 9th Floor, Stamford, Connecticut 06902, United States ("**Client**"). For the purpose of this Product Agreement, references in the Master Agreement to "Patheon" and "Client" mean the entities defined respectively as Patheon and Client in this Product Agreement.

The terms and conditions of the Master Agreement are incorporated into this Product Agreement except to the extent this Product Agreement expressly modifies specific provisions in the Master 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.

Initial Product Term: will be from the Effective Date until December 31, 2024

Manufacturing Site: The Manufacturing Services will be performed at 5900 Martin Luther King Jr. Highway, Greenville, NC 27834, USA

Notices: (if different to Section 13.7 of the Master Agreement): See Section 13.7 of the Master Agreement

API Name: CR845

API Credit Value: Client's actual cost for API not to exceed [***]. API value to be provided by Client and supported by such reasonable evidence as Patheon requests.

Local Currency: USD

Billing Currency: USD

Initial Exchange Rate: 1.00 Euro to 1.15 USD.

Inflation Index: See Appendix 4 of the Master Agreement

Governing Law: See Section 13.15 of the Master Agreement

Modifications to the Master Agreement (if any): None

Schedule A – Commercial Supply Pricing Proposal: Description of the Manufacturing Services and related terms of this Product Agreement.

In case of conflict between Schedule A and the other parts of this Product Agreement, those other parts will prevail.

This Agreement is signed by the authorized representatives of the parties on the dates shown below and will take effect from the later of those dates (the "**Effective Date**").

PATHEON MANUFACTURING SERVICES LLC		**CARA THERAEPEUTICS INC.**	
By:	/s/ Scott Brown	By:	/s/ Derek Chalmers
Name:	Scott Brown	Name:	Derek Chalmers
Title:	Director, POS	Title:	CEO
Date:	09 Jul 2019	Date:	June 27, 2019

Schedule A – Commercial Supply Pricing Proposal

Revision History

Proposal Number	Date Issued	Key Revisions
C-MNC-62877-R2	March 30, 2018	2018 commercial pricing

Contents

Part A:

Project Overview

1. Executive Summary of the Opportunity

Patheon is providing updated commercial pricing for CR845 Sterile Liquid Vials out of Patheon's Monza and Greenville facilities.

Patheon will be responsible for the following core services:

1.1 Supply of raw materials and packaging components, with the exception of the Active Pharmaceutical Ingredient ("API"), which is to be furnished by Cara Therapeutics.

1.2 Bulk manufacturing, filling, sealing and bulk packaging of CR845 sterile liquid vials.

1.3 API identification test and all QC testing requirements for raw materials, packaging components and finished product.

2. Target Site – Monza Operations

Patheon's Monza Operations, features four separate sterile areas. One sterile area houses a state of the art pre-filled syringe and cartridge filling line capable of filling a range of nested syringes and cartridges from 0.5mL to 20mL in size, and with a fill range of between 0.1mL and 20mL. The remaining three sterile areas house seven lyophilization units ranging in size from 312 ft² (29 m²) to 431 ft² (40 m²) and offering a combined lyophilization production capacity of 2562 ft² (238 m²). These state-of-the-art lyophilization systems are ideal for the commercial manufacture of biopharmaceuticals and small molecules. The facility is also designed for the aseptic filling of small volume parenterals (SVP).

Monza Commercial Operations is a centre of excellence, offering extensive technology transfer and commercial manufacturing experience in sterile liquid products in vials, pre-filled syringes and cartridges and also sterile lyophilized vials. Monza supplies all the major international markets, including US, EU and Japan.The facility also provides high-volume manufacturing capabilities for a range of conventional solid dosage forms such as tablets, capsules, and granules. All manufacturing services are fully supported with comprehensive in-house analytical and bio-analytical capabilities. Monza also offers compliance with controlled drug regulations in Europe and US as well as disposable manufacturing technologies and fully integrated secondary packaging services.

