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 SEPTEMBER 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 November 1, 2019 was: 46,678,977.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 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)

	September 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 34,705	$ 15,081
Marketable securities	158,384	146,302
Income tax receivable	1,033	664
Other receivables	784	926
Prepaid expenses	8,556	4,805
Restricted cash, current	—	361
Total current assets	203,462	168,139
Operating lease right-of-use asset	3,192	—
Marketable securities, non-current	55,985	21,396
Property and equipment, net	748	880
Restricted cash	408	408
Total assets	$ 263,795	$ 190,823
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 20,581	$ 13,622
Operating lease liability, current	945	—
Current portion of deferred revenue	26,773	26,825
Total current liabilities	48,299	40,447
Operating lease liability, non-current	3,602	—
Deferred revenue, non-current	—	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 September 30, 2019 and December 31, 2018, zero shares issued and outstanding at September 30, 2019 and December 31, 2018	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at September 30, 2019 and December 31, 2018, 46,673,977 shares and 39,547,558 shares issued and outstanding at September 30, 2019 and December 31, 2018, respectively	46	39
Additional paid-in capital	583,811	428,059
Accumulated deficit	(372,116)	(294,354)
Accumulated other comprehensive income (loss)	153	(114)
Total stockholders' equity	211,894	133,630
Total liabilities and stockholders' equity	$ 263,795	$ 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		Nine Months Ended	
	September 30, 2019	September 30, 2018	September 30, 2019	September 30, 2018
Revenue:				
License and milestone fees	$ 5,785	$ 5,029	$ 15,235	$ 7,903
Clinical compound revenue	—	33	140	33
Total revenue	5,785	5,062	15,375	7,936
Operating expenses:				
Research and development	35,992	22,303	83,956	52,732
General and administrative	4,226	3,227	13,128	10,609
Total operating expenses	40,218	25,530	97,084	63,341
Operating loss	(34,433)	(20,468)	(81,709)	(55,405)
Other income	1,261	1,002	3,297	1,780
Loss before benefit from income taxes	(33,172)	(19,466)	(78,412)	(53,625)
Benefit from income taxes	330	66	650	264
Net loss	$ (32,842)	$ (19,400)	$ (77,762)	$ (53,361)
Net loss per share:				
Basic and Diluted	$ (0.74)	$ (0.51)	$ (1.88)	$ (1.54)
Weighted average shares:				
Basic and Diluted	44,517,134	38,034,216	41,314,044	34,696,835
Other comprehensive income, net of tax of $0:				
Change in unrealized gains (losses) on available-for-sale marketable securities	(12)	70	267	83
Total comprehensive loss	$ (32,854)	$ (19,330)	$ (77,495)	$ (53,278)

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 Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Accumulated 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
Sale of common stock in a follow-on public offering ($19.00 per share), net of underwriting discounts and commissions and offering expenses of $6,248	5,175,000	5	92,072	—	—	92,077
Stock-based compensation expense	—	—	1,819	—	—	1,819
Shares issued upon exercise of stock options	155,301	—	1,888	—	—	1,888
Net loss	—	—	—	(19,400)	—	(19,400)
Other comprehensive income	—	—	—	—	70	70
Balance at September 30, 2018	39,389,515	$ 39	$ 423,180	$ (273,702)	$ 13	$ 149,530

	Common Stock		Additional Paid-In		Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Accumulated 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
Sale of common stock in a follow-on public offering ($23.00 per share), net of underwriting discounts and commissions and offering expenses of $8,950	6,325,000	6	136,519	—	—	136,525
Issuance of common stock upon entry into License Agreement with Enteris Biopharma, Inc. ($23.42 per share)	170,793	—	4,000	—	—	4,000
Stock-based compensation expense	—	—	2,835	—	—	2,835
Shares issued upon exercise of stock options	150,268	—	1,843	—	—	1,843
Net loss	—	—	—	(32,842)	—	(32,842)
Other comprehensive loss	—	—	—	—	(12)	(12)
Balance at September 30, 2019	46,673,977	$ 46	$ 583,811	$ (372,116)	$ 153	$ 211,894

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Nine Months Ended	
	September 30, 2019	September 30, 2018
Operating activities		
Net loss	$ (77,762)	$ (53,361)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Stock-based compensation expense	9,182	5,759
Depreciation and amortization	150	318
Amortization expense component of lease expense	445	—
Noncash expense related to oral formulation license agreement	4,000	—
Accretion of available-for-sale marketable securities	(1,168)	(1,177)
Realized loss on sale of available-for-sale marketable securities	—	32
Deferred rent costs	—	(89)
Deferred revenue	(15,235)	47,542
Changes in operating assets and liabilities:		
Income tax receivable	(369)	192
Other receivables	142	(70)
Prepaid expenses	(3,751)	(2,583)
Accounts payable and accrued expenses	6,958	5,497
Operating lease liability	(651)	—
Net cash (used in) provided by operating activities	(78,059)	2,060
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	195,839	85,500
Proceeds from sale of available-for-sale marketable securities	—	28,250
Purchases of available-for-sale marketable securities	(241,075)	(138,689)
Purchases of property and equipment	(18)	(49)
Net cash used in investing activities	(45,254)	(24,988)
Financing activities		
Proceeds from the sale of common stock in a follow-on public offering, net of issuance costs	136,525	92,077
Proceeds from the sale of common stock under license agreement	—	14,556
Proceeds from the exercise of stock options	6,051	3,636
Net cash provided by financing activities	142,576	110,269
Net increase in cash, cash equivalents and restricted cash	19,263	87,341
Cash, cash equivalents and restricted cash at beginning of period	15,850	10,157
Cash, cash equivalents and restricted cash at end of period	$ 35,113	$ 97,498
Noncash investing and financing activities		
Shares of common stock issued in connection with oral formulation license agreement	$ 4,000	$ —
Shares of common stock issued in exchange for consulting services	197	—

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
(unaudited)

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 September 30, 2019, the Company had raised aggregate net proceeds of approximately $519,700 from several rounds of equity financing, including its initial public offering, or IPO, which closed in February 2014 and four follow-on public offerings of common stock, which closed in July 2019, 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 September 30, 2019, the Company had unrestricted cash and cash equivalents and marketable securities of $249,074 and an accumulated deficit of $372,116. 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 $32,842 and $19,400 for the three months ended September 30, 2019 and 2018, respectively, and $77,762 and $53,361 for the nine months ended September 30, 2019 and 2018, respectively, and had net cash (used in) provided by operating activities of $(78,059) and $2,060 for the nine months ended September 30, 2019 and 2018, respectively.

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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
(unaudited)

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

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
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(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 will adopt ASU 2018-18 on January 1, 2020, and 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 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. The Company will adopt ASU 2016-13 on January 1, 2020 and believes ASU 2016-13 will primarily impact the Company's assessment of any potential impairment of its investments in debt securities, specifically its assessment of whether any portion of an unrealized loss in a given period relates to a credit loss.