Site Regulatory History

Date of Inspection	Regulatory Authority	Inspection Type
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

3. Target Site – Greenville Operations

Patheon's Greenville Operations, North Carolina USA, supports both commercial manufacturing and pharmaceutical development services (PDS) in both sterile and oral solid dosage forms. The Sterile North facility has 340,519 square feet of floor space and features five separate CTM & Commercial manufacturing suites housing ten lyophilization units ranging in size from 24ft² (2.23m²) to 640ft² (59m²). Additionally, two 8ft² (0.74m²) lyophilization units are utilized for development and lyo cycle optimization activities. These state-of-the-art lyophilization systems are ideal for the large-scale production of biopharmaceuticals and small molecules, and the facility is also designed for the aseptic filling of small volume parenterals (SVP).

Greenville Operations also serves as a Center of Excellence for sterile products, immediate and sustained release solid oral dosage forms, as well as controlled substances (Sterile and OSD). With U.S. DEA manufacturing registrations (Schedule I to V), analytical registrations (Schedule I to V), and distribution registrations (Schedule II to IV), the facility is equipped to fully accommodate controlled drug product requirements.

Site Regulatory History

Date of Inspection	Regulatory Authority	Inspection Type
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

4. Product Features and Assumptions

4.1 API: CR845

- Indication: pruritus
- Patheon's preliminary categorisation: Category 3A

4.2 Key product parameter overview:

Product	Vial Size	Fill Volume	Packaging Configuration
CR845 sterile liquid vials	2R	1.5mL	Bulk unlabeled vials

4.3 Territories –U.S.A.

4.4 Commercial launch date: [***]

Part B: Pricing

1. Annual Volume Forecasts

Cara Therapeutics has provided a (from 2017) projected annual volume forecast as outlined in the table below.

Product	Annual Volume Forecast (Vials)*				
	2020	2021	2022	2023	2024
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]

*Note: Reported for total units for EU-US.

The forecast presented above is a critical driver for important parameters such as batch size, campaign length, equipment train and site selection, as well as influencing the business model outlined within this proposal. Adjustments to the forecast will likely have a material impact on unit pricing and other business considerations described herein, leading to a review by Patheon and revision of the proposal.

2. Pricing Tables

2.1 **Monza** Bulk Vial Prices:

Product	Batch Size (Vials)	Campaign Length (Batches)	Filling Shifts	Price Per Vial (Bulk)		
				Material Price	Conversion Price	Bulk Price
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]	[***]
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]	[***]

*Note: Patheon intends to include both batch sizes for manufacturing flexibility and with 3 Shifts Patheon can increase the batch size up to [***].

2.2 **Greenville** Bulk Vial Prices:

Product	Batch Size (Vials)	Campaign Length (Batches)	Price Per Vial (Bulk)		
			Material Price	Conversion Price	Bulk Price
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]

3. Costs Included in Price

3.1 Product manufactured, tested and packaged according to the approved and registered specifications.

3.2 **Monza Pricing**: Estimated material costs. Material costs included in the proposal are best estimates based on Patheon's current standards and specifications and do not include any extraordinary or custom raw materials. Final material costs will be provided after confirmation of specifications and formal quotations have been received from the suppliers. The cost of materials to Cara Therapeutics will be Patheon's direct costs plus [***] markup as a handling fee.

3.3 **Greenville Pricing**: Estimated material costs (excluding API). Materials to be purchased by Patheon will be supplied by Patheon approved suppliers.

3.4 Procurement, storage, inventory control and Quality Control ("QC") testing of all required raw materials & packaging materials to supply the CR845 sterile liquid vials , including storage of client-supplied components to meet firm order requirements or such time as agreed between the parties to accommodate long lead time items.

3.5 Qualification and auditing of all raw material and component suppliers (with the exception of client-supplied raw material and component suppliers).

3.6 Active Pharmaceutical Ingredients (API) identity test according to Patheon standard incoming process. If Cara Therapeutics stipulates a vendor, Cara Therapeutics will audit and approve the Vendor and ensure cGMP compliance. If Patheon is to release an API or other client stipulated material based on "ID only," Cara Therapeutics will ensure the required verification testing by an independent laboratory has been completed.

3.7 Batch Record copies for validation batches, first ten commercial batches, and one commercial batch per Year thereafter.

3.8 First Product Approval Inspection (“PAI”) and copy of FDA Report. Additional PAI support will be subject to additional fees.

3.9 Continued process verification (CPV) Data Collection, Data Analysis, Reporting (one set of analysis and report per year).