3. Available-for-Sale Marketable Securities

As of September 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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
(unaudited)

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

As of September 30, 2019

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 12,842	$ 27	$ (9)	$ 12,860
U.S. government agency obligations	22,426	12	(11)	22,427
Corporate bonds	108,108	145	(27)	108,226
Commercial paper	65,340	19	(3)	65,356
Municipal bonds	5,500	—	—	5,500
Total available-for-sale marketable securities	$ 214,216	$ 203	$ (50)	$ 214,369

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

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 September 30, 2019, the Company's marketable debt securities mature at various dates through September 2021. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows.

Contractual maturity	As of September 30, 2019 Amortized Cost	As of September 30, 2019 Fair Value	As of December 31, 2018 Amortized Cost	As of December 31, 2018 Fair Value
Less than one year	$ 158,274	$ 158,384	$ 146,363	146,302
One year to two years	55,942	55,985	21,449	21,396
Total	$ 214,216	$ 214,369	$ 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.

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NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
(unaudited)

As of September 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
U.S. Treasury securities	$ 3,177	$ (9)	$ —	$ —	$ 3,177	$ (9)
U.S. government agency obligations	5,487	(11)	—	—	5,487	(11)
Corporate bonds	27,689	(27)	—	—	27,689	(27)
Commercial paper	11,906	(3)	—	—	11,906	(3)
Total	$ 48,259	$ (50)	$ —	$ —	$ 48,259	$ (50)

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 September 30, 2019 and December 31, 2018, the Company held a total of 23 out of 84 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 September 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.

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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 nine months ended September 30, 2019 and September 30, 2018.

	Total Accumulated Other Comprehensive Income (Loss)
Balance, December 31, 2018	$ (114)
Other comprehensive income before reclassifications	267
Amount reclassified from accumulated other comprehensive income	—
Net current period other comprehensive income	267
Balance, September 30, 2019	$ 153
Balance, December 31, 2017	$ (70)
Other comprehensive income before reclassifications	51
Amount reclassified from accumulated other comprehensive loss	32
Net current period other comprehensive income	83
Balance, September 30, 2018	$ 13

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

Component of AOCI	Three Months Ended September 30, 2019	Three Months Ended September 30, 2018	Nine Months Ended September 30, 2019	Nine Months Ended September 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	$ —	$ (17)	$ —	$ (32)	Other income
	—	—	—	—	Benefit from income taxes
	$ —	$ (17)	$ —	$ (32)	

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

5. Fair Value Measurements

As of September 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.

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 September 30, 2019 or December 31, 2018.

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

Fair value measurement as of September 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	$ 34,705	$ 34,705	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	12,860	—	12,860	—
U.S. government agency obligations	22,427	—	22,427	—
Corporate bonds	108,226	—	108,226	—
Commercial paper	65,356	—	65,356	—
Municipal bonds	5,500	—	5,500	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 249,482	$ 35,113	$ 214,369	$ —

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 nine months ended September 30, 2019. There were no transfers of financial assets between Levels 1, 2, or 3 classifications during the nine months ended September 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

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balance to serve as collateral for the letter of credit issued to the landlord by the bank. As of September 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 thereafter, upon request from the Company, was eligible to 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. In July 2019, the Company was granted the reduction in the balance of the letter of credit. As of September 30, 2019, the Company had $408 of restricted cash related to the Stamford Lease in long-term assets. As of 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.

	September 30, 2019	December 31, 2018
Cash and cash equivalents	$ 34,705	$ 15,081
Restricted cash, current assets	—	361
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 35,113	$ 15,850

7. Prepaid expenses

As of September 30, 2019, prepaid expenses were $8,556, consisting of $7,751 of prepaid R&D clinical costs, $481 of prepaid insurance and $324 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:

	September 30, 2019	December 31, 2018
Accounts payable	$ 9,536	$ 4,371
Accrued research projects	7,748	6,079
Accrued professional fees	566	802
Accrued compensation and benefits	2,731	2,370
Total	$ 20,581	$ 13,622

9. Stockholders' Equity

On August 20, 2019, the Company entered into a Non-Exclusive License Agreement, or the License Agreement, with Enteris Biopharma, Inc., or Enteris (see Note 15, *Commitments and Contingencies* for additional information regarding the License Agreement). As consideration for the licensed rights under the License Agreement, the Company paid an upfront fee equal to $8,000, consisting of $4,000 in cash and $4,000 in shares of the Company's common stock. In connection with the License Agreement, on August 20, 2019, the Company entered into a Common Stock Purchase Agreement, or the Purchase Agreement, with Enteris and its affiliate, EBP Holdco LLC, collectively referred to as

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Purchaser, pursuant to which the Company issued and sold to Purchaser 170,793 shares of its common stock in a private placement in satisfaction of the $4,000 portion of the upfront fee payable in shares of the Company's common stock pursuant to the License Agreement, and for no additional consideration, based on a purchase price of $23.42 per share, which was equal to the 30-day volume weighted average price of the Company's common stock on August 20, 2019. In addition, if the Company exercises its right, but not obligation, to terminate its obligation to pay any royalties under the License Agreement in exchange for a lump sum payment in cash, it may elect to make 50% of the payment in stock by issuing additional shares of the Company's common stock valued at the 30-day volume weighted average price of the Company's common stock as of such exercise. Pursuant to its obligations under the Purchase Agreement, the Company effected the registration and sale of the shares issued and sold to Purchaser thereunder in accordance with the applicable requirements of the Securities Act of 1933, as amended, or the Securities Act, through the filing of an automatic shelf registration statement on Form S-3ASR (File No. 333-233666) with the SEC on September 9, 2019. In addition, the Purchase Agreement includes customary representations, warranties and covenants by the Company (see Note 15, *Commitments and Contingencies*).

On July 24, 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 included 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. The Company closed this offering on July 29, 2019, including the full exercise of the underwriters' option to purchase 825,000 additional shares of common stock. The Company received net proceeds of approximately $136,525, after deducting $8,950 of underwriting discounts and commissions and estimated offering expenses payable by the Company.

This offering was made pursuant to the Company's Shelf 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 $300,000 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 provided 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 per share. The services provided by the consultant were performed during the six-month period following the Effective Date. During the three and nine months ended September 30, 2019, stock-based compensation expense of $98 and $197, respectively, 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

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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

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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 nine months ended September 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 this period. There were no sales of clinical compound to Maruishi during the three months ended September 30, 2019. During each of the three and nine months ended September 30, 2018, the Company recognized clinical compound revenue of $33 from the sale of clinical compound to Maruishi and as a result, the Company incurred R&D expense of $30 during those periods.

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 September 30, 2019, the Company had deferred revenue, current of $26,773 related to the performance obligations from the VFMCRP Agreement and had no balances of receivables, other assets or deferred revenue, non-current 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 September 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.

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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 nine months ended September 30, 2019, $5,785 and $15,235, 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 September 30, 2019, $28,671 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 September 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.

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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 $26,773 at September 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 three and nine months ended September 30, 2019 and 2018, no milestone events were probable of occurrence or achieved.

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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.

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 nine months ended September 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 September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Basic:				
Weighted average common shares outstanding	44,517,134	38,034,216	41,314,044	34,696,835
Diluted:				
Weighted average common shares outstanding - Basic	44,517,134	38,034,216	41,314,044	34,696,835
Common stock options*	—	—	—	—
Denominator for diluted net loss per share	44,517,134	38,034,216	41,314,044	34,696,835

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

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Net loss	$ (32,842)	$ (19,400)	$ (77,762)	$ (53,361)
Weighted-average common shares outstanding:				
Basic and Diluted	44,517,134	38,034,216	41,314,044	34,696,835
Net loss per share, Basic and Diluted	$ (0.74)	$ (0.51)	$ (1.88)	$ (1.54)

As of September 30, 2019 and 2018, 4,575,454 and 3,780,390 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 September 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 nine months ended September 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*).

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.

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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 nine months ended September 30, 2019, $123 and $164, respectively, 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 September 30, 2019.

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 nine months ended September 30, 2019, consisting of $590 relating to G&A expense and $604 relating to R&D expense. Since there was no additional vesting of these executive restricted stock units during the three months ended September 30, 2019, no additional stock-based compensation expense was recognized in the respective period.

Stock Options

Under the 2014 Plan, the Company granted 20,000 and 165,000 stock options during the three months ended September 30, 2019 and 2018, respectively, and 1,218,000 and 897,500 stock options during the nine months ended September 30, 2019 and 2018, respectively. The fair values of stock options granted during the three and nine months ended September 30, 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 September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Risk-free interest rate	1.62%	2.73% - 2.99%	1.62% - 2.62%	2.51% - 2.99%
Expected volatility	71.8%	82.6% - 87.6%	71.8% - 75.2%	82.6% - 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)	—	—	—	—

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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 September 30, 2019 and 2018 was $15.29 and $14.51, respectively, and during the nine months ended September 30, 2019 and 2018 was $11.35 and $11.25, 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 September 30, 2018 are as follows:

	January 1, 2019	September 30, 2018
Risk-free interest rate	2.59% - 2.62%	2.06% - 3.02%
Expected volatility	58.9% - 84.6%	77.4% - 80.9%
Expected dividend yield	0%	0%
Expected life of non-employee options (in years)	0.81 - 8.19	0.26 - 8.44

During the three and nine months ended September 30, 2019 and 2018, the Company recognized compensation expense relating to stock options as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Research and development	$ 1,391	$ 901	$ 3,799	2,401
General and administrative	1,322	918	3,829	3,358
Total stock option expense	$ 2,713	$ 1,819	$ 7,628	$ 5,759

The following were excluded from the table above as they are not related to stock options: compensation expense for i) the issuance of common stock relating to the consulting agreement for $98 and $197, respectively, in G&A expense for the three and nine months ended September 30, 2019; ii) the vesting of executives' restricted stock units for $604 in R&D expense and $590 in G&A expense for the nine months ended September 30, 2019; and iii) compensation expense relating to the Board of Directors' restricted stock units for $123 and $164, respectively, in G&A expense for the three and nine months ended September 30, 2019.

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 nine months ended September 30, 2019 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2018	4,004,422	$ 13.34
Granted	1,218,000	16.88
Exercised	(546,265)	11.08
Forfeited	(100,703)	16.22
Outstanding, September 30, 2019	4,575,454	$ 14.50
Options exercisable, September 30, 2019	2,126,935	

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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 nine months ended September 30, 2019 and 2018.

14. Income Taxes

For the three months ended September 30, 2019 and 2018, pre-tax losses were $33,172 and $19,466, respectively, and for the nine months ended September 30, 2019 and 2018, pre-tax losses were $78,412 and $53,625, respectively. The Company recognized a full tax valuation allowance against its deferred tax assets as of September 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 $330 and $66 for the three months ended September 30, 2019 and 2018, respectively, and $650 and $264 for the nine months ended September 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 September 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

License Agreement

On August 20, 2019, the Company entered into the License Agreement with Enteris, pursuant to which Enteris granted to the Company a non-exclusive, royalty-bearing license, including the right to grant sublicenses, under certain proprietary technology and patent rights related to or covering formulations for oral delivery of peptide active pharmaceutical ingredients with functional excipients to enhance permeability and/or solubility, known as Enteris’s Peptelligence® technology, to develop, manufacture and commercialize products using such technology worldwide, excluding Japan and South Korea.

As consideration for the licensed rights under the License Agreement, the Company paid an upfront fee equal to $8,000, consisting of $4,000 in cash and $4,000 in shares of the Company’s common stock pursuant to the Purchase Agreement (see Note 9, *Stockholders’ Equity*). As a result, the Company recognized R&D expense of $8,000 related to the License Agreement during the three and nine months ended September 30, 2019.

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The Company is also obligated, pursuant to the License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. Until the second anniversary of the entry into the License Agreement, the Company has the right, but not the obligation, to terminate its obligation to pay any royalties under the License Agreement in exchange for a lump sum payment in cash, or the Royalty Buyout. Subject to certain conditions, the Company may elect to pay 50% of the lump sum due under the Royalty Buyout in shares of the Company's common stock pursuant to the Purchase Agreement. During each of the three and nine months ended September 30, 2019, no milestone payments or royalties were paid to Enteris by the Company.

The License Agreement will expire on a country-by-country, licensed product-by-licensed product basis upon the later of (1) the expiration (or invalidation) of all valid claims in licensed patent rights that cover such product in such country, (2) the end of the calendar quarter in which generic competition (as defined in the License Agreement) occurs for such product in such country and (3) ten years from the first commercial sale of such product.

Either party may terminate the License Agreement upon written notice if the other party has failed to remedy a material breach within 60 days (or 30 days in the case of a material breach of a payment obligation). Enteris may terminate the License Agreement upon 30 days' written notice to the Company if the Company or any of its affiliates formally challenge the validity of any licensed patent rights or assists a third party in doing so. The Company may terminate the License Agreement for any reason or no reason (a) prior to receipt of first regulatory approval for a licensed product in the United States for any indication upon 30 days' prior written notice to Enteris or (b) on or after receipt of first regulatory approval for a licensed product in the United States for any indication upon 60 days' prior written notice to Enteris.

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.

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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.

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 $737 for the three and nine months ended September 30, 2018, respectively.

In connection with the signing of the Stamford Lease, the Company entered into a standby letter of credit agreement 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

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(unaudited)

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 September 30, 2019, consisting of $164 relating to R&D lease expense and $70 relating to G&A lease expense. For the nine months ended September 30, 2019, $702 of operating lease cost was recognized, consisting of $492 relating to R&D lease expense and $210 relating to G&A lease expense.