4. Costs Not Included in Price

4.1 API, reference standards, and client-supplied materials to be supplied by Cara Therapeutics at no cost to Patheon.

4.2 API complete QC testing or special API testing requests. NOTE this testing will be mandatory if Cara Therapeutics has not performed the verification testing specified in 3.6.

4.3 Stability testing program − Patheon can store and test in accordance with an agreed protocol and ICH guidelines.

4.4 Any additional data or report requested by Cara Therapeutics beyond the scope of cGMPs and customary FDA or other regulatory agencies requirements will be subject to an additional fee to be agreed upon between Patheon and Cara Therapeutics.

4.5 Regulatory support (such as preparation of Annual Report and Chemistry, Manufacturing, and Controls (“CMC”) files). Regulatory support work is subject to an additional fee and will be charged at a rate of [***].

4.6 Label copy change and batch record changes initiated by Cara Therapeutics.

4.7 Any specific visual inspection of the bulk or of the finished products outside of standard release testing.

4.8 Testing required to support OOS results or stability failures, testing required in support of complaint investigations and testing of products which exceeds routine testing that are not related to Patheon’s performance.

4.9 Copy of the Product Quality Review Report. Pricing of this service will depend on the level of complexity required by Cara Therapeutics.

5. Capital Requirements

Greenville capital requirements have been provided in the CTM/Registration Proposal for Cara Therapeutics, Inc. (P-GRP-92560-R4).

Part C: Key Technical Parameters

The following technical parameters apply to the production of CR845 sterile liquid vials and the materials used therein.

1. Manufacturing Parameters

Manufacturing Parameters		
[***]	[***]	[***]
[***]	[***]	
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	
[***]	[***]	[***]
[***]	[***]	
[***]	[***]	
[***]	[***]	[***]
[***]	[***]	

2. Packaging Parameters

2.1 **Primary packaging components:**

Component	Specification
[***]	[***]
[***]	[***]
[***]	[***]

2.2 **Secondary packaging** – Patheon standard bulk packaging.

2.3 **Tertiary packaging** – According to Patheon's standard shipment preparations.

3. Testing Conditions

3.1 Testing for raw materials, packaging components and finished product are based on information provided by Cara Therapeutics and Patheon's best estimates.

3.2 It is assumed that the API would only require ID testing

3.3 It is assumed that QC test methods are fully validated and robust at the time of commercial manufacture.

Testing Requirements	
In-Process Controls	**Finished Product Testing**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

3.4 Micro testing on the finished product has been included.

3.5 Testing labour may be subject to change after the final agreement on testing specifications and requirements.

4. Supply Chain

4.1 Patheon will procure components and excipients for the manufacture of CR845 sterile liquid vials from Patheon qualified suppliers. Should Cara Therapeutics require Patheon to source any materials from specified suppliers, then these suppliers will remain under the quality audit control of Cara Therapeutics unless an agreement is reached for Patheon to take on this responsibility.

4.2 Components and excipients will be supplied by Patheon in accordance with the specifications agreed. Patheon will issue formal Patheon specifications for each material.

4.3 Each lot of incoming components and excipients will be sampled and tested according to the agreed specifications.

4.4 The API will be provided free issue/released to Patheon by Cara Therapeutics or its qualified supplier.

4.5 **Monza only:** Patheon assumes the API will be delivered from within the EU. Patheon will not act as the importer of record for API imported into the EU.

4.6 The API and all excipients used for the manufacture will be GMP grade and from TSE/BSE certified sources.

4.7 Finished product will be made available at Patheon's proposed manufacturing site (supplied EXW according to Incoterms® 2010).

[End of Product Agreement]

Product Agreement for CR 845 Sterile Liquid Vials

This Product Agreement (this "**Product Agreement**") is issued under the Master Manufacturing Services Agreement dated June 27, 2019 between Patheon UK Limited and Cara Therapeutics Inc (the "**Master Agreement**"), and is entered into on 28 June 2019 (the "**Effective Date**") between Patheon UK Limited, a corporation existing under the laws of England, having a principal place of business at Kingfisher Drive, Covingham, Swindon, SN3 5BZ, England ("**Patheon**") and Cara Therapeutics Inc a company existing under the laws of Delaware with its principal place of business at 4 Stamford Plaza, 107 Elm Street, 9th Floor, Stamford, Connecticut 06902, United States ("**Client**"). For the purpose of this Product Agreement, references in the Master Agreement to "Patheon" and "Client" mean the entities defined respectively as Patheon and Client in this Product Agreement.