Other information related to the Stamford Lease was as follows:

	Three Months Ended September 30, 2019	Nine Months Ended September 30, 2019
Cash paid for amounts included in the measurement of lease liability:		
Operating cash outflows relating to operating lease	$ (306)	$ (909)
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ 3,636
Remaining lease term-operating lease (years)	4.2	4.2
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 September 30, 2019, were as follows:

Year Ending December 31,	
2019 (Excluding the nine months ended September 30)	$ 306
2020	1,239
2021	1,264
2022	1,288
2023	1,164
Total future minimum lease payments, undiscounted	5,261
Less imputed interest	(714)
Total	$ 4,547
Operating lease liability reported as of September 30, 2019:	
Operating lease liability - current	$ 945
Operating lease liability - non-current	3,602
Total	$ 4,547

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 anticipated use of Enteris' Peptelligence® technology to develop, manufacture and commercialize Oral KORSUVA (CR845/difelikefalin);

- 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

License Agreement

On August 20, 2019, we entered into a Non-Exclusive License Agreement, or the License Agreement, with Enteris Biopharma, Inc., or Enteris. Pursuant to the License Agreement, Enteris granted to us a non-exclusive, royalty-bearing license, including the right to grant sublicenses, under certain proprietary technology and patent rights related to or covering formulations for oral delivery of peptide active pharmaceutical ingredients with functional excipients to enhance permeability and/or solubility, known as Enteris's Peptelligence® technology, to develop, manufacture and commercialize products using such technology worldwide, excluding Japan and South Korea.

As consideration for the licensed rights under the License Agreement, we paid an upfront fee equal to $8.0 million, consisting of $4.0 million in cash and $4.0 million in shares of our common stock pursuant to the Purchase Agreement (as defined below). As a result, the Company recognized $8.0 million of research and development, or R&D, expense related to the License Agreement during the three and nine months ended September 30, 2019.

We are also obligated, pursuant to the License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. Until the second anniversary of the entry into the License Agreement, we have the right, but not the obligation, to terminate our obligation to pay any royalties under the License Agreement in exchange for a lump sum payment in cash, or the Royalty Buyout. Subject to certain conditions, we may elect to pay 50% of the lump sum due under the Royalty Buyout in shares of our common stock pursuant to the Purchase Agreement.

The License Agreement will expire on a country-by-country, licensed product-by-licensed product basis upon the later of (1) the expiration (or invalidation) of all valid claims in licensed patent rights that cover such product in such country, (2) the end of the calendar quarter in which generic competition (as defined in the License Agreement) occurs for such product in such country and (3) ten years from the first commercial sale of such product.

Either party may terminate the License Agreement upon written notice if the other party has failed to remedy a material breach within 60 days (or 30 days in the case of a material breach of a payment obligation). Enteris may terminate the License Agreement upon 30 days' written notice to us if we or any of our affiliates formally challenge the validity of any licensed patent rights or assists a third party in doing so. We may terminate the License Agreement for any reason or no reason (a) prior to receipt of first regulatory approval for a licensed product in the United States for any indication upon 30 days' prior written notice to Enteris or (b) on or after receipt of first regulatory approval for a licensed product in the United States for any indication upon 60 days' prior written notice to Enteris.

Stock Purchase Agreement

In connection with the License Agreement, on August 20, 2019, we entered into a Stock Purchase Agreement, or the Purchase Agreement, with Enteris and its affiliate, EBP Holdco LLC, collectively referred to as Purchaser, pursuant to which we issued and sold to Purchaser 170,793 shares of our common stock in a private placement, or the Private Placement. Such shares were issued in satisfaction of the $4.0 million portion of the upfront fee payable in shares of our common stock pursuant to the License Agreement and for no additional consideration, based on a purchase price of $23.42 per share, which was equal to the 30-day volume weighted average price of our common stock on August 20, 2019. In addition, if we exercise our Royalty Buyout option, we may elect to make 50% of the payment in stock by issuing additional shares of our common stock valued at the 30-day volume weighted average price of our common stock as of such exercise. Pursuant to the Purchase Agreement, we used commercially reasonable efforts to effect the registration and sale of the shares issued and sold to Purchaser thereunder in accordance with the applicable requirements of the Securities Act of 1933, as amended, or the Securities Act, which included the filing of registration statement with the SEC on September 9, 2019. In addition, the Purchase Agreement includes customary representations, warranties and covenants by us.

Follow-on Public Offering

On July 24, 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 included 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. We closed this offering on July 29, 2019, including the full exercise of the underwriters' option to purchase 825,000 additional shares of common stock. We received net proceeds of approximately $136.5 million, after deducting approximately $9.0 million of underwriting discounts and commissions and estimated offering expenses payable by us.

This offering was pursuant to our Shelf 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.

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; interim assessment complete – target enrollment increased to 430 patients • 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™-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 the 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 October 2019, we completed an interim statistical assessment of KALM-2 and based on the recommendation of the Independent Data Monitoring Committee, or IDMC, the size of the trial has been increased from the original enrollment target of 350 patients to a new target of 430 patients. 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. Based on the current status of our completed and ongoing efficacy and safety trials, we expect to file the NDA for KORSUVA (CR845/difelikefalin) injection in the second half of 2020.

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 allows 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. In October 2019, we completed an interim statistical assessment of KALM-2 and based on the recommendation of the IDMC, the target size of the trial has been increased to 430 patients versus the original enrollment target of 350 patients. The IDMC's recommendation was based on the results of a prespecified interim conditional power assessment that was conducted after approximately 50 percent of the originally

targeted patients completed the designated 12-week treatment period. Based on current projections, we expect to complete enrollment of 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 was 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. The study is now fully enrolled at 288 patients. Currently, approximately 185 patients have completed at least six months of treatment and over 100 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 250 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. We continue to screen patients in the ongoing Phase 2 trial of Oral KORSUVA and aim to have top-line data from this trial in 2020.

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. We expect to report the top-line results from this trial in 2020.

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 Nine Months Ended September 30, 2019 and 2018

Revenue

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
License and milestone fees revenue	$ 5,785	$ 5,029	15%	$ 15,235	$ 7,903	93%
Clinical compound revenue	—	33	-100%	140	33	324%
Total revenue	$ 5,785	$ 5,062	14%	$ 15,375	$ 7,936	94%

License and milestone fees revenue

License and milestone fees revenue for the three and nine months ended September 30, 2019 was $5.8 million and $15.2 million, respectively. License and milestone fees revenue for the three and nine months ended September 30, 2018 was $5.0 million and $7.9 million, respectively. License and milestone fees revenue for the three and nine months ended September 30, 2019 and September 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 nine months ended September 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 September 30, 2019. Clinical compound revenue for the three and nine months ended September 30, 2018 was $33 thousand which was related to the sale of clinical compound to Maruishi.

Research and Development Expense

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 21,884	$ 17,955	22%	$ 57,168	$ 40,041	43%
Consultant services in support of clinical trials	1,014	792	28%	3,394	2,248	51%
Stock-based compensation	1,391	901	54%	4,402	2,401	83%
Depreciation and amortization	28	58	-52%	83	258	-68%
Other R&D operating expenses	11,675	2,597	350%	18,909	7,784	143%
Total R&D expense	$ 35,992	$ 22,303	61%	$ 83,956	$ 52,732	59%

For the three months ended September 30, 2019 compared to the three months ended September 30, 2018, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $7.3 million, mainly from activities related to the Phase 3 efficacy trial and up to 12 week Phase 3 safety trial 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 the Phase 2 efficacy trial for CLD-aP. There was also an increase of $1.3 million in drug manufacturing costs. Those costs were partially offset by a decrease of $4.4 million, mainly from the Phase 3 efficacy study in hemodialysis patients with CKD-aP, the Phase 2/3 I.V. CR845/difelikefalin adaptive clinical trial in post-operative pain and costs associated with certain Phase 1 studies. The increase in stock-based compensation expense was primarily the result of additional stock option grants to R&D

employees. The increase in other R&D operating expenses primarily resulted from the upfront payment of $8.0 million upon entering into the License Agreement with Enteris and an increase in payroll and related costs associated with R&D personnel.