The terms and conditions of the Master Agreement are incorporated into this Product Agreement except to the extent this Product Agreement expressly modifies specific provisions in the Master 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.

Initial Product Term: will be from the Effective Date until December 31, 2024

Manufacturing Site: The Manufacturing Services will be performed at Vtiale GB Stucchi,110, I-20052 Monza Italy

Notices: (if different to Section 13.7 of the Master Agreement): See Section 13.7 of the Master Agreement

API Name: CR845

API Credit Value: Client's actual cost for API not to exceed [***]. API value to be provided by Client and supported by such reasonable evidence as Patheon requests.

Local Currency: EURO

Billing Currency: USD

Initial Exchange Rate: 1.00 Euro to 1.15 USD.

Inflation Index: See Appendix 4 of the Master Agreement

Governing Law: See Section 13.15 of the Master Agreement

Modifications to the Master Agreement (if any): None

Schedule A – Commercial Supply Pricing Proposal: Description of the Manufacturing Services and related terms of this Product Agreement.

In case of conflict between Schedule A and the other parts of this Product Agreement, those other parts will prevail.

This Agreement is signed by the authorized representatives of the parties on the dates shown below and will take effect from the later of those dates (the "**Effective Date**").

PATHEON UK LIMITED		**CARA THERAPEUTICS INC.**	
By:	/s/ A. Robinson	By:	/s/ Derek Chalmers
Name:	Andrew Robinson	Name:	Derek Chalmers
Title:	Director	Title:	CEO
Date:	08 July 2019	Date:	June 27, 2019

Schedule A – Commercial Supply Pricing Proposal

Revision History

Proposal Number	Date Issued	Key Revisions
C-MNC-62877-R2	March 30, 2018	2018 commercial pricing

Contents

Part A:

Project Overview

1. Executive Summary of the Opportunity

Patheon is providing updated commercial pricing for CR845 Sterile Liquid Vials out of Patheon's Monza and Greenville facilities.

Patheon will be responsible for the following core services:

1.1 Supply of raw materials and packaging components, with the exception of the Active Pharmaceutical Ingredient ("API"), which is to be furnished by Cara Therapeutics.

1.2 Bulk manufacturing, filling, sealing and bulk packaging of CR845 sterile liquid vials.

1.3 API identification test and all QC testing requirements for raw materials, packaging components and finished product.

2. Target Site – Monza Operations

Patheon's Monza Operations, features four separate sterile areas. One sterile area houses a state of the art pre-filled syringe and cartridge filling line capable of filling a range of nested syringes and cartridges from 0.5mL to 20mL in size, and with a fill range of between 0.1mL and 20mL. The remaining three sterile areas house seven lyophilization units ranging in size from 312 ft² (29 m²) to 431 ft² (40 m²) and offering a combined lyophilization production capacity of 2562 ft² (238 m²). These state-of-the-art lyophilization systems are ideal for the commercial manufacture of biopharmaceuticals and small molecules. The facility is also designed for the aseptic filling of small volume parenterals (SVP).

Monza Commercial Operations is a centre of excellence, offering extensive technology transfer and commercial manufacturing experience in sterile liquid products in vials, pre-filled syringes and cartridges and also sterile lyophilized vials. Monza supplies all the major international markets, including US, EU and Japan. The facility also provides high-volume manufacturing capabilities for a range of conventional solid dosage forms such as tablets, capsules, and granules. All manufacturing services are fully supported with comprehensive in-house analytical and bio-analytical capabilities. Monza also offers compliance with controlled drug regulations in Europe and US as well as disposable manufacturing technologies and fully integrated secondary packaging services.

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[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
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Patheon's Greenville Operations, North Carolina USA, supports both commercial manufacturing and pharmaceutical development services (PDS) in both sterile and oral solid dosage forms. The Sterile North facility has 340,519 square feet of floor space and features five separate CTM & Commercial manufacturing suites housing ten lyophilization units ranging in size from 24ft² (2.23m²) to 640ft² (59m²). Additionally, two 8ft² (0.74m²) lyophilization units are utilized for development and lyo cycle optimization activities. These state-of-the-art lyophilization systems are ideal for the large-scale production of biopharmaceuticals and small molecules, and the facility is also designed for the aseptic filling of small volume parenterals (SVP).