For the nine months ended September 30, 2019 compared to the nine months ended September 30, 2018, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $27.1 million, mainly from activities related to the two Phase 3 efficacy trials and up to 12 week Phase 3 safety trial 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 $8.4 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. 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 during the nine months ended September 30, 2019. The increase in other R&D operating expenses primarily resulted from the upfront payment of $8.0 million upon entering into the License Agreement with Enteris and 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 nine months ended September 30, 2019 and 2018:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
I.V. CR845 - Pruritus	$ 15,847	$ 11,187	42%	$ 43,035	$ 23,045	87%
I.V. CR845 - Pain	(1)	2,018	-100%	358	5,986	-94%
Oral CR845 - Pruritus	7,044	5,510	28%	17,138	11,073	55%
Oral CR845 - Pain	8	32	-76%	30	2,185	-99%
Internal research and development expenses	13,094	3,556	268%	23,395	10,443	124%
Total research and development expenses	$ 35,992	$ 22,303	61%	$ 83,956	$ 52,732	59%

General and Administrative Expenses

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 1,074	$ 702	53%	$ 2,906	$ 2,184	33%
Stock-based compensation	1,543	918	68%	4,781	3,358	42%
Depreciation and amortization	22	21	6%	67	60	11%
Other G&A operating expenses	1,587	1,586	0%	5,374	5,007	7%
Total G&A expense	$ 4,226	$ 3,227	31%	$ 13,128	$ 10,609	24%

For the three months ended September 30, 2019 compared to the three months ended September 30, 2018, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs and accounting fees. The increase in stock-based compensation expense was primarily the result of additional stock option grants to G&A employees, additional stock-based compensation expense relating to restricted stock units granted to the members of our Board of Directors in June 2019, and stock-based compensation expense resulting from issuing shares of our common stock for consulting services performed during the three months ended September 30, 2019. Other G&A operating expenses remained consistent between the respective periods.

For the nine months ended September 30, 2019 compared to the nine months ended September 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, additional stock-based compensation expense relating to the vesting of restricted stock units granted to G&A executive officers, additional stock-based compensation expense relating to restricted stock units granted to the members of our Board of Directors in June 2019, and stock-based compensation expense resulting from issuing shares of our common stock for consulting services performed during the nine months ended September 30, 2019. 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 September 30,			Nine Months Ended September 30,		
	2019	2018	% change	2019	2018	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other Income	$ 1,261	$ 1,002	26%	$ 3,297	$ 1,780	85%

During the three months ended September 30, 2019 compared to the three months ended September 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 nine months ended September 30, 2019 compared to the nine months ended September 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 September 30, 2019 and 2018, pre-tax losses were $33.2 million and $19.5 million, respectively, and we recognized a benefit from income taxes of $330 thousand and $66 thousand, respectively. For the nine months ended September 30, 2019 and 2018, pre-tax losses were $78.4 million and $53.6 million, respectively, and we recognized a benefit from income taxes of $650 thousand and $264 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 September 30, 2019 and December 31, 2018.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception and through September 30, 2019, we have raised an aggregate of approximately $623.2 million to fund our operations, including (1) net proceeds of $446.4 million from the sale of shares of our common stock in five 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 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 $136.5 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 September 30, 2019, we had $249.1 million in unrestricted cash and cash equivalents and available-for-sale marketable securities. 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 September 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 September 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 September 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 $32.8 million and $19.4 million for the three months ended September 30, 2019 and 2018, respectively, and $77.8 million and $53.4 million for the nine months ended September 30, 2019 and 2018, respectively. As of September 30, 2019, we had an accumulated deficit of $372.1 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 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 September 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 nine months ended September 30, 2019 and 2018:

	Nine Months Ended September 30,	
	2019	2018
	Dollar amounts in thousands	
Net cash (used in) provided by operating activities	$ (78,059)	$ 2,060
Net cash used in investing activities	(45,254)	(24,988)
Net cash provided by financing activities	142,576	110,269
Net increase in cash, cash equivalents and restricted cash	$ 19,263	$ 87,341

Net cash (used in) provided by operating activities

Net cash used in operating activities for the nine months ended September 30, 2019 consisted primarily of a net loss of $77.8 million and a $2.6 million cash outflow from net non-cash charges, partially offset by a $2.3 million cash inflow from net changes in operating assets and liabilities. Net non-cash charges primarily consisted of a decrease of $15.2 million in deferred revenue associated with our VFMCRP Agreement and $1.2 million related to accretion of

available-for-sale securities, partially offset by stock-based compensation expense of $9.2 million and a noncash expense of $4.0 million related to the License Agreement with Enteris. The change in operating assets and liabilities primarily consisted of a cash inflow of $7.0 million from an increase in accounts payable and accrued expenses, partially offset by a cash outflow of $3.8 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs and a cash outflow of $0.7 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 cash provided by operating activities for the nine months ended September 30, 2018 consisted primarily of a $52.4 million cash inflow from net non-cash charges and a $3.0 million inflow from net changes in operating assets and liabilities, partially offset by a net loss of $53.4 million. Net non-cash charges primarily consisted of an increase in deferred revenue of $47.5 million related to the VFMCRP Agreement and stock-based compensation expense of $5.8 million, partially offset by $1.2 million related to amortization/accretion of available-for-sale securities. The net change in operating assets and liabilities primarily consisted of a cash inflow of $5.5 million from an increase in accounts payable and accrued expenses, partially offset by a cash outflow of $2.6 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs.

Net cash used in investing activities

Net cash used in investing activities was $45.3 million for the nine months ended September 30, 2019, which primarily included cash outflows of $241.1 million for the purchases of available-for-sale marketable securities, partially offset by $195.8 million from maturities of available-for-sale marketable securities.

Net cash used in investing activities was $25.0 million for the nine months ended September 30, 2018, which primarily included cash outflows of $138.7 million for the purchase of available-for-sale marketable securities, partially offset by cash inflows of $85.5 million from maturities of available-for-sale marketable securities and $28.3 million from the sale of available-for-sale marketable securities.

Net cash provided by financing activities

Net cash provided by financing activities for the nine months ended September 30, 2019 consisted of $136.5 million of net proceeds from the issuance and sale of our common stock in July 2019 and proceeds of $6.1 million received from the exercise of stock options.

Net cash provided by financing activities for the nine months ended September 30, 2018 consisted of $92.1 million of net proceeds from the issuance and sale of our common stock in July 2018, proceeds of $14.6 million from the sale of our common stock relating to the VFMCRP Agreement and $3.6 million received from the exercise of stock options.

Significant Contractual Obligations and Commitments

Contractual obligations and commitments as of September 30, 2019 consisted of the License Agreement we entered into in August 2019, the MSA we entered into in July 2019 and 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*, 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 nine months ended September 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 September 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 September 30, 2019, we had invested $214.4 million of our cash reserves in such marketable securities. Those marketable securities include $214.4 million of investment grade debt instruments with a yield of approximately 2.23% and maturities through September 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 September 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 September 30, 2019. Based on such evaluation, our Chief Executive Officer

and Chief Financial Officer have concluded that, as of September 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 nine months ended September 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 September 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 nine months ended September 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 †#	Non-Exclusive License Agreement, dated August 20, 2019, between the Registrant and Enteris Biopharma, Inc.
10.2 #	Common Stock Purchase Agreement, dated August 20, 2019, by and among the Registrant and Enteris Biopharma, Inc. and EBP Holdco LLC (3)
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.

(3) Filed as exhibit 4.3 to the Registrant's automatic shelf registration statement on Form S-3/ASR filed with the Securities and Exchange Commission on September 9, 2019 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, and certain exhibits and schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The Registrant hereby undertakes to furnish supplementally a copy of any omitted exhibit or schedule upon request by the Securities and Exchange Commission.

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: November 5, 2019

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

Date: November 5, 2019

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

Exhibit 10.1

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.

Execution Version

Non-Exclusive License Agreement

between

ENTERIS BIOPHARMA, INC.

and

CARA THERAPEUTICS, INC.

Dated as of August 20, 2019

Table of Contents

Exhibits and Schedules

Exhibit A	Wire Instructions
Exhibit B	Form Stock Purchase Agreement
Exhibit C	Project Plan

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NON-EXCLUSIVE LICENSE AGREEMENT

This NON-EXCLUSIVE LICENSE AGREEMENT ("**Agreement**") is made August 20, 2019 (the "**Effective Date**") by and between CARA THERAPEUTICS, INC., incorporated and registered in the State of Delaware and having offices at 4 Stamford Plaza, 107 Elm Street, 9th Floor, Stamford, CT 06902, USA (hereinafter referred to as "**Cara**"), and ENTERIS BIOPHARMA, INC., incorporated and registered in the State of Delaware and having offices at 83 Fulton St., Boonton, NJ 07005, USA (hereinafter referred to as "**Enteris**"). Each of Enteris and Cara is sometimes referred to individually herein as a "**Party**" and collectively as the "**Parties**."

RECITALS

A. Enteris owns or otherwise controls certain proprietary technology and patent rights (defined below as Licensed Technology) claiming or covering formulations for oral delivery of peptide active pharmaceutical ingredients with functional excipients to enhance permeability and/or solubility, including in any oral solid dosage forms, and the development and manufacture of drug products using such formulations;

B. Cara wishes to obtain a non-exclusive license under the Licensed Technology on the terms and conditions of this Agreement; and

C. Enteris is willing to grant to Cara the requested license rights and Cara is willing to accept such rights pursuant to the terms and conditions of this Agreement.

NOW THEREFORE, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, it is hereby agreed by and between the Parties as follows:

ARTICLE 1
DEFINITIONS

In this Agreement the following words and phrases shall have the following meanings unless the context requires otherwise:

"**AAA**" shall have the meaning set forth in Article 11.

"**Affiliate**" means, with respect to a particular Party, any person, company, partnership or other entity, whether or not incorporated or in existence at the Effective Date, that directly or indirectly controls, is controlled by or is under common control with such Party to this Agreement. The term "**control**" for the purposes of this definition (with correlative meanings for the terms "controlled by" and "under common control with") means that the applicable person, company, partnership, or other entity owns fifty percent (50%) or more (including ownership by trusts with substantially the same beneficial interests) of the voting and equity rights of the applicable Party, or otherwise has the legal power to direct or cause the direction of the general management and policies of such Party.

"**Agreement**" shall have the meaning set forth in the Recitals.

"**Applicable Laws**" means any national, international, federal, state or local laws, treaties, statutes, ordinances, rules and regulations, including any rules, regulations, guidance, guidelines or requirements of any national, international, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, national securities exchanges or securities listing organizations, that are in effect from time to time during the Term and apply to a particular activity or obligation hereunder.

"**Assist**" means knowingly providing, directly or indirectly, a Third Party with (a) any analysis of the Licensed Patent Rights or any portion thereof; (b) prior art or analysis of any prior art to any of the Licensed Patent Rights; (c) any documents in a Party's possession, custody, or control relating to the Licensed Patent Rights, in whole or in part, or to any prior art to any of the Licensed Patent Rights; or (d) financial or technical support, in each case in connection with a Challenge by such Third Party of the Licensed Patent Rights or any portion thereof.

"**Bankruptcy Code**" means, as applicable, the U.S. Bankruptcy Code, as amended from time to time, and the rules and regulations and guidelines promulgated thereunder, or the bankruptcy laws of any other Governmental Authority, as amended from time to time, and the rules and regulations and guidelines promulgated thereunder, or any applicable bankruptcy laws of any other country or competent Governmental Authority, as amended from time to time, and the rules and regulations and guidelines promulgated thereunder.

"**Business Day**" means any day, other than a Saturday or Sunday, on which banking institutions in New York, New York are open for business.

"**Calendar Quarter**" means the period beginning on the Effective Date and ending on the last day of the calendar quarter in which the Effective Date falls, and thereafter each successive period of three (3) consecutive calendar months beginning on January 1, April 1, July 1, or October 1 and ending, respectively on March 31, June 30, September 30 and December 31; provided, that, the final Calendar Quarter shall end on the last day of the Term.

"**Calendar Year**" means the period beginning on the Effective Date and ending on December 31 of the calendar year in which the Effective Date falls, and thereafter each successive period of twelve (12) months commencing on January 1 and ending on December 31; provided, that, the final Calendar Year shall end on the last day of the Term.

"**Cara Indemnitees**" shall have the meaning set forth in Section 7.5(b).

"**Cara Indemnity Claims**" shall have the meaning set forth in Section 7.5(b).

"**Challenge**" means to contest, or knowingly to Assist a Third Party in its contest, of the validity or enforceability of the Licensed Patent Rights, in whole or in part, in any court, arbitration proceeding or other legal, judicial, or administrative tribunal, including the United States Patent and Trademark Office and the United States International Trade Commission. For the avoidance of doubt, for the purposes of this definition, the term "**contest**" means: (a) filing an action under 28 U.S.C. §§ 2201-2202 seeking a declaration of invalidity or unenforceability of any Licensed Patent Rights; (b) citation to the United States Patent and Trademark Office pursuant to 35 U.S.C.

§ 301 of prior art patents or printed publications or statements of the patent owner concerning the scope of any of the Licensed Patent Rights; (c) filing a request under 35 U.S.C. § 302 for re-examination of any of the Licensed Patent Rights; (d) filing, or joining in, a petition under 35 U.S.C. § 311 to institute inter partes review of any Licensed Patent Rights or any portion thereof; (e) filing, or joining in, a petition under 35 U.S.C. § 321 to institute post-grant review of the Licensed Patent Rights or any portion thereof; (f) provoking or becoming a party to an interference with an application for any of the Licensed Patent Rights pursuant to 35 U.S.C. § 135; or (g) filing or commencing any re-examination, opposition, cancellation, nullity or similar proceedings against any of the Licensed Patent Rights in any country.