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[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	[***]

4. Product Features and Assumptions

4.1 API: CR845

- Indication: pruritus
- Patheon's preliminary categorisation: Category 3A

4.2 Key product parameter overview:

Product	Vial Size	Fill Volume	Packaging Configuration
CR845 sterile liquid vials	2R	1.5mL	Bulk unlabeled vials

4.3 Territories –U.S.A.

4.4 Commercial launch date: [***]

Part B: Pricing

1. Annual Volume Forecasts

Cara Therapeutics has provided a (from 2017) projected annual volume forecast as outlined in the table below.

Product	Annual Volume Forecast (Vials)*				
	2020	2021	2022	2023	2024
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]

*Note: Reported for total units for EU-US.

The forecast presented above is a critical driver for important parameters such as batch size, campaign length, equipment train and site selection, as well as influencing the business model outlined within this proposal. Adjustments to the forecast will likely have a material impact on unit pricing and other business considerations described herein, leading to a review by Patheon and revision of the proposal.

2. Pricing Tables

2.1 **Monza** Bulk Vial Prices:

Product	Batch Size (Vials)	Campaign Length (Batches)	Filling Shifts	Price Per Vial (Bulk)		
				Material Price	Conversion Price	Bulk Price
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]	[***]
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]	[***]

*Note: Patheon intends to include both batch sizes for manufacturing flexibility and with 3 Shifts Patheon can increase the batch size up to [***].

2.2 **Greenville** Bulk Vial Prices:

Product	Batch Size (Vials)	Campaign Length (Batches)	Price Per Vial (Bulk)		
			Material Price	Conversion Price	Bulk Price
CR845 sterile liquid vials	[***]	[***]	[***]	[***]	[***]

3. Costs Included in Price

3.1 Product manufactured, tested and packaged according to the approved and registered specifications.

3.2 **Monza Pricing**: Estimated material costs. Material costs included in the proposal are best estimates based on Patheon's current standards and specifications and do not include any extraordinary or custom raw materials. Final material costs will be provided after confirmation of specifications and formal quotations have been received from the suppliers. The cost of materials to Cara Therapeutics will be Patheon's direct costs plus [***] markup as a handling fee.

3.3 **Greenville Pricing**: Estimated material costs (excluding API). Materials to be purchased by Patheon will be supplied by Patheon approved suppliers.

3.4 Procurement, storage, inventory control and Quality Control ("QC") testing of all required raw materials & packaging materials to supply the CR845 sterile liquid vials , including storage of client-supplied components to meet firm order requirements or such time as agreed between the parties to accommodate long lead time items.

3.5 Qualification and auditing of all raw material and component suppliers (with the exception of client-supplied raw material and component suppliers).

3.6 Active Pharmaceutical Ingredients (API) identity test according to Patheon standard incoming process. If Cara Therapeutics stipulates a vendor, Cara Therapeutics will audit and approve the Vendor and ensure cGMP compliance. If Patheon is to release an API or other client stipulated material based on "ID only," Cara Therapeutics will ensure the required verification testing by an independent laboratory has been completed.

3.7 Batch Record copies for validation batches, first ten commercial batches, and one commercial batch per Year thereafter.

3.8 First Product Approval Inspection ("PAI") and copy of FDA Report. Additional PAI support will be subject to additional fees.

3.9 Continued process verification (CPV) Data Collection, Data Analysis, Reporting (one set of analysis and report per year).

4. Costs Not Included in Price

4.1 API, reference standards, and client-supplied materials to be supplied by Cara Therapeutics at no cost to Patheon.

4.2 API complete QC testing or special API testing requests. NOTE this testing will be mandatory if Cara Therapeutics has not performed the verification testing specified in 3.6.

4.3 Stability testing program − Patheon can store and test in accordance with an agreed protocol and ICH guidelines.

4.4 Any additional data or report requested by Cara Therapeutics beyond the scope of cGMPs and customary FDA or other regulatory agencies requirements will be subject to an additional fee to be agreed upon between Patheon and Cara Therapeutics.