"**Change of Scope**" shall have the meaning set forth in Section 3.2(c).

"**CMO**" means the third party manufacturer that Cara selects for commercial Manufacturing.

"**Commercialization**" or "**Commercialize**" means any and all activities directed to the offering for sale and sale of a Product, from the initial launch, including (a) activities directed to marketing, promoting, detailing, distributing, Manufacturing, importing, selling and offering to sell that Product in the Territory (including pre-approval marketing activities); (b) conducting Phase IV clinical trials with respect to that Product; (c) interacting with Regulatory Authorities regarding any of the foregoing; and (d) seeking pricing approvals and reimbursement approvals (as applicable) for that Product in the Territory. When used as a verb, "to Commercialize" and "Commercializing" means to engage in Commercialization and "Commercialized" has a corresponding meaning.

"**Commercially Reasonable Efforts**" means, with respect to the applicable task or activity under this Agreement, the application of efforts and resources that are generally consistent with those that a comparable company in the pharmaceutical industry generally would devote to accomplish such task or activity relating to products that are at a similar stage of development and have similar commercial potential as Product, taking into account all applicable competition, market, scientific, technical, intellectual property, regulatory, and commercial factors (including potential and actual economic return for the product), all based on then-prevailing conditions.

"**Completion of Analytical Procedures Transfer"** means the date of the full and complete transfer of the analytical procedures by Enteris to the CMO designated by Cara as specified in and in accordance with Section 3.2(a), as summarized in Section I (Transfer of Analytical Procedures) of the Project Plan.

"**Completion of Manufacturing Process Transfer**" means the date of the full and complete transfer of the Manufacturing process by Enteris to the CMO designated by Cara as specified in and in accordance with Section 3.2(a), as summarized in Section II (Transfer of Manufacturing Process) of the Project Plan.

"**Confidential Information**" means, for a particular Party, any and all confidential and proprietary information, including any Know-how, disclosed by such Party to the other in writing, orally or in any other form in connection with this Agreement, which may include samples,

documents, drawings, specifications data, graphics, technical know-how, letters, electronically transmitted documents, e-mails, etc. Confidential Information of a Party includes the Proprietary Materials of such Party. In the case of Enteris, Confidential Information includes Licensed Know-how and Improvements. In the case of Cara, Confidential Information includes any information disclosed by Cara relating to any Drug and Product(s) produced with the support of the Licensed Technology. With respect to each Party, Confidential Information includes this Agreement and the terms of this Agreement.

"**Control**" or "**Controlled**" means, with respect to Know-how or Patent Rights, that the applicable Party, either directly or through any of its Affiliates, owns or has a license (or sublicense) to or under, and has the right to grant to the other Party access to and a license or sublicense under, such Know-how or Patent Rights as provided herein without the payment of additional consideration to, or violating the terms of any agreement or arrangement with any Third Party, and without violating any Applicable Laws. For clarity, no Party (or Affiliate of a Party, as applicable) shall be deemed to Control any Know-how or Patent Rights by virtue of the license grants to that Party from or by the other Party as set forth in this Agreement.

"**Debarred Entity**" shall have the meaning set forth in Section 7.1(e).

"**Development**" or "**Develop**" means, with respect to a Product, all non clinical and clinical drug development activities that are undertaken after the Effective Date, including (a) the preparation and filing of Regulatory Filings and all regulatory affairs related to the foregoing, (b) obtaining, maintaining or expanding Regulatory Approvals of a Product, or (c) developing the ability to manufacture clinical and commercial quantities of a Product. This includes: (i) preclinical testing, toxicology, and clinical trials; (ii) preparation, submission, review, and development of data or information for the purpose of submission to a Regulatory Authority to obtain, maintain or expand Regulatory Approvals of a Product; and (iii) Manufacturing Process Development associated with the supply of a Product for preclinical testing and clinical trials, and related quality assurance and technical support activities. When used as a verb, "Developing" means to engage in Development and "Developed" has a corresponding meaning. For clarity, "Development" shall not include any Commercialization activities.

"**Dispute**" shall have the meaning set forth in Section 11.1.

"**Drug**" means CR845 (difelikefalin), and any salt forms, esters, prodrugs, biologically active metabolites or biologically active structural analogs, solvates, hydrates and crystalline forms thereof.

"**Effective Date**" shall have the meaning set forth in the Recitals.

"**EMA**" means the European Medicines Agency or any successor agency or authority thereto.

"**End of Phase 2 Meeting**" means the end of Phase 2 meeting with the FDA, as described in 21 C.F.R. § 312.47(b), intended to determine the safety of proceeding to Phase 3, to evaluate

the Phase 3 plan and protocols, and to identify any additional information necessary to support a marketing application for the uses under investigation.

"**Enteris DMF**" means that certain [***] and the information contained therein.

"**Enteris Indemnitees**" shall have the meaning set forth in Section 7.5(a).

"**Enteris Indemnity Claims**" shall have the meaning set forth in Section 7.5(a).

"**FDA**" means the United States Food and Drug Administration, or any successor entity thereto having substantially the same functions.

"**FDCA**" means the United States Federal Food, Drug, and Cosmetic Act, enacted in 1938 as Public Law 75-717, as such may have been amended, and which is contained in Title 21 of the U.S. Code, Section 301 et seq., as amended, and the regulations promulgated thereunder from time to time.

"**Field**" means all fields and uses, including all prophylactic, therapeutic and diagnostic uses for all human diseases, conditions and indications.

"**Force Majeure**" means any occurrence beyond the reasonable control of a Party that (a) prevents or substantially interferes with the performance by such Party of any of its obligations hereunder and (b) occurs by reason of any act of God, flood, fire, explosion, earthquake, casualty or accident, or war, revolution, civil commotion, act of terrorism, blockage or embargo, or any injunction, law, order, proclamation, regulation, ordinance, demand or requirement of any government or of any subdivision, authority or representative of any such government.

"**Generic Competition**" means and shall be deemed to exist in a particular country in the Territory with respect to a particular Product in a given Calendar Quarter if in such country during such Calendar Quarter one or more Generic Products (other than a Generic Product sold by Cara or its Affiliates or by a Sub-licensee under a license granted by Cara or its Affiliates) in the aggregate account (on a units sold basis) for more than [***] of the sum of (a) the aggregate unit sales of such Product sold by Cara or its Affiliates or Sub-licensees in such country, and (b) the aggregate unit sales of such Generic Products in such country, each in such Calendar Quarter, based on data provided by IQVIA (formerly, Quintiles IMS Holding, Inc.), or if such data is not available, such other reliable data source as reasonably agreed upon by Cara and Enteris. If no data is commercially available, then the Parties shall reasonably agree upon a commercially reasonable methodology for estimating the percentage unit-based market share of Generic Products in such country during the applicable time period.