4.5 Regulatory support (such as preparation of Annual Report and Chemistry, Manufacturing, and Controls ("CMC") files). Regulatory support work is subject to an additional fee and will be charged at a rate of [***].

4.6 Label copy change and batch record changes initiated by Cara Therapeutics.

4.7 Any specific visual inspection of the bulk or of the finished products outside of standard release testing.

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4.9 Copy of the Product Quality Review Report. Pricing of this service will depend on the level of complexity required by Cara Therapeutics.

5. Capital Requirements

Greenville capital requirements have been provided in the CTM/Registration Proposal for Cara Therapeutics, Inc. (P-GRP-92560-R4).

Part C: Key Technical Parameters

The following technical parameters apply to the production of CR845 sterile liquid vials and the materials used therein.

1. Manufacturing Parameters

Manufacturing Parameters		
[***]	[***]	[***]
[***]	[***]	
[***]	[***]	[***]
[***]	[***]	[***]
[***]	[***]	
[***]	[***]	[***]
[***]	[***]	
[***]	[***]	
[***]	[***]	[***]
[***]	[***]	

2. Packaging Parameters

2.1 **Primary packaging components:**

Component	Specification
[***]	[***]
[***]	[***]
[***]	[***]

2.2 **Secondary packaging** – Patheon standard bulk packaging.

2.3 **Tertiary packaging** – According to Patheon's standard shipment preparations.

3. Testing Conditions

3.1 Testing for raw materials, packaging components and finished product are based on information provided by Cara Therapeutics and Patheon's best estimates.

3.2 It is assumed that the API would only require ID testing

3.3 It is assumed that QC test methods are fully validated and robust at the time of commercial manufacture.

Testing Requirements	
In-Process Controls	**Finished Product Testing**
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

3.4 Micro testing on the finished product has been included.

3.5 Testing labour may be subject to change after the final agreement on testing specifications and requirements.

4. Supply Chain

4.1 Patheon will procure components and excipients for the manufacture of CR845 sterile liquid vials from Patheon qualified suppliers. Should Cara Therapeutics require Patheon to source any materials from specified suppliers, then these suppliers will remain under the quality audit control of Cara Therapeutics unless an agreement is reached for Patheon to take on this responsibility.

4.2 Components and excipients will be supplied by Patheon in accordance with the specifications agreed. Patheon will issue formal Patheon specifications for each material.

4.3 Each lot of incoming components and excipients will be sampled and tested according to the agreed specifications.

4.4 The API will be provided free issue/released to Patheon by Cara Therapeutics or its qualified supplier.

4.5 **Monza only:** Patheon assumes the API will be delivered from within the EU. Patheon will not act as the importer of record for API imported into the EU.

4.6 The API and all excipients used for the manufacture will be GMP grade and from TSE/BSE certified sources.

4.7 Finished product will be made available at Patheon's proposed manufacturing site (supplied EXW according to Incoterms® 2010).

[End of Product Agreement]

EXHIBIT 31.1

Certification of Chief Executive Officer Pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Derek Chalmers, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Cara Therapeutics, 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 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 7, 2019

By: /s/ Derek Chalmers
DEREK CHALMERS, Ph.D., D.Sc.
CHIEF EXECUTIVE OFFICER

EXHIBIT 31.2

Certification of Chief Financial Officer Pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Mani Mohindru, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Cara Therapeutics, 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 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 7, 2019

By: /s/ Mani Mohindru
MANI MOHINDRU, Ph.D.
CHIEF FINANCIAL OFFICER

EXHIBIT 32.1

CERTIFICATIONS OF
CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
OF CARA THERAPEUTICS, INC.
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 Cara Therapeutics, Inc. (the "Company") for the quarter ended June 30, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Derek Chalmers, Ph.D., D.Sc., as Chief Executive Officer of the Company, and Mani Mohindru, Ph.D., as Chief Financial Officer of the Company, each 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 or her knowledge, based upon a review of the Report:

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

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

/s/ DEREK CHALMERS
Name: Derek Chalmers, Ph.D., D.Sc.
Title: Chief Executive Officer
Date: August 7, 2019

/s/ MANI MOHINDRU
Name: Mani Mohindru, Ph.D.
Title: Chief Financial Officer
Date: August 7, 2019