"**Generic Product**" means, with respect to a particular Product and a particular country, any pharmaceutical product (other than the Product) that contains the same active ingredient(s) in the same or substantially the same formulation and in a comparable quality and quantity as such Product, and is approved under an Abbreviated New Drug Application (ANDA) or any foreign equivalent thereof.

"**Governmental Authority**" means any multi-national, national, federal, state, local, municipal, provincial or other governmental, regulatory, administrative, judicial, public or statutory instrumentality, court or governmental tribunal, agency, commission, authority, body or entity, or any political subdivision thereof, having legal jurisdiction over the matter or party in question.

"**Improvement**" means any Invention that constitutes a specific enhancement or improvement to or modification of the proprietary Licensed Technology (including Peptelligence® Formulation Technology), whether or not patentable.

"**IND**" means (a) an Investigational New Drug Application as defined in the FDCA or any successor application or procedure required to initiate clinical testing of the Product in humans in the United States; (b) a counterpart of an Investigational New Drug Application that is required in any other country or region in the Territory before beginning clinical testing of the Product in humans in such country or region; and (c) all supplements and amendments to any of the foregoing.

"**Indemnified Party**" shall have the meaning set forth in Section 7.5(c).

"**Indemnifying Party**" shall have the meaning set forth in Section 7.5(c).

"**Infringement**" shall have the meaning set forth in Section 5.4(a)

"**Infringement Notice**" shall have the meaning set forth in Section 5.4(a).

"**Invention**" means any new or useful process, machine, method of manufacture, or composition of matter, whether or not patentable, or any idea, invention, discovery, improvement, enhancement, modification or derivative work, whether or not patentable or copyrightable, including in respect of, relating to or comprising a Product, that is conceived and/or first reduced to practice (actually or constructively), whether or not patentable, by or on behalf of Cara (including by an Affiliate, Sub-licensee or other Third Party) in connection with the Development, Manufacture and/or Commercialization of Products.

"**Know-how**" means any and all proprietary technical and other information, whether or not patentable, including ideas, concepts, know-how, inventions, discoveries, data, formulae, processes, trade secrets, specifications, procedures for experiments and tests and other protocols, results of experimentation and testing, manufacturing and purification techniques and protocols.

"**Licensed Know-how**" means any and all Know-how comprising, relating to or using the Peptelligence® Formulation Technology (including any formulations developed by Enteris using the Peptelligence® Formulation Technology, and any manufacturing processes of Enteris of drugs using such formulations), that is Controlled by Enteris, prior to or during the Term, including any Improvements, that is necessary or useful for the Development, Manufacture, use or sale of the Product. To the extent that Cara exercises its right to a Royalty Buyout, "Licensed Know-how" shall exclude Improvements to such Know-how that are made by Enteris after the date on which Enteris receives a payment from Cara in connection with such Royalty Buyout.

"**Licensed Patent Rights**" means any and all Patent Rights that claim or cover any Licensed Know-how, including the Peptelligence® Formulation Technology (including any formulations developed by Enteris using the Peptelligence® Formulation Technology, and any manufacturing processes of Enteris for drugs using such formulations), that are Controlled by Enteris prior to or during the Term, and including any Improvements, that is necessary or useful for the Development, Manufacture, use or sale of the Product; provided, however, to the extent that Cara exercises its right to a Royalty Buyout, "Licensed Patent Rights" shall exclude Improvements claimed or covered in any such Patent Rights that are made by Enteris after the date on which Enteris receives a payment from Cara in connection with such Royalty Buyout.

"**Licensed Technology**" means the Licensed Know-how and the Licensed Patent Rights.

"**Losses**" shall have the meaning set forth in Section 7.5(a).

"**MAA**" means any application for Regulatory Approval submitted to the EMA pursuant to the centralized approval procedure to obtain European Commission approval for the marketing of the Product in the European Union, or any successor application or procedure required to sell the Product in the European Union.

"**Manufacture**" means, with respect to the Product, any activities related to the formulation, production, manufacture, processing, filling, finishing, packaging, labeling, release, shipping, holding, conduct of Manufacturing Process Development, stability testing, quality assurance, release testing and quality control of such Product or any intermediate thereof for Development or Commercialization, and regulatory activities related to any of the foregoing. When used as a verb, "Manufacturing" means to engage in Manufacture.

"**Manufacturing Process Development**" means the development, qualification, validation and scale-up of the process used to manufacture the Product and analytic development and product characterization with respect thereto.

"**Manufacturing Services Agreement**" means that certain Phase 2 Clinical Manufacturing Services Agreement dated July 1, 2015, by and between Enteris BioPharma, Inc., and Cara Therapeutics, Inc., as amended from time to time.

"**NDA**" means a New Drug Application, as defined in the FDCA and regulations promulgated thereunder, or any successor application or procedure required to sell the Product in the United States.

"**Net Sales**" means the gross amount billed or invoiced by Cara or any of its Affiliates or Sub-licensees (each, a "**Seller**") to Third Parties (excluding sales of Products among Cara, its Affiliates and Sub-licensees for resale to Third Parties), throughout the Territory for sales or other dispositions or transfers for value of Products, less [***]. In addition, Net Sales are subject to the following:

[***]

In the case of pharmacy incentive programs, hospital performance incentive program chargebacks, disease management programs, similar programs or discounts on products, all discounts shall be allocated among products on the basis on which such discounts were actually granted or, if such basis cannot be determined, in proportion to the respective list prices of such products.

For purposes of this Agreement, "sale" shall mean any commercial transfer or other commercial distribution or disposition, but shall not include transfers or other distributions or dispositions of Products at no charge (or at cost) for academic research, preclinical, clinical, or regulatory purposes (including the use of Products in clinical trials) or in connection with patient assistance programs or other charitable purposes or to physicians or hospitals for promotional purposes (including free samples to a level and in an amount which is customary in the industry and/or which is reasonably proportional to the market for such Product).

Net Sales (including the deductions) shall be determined from the books and records of Cara, its Affiliates and its Sub-licensees, in all cases maintained in accordance with the relevant accounting standards, consistently applied. Such amounts shall be calculated using the same accounting principles used by Cara (or the applicable Affiliate or Sub-licensee) for other Cara (or its Affiliate or Sub-licensee) products for financial reporting purposes.

"**One Year Royalty Buyout**" shall have the meaning in Section 6.5(c)(i).

"**Patent Rights**" means issued patents and pending patent applications (which, for purposes of this Agreement, include certificates of invention, applications for certificates of invention and priority rights) in any country or region, including all provisional applications, substitutions, continuations, continuations-in-part, divisions, renewals, all letters patent granted thereon, and all reissues, re-examinations and extensions thereof, and all foreign counterparts of any of the foregoing, and all the rights and interests in and to any of the foregoing.

"**Peptelligence® Formulation Technology**" means Enteris' proprietary technology relating to the methods and processes used by Enteris concerning the formulation, development, testing, manufacturing and/or packaging of active pharmaceutical ingredients, including: (i) the development of formulations for oral delivery of peptide active pharmaceutical ingredients in an enteric coated capsule or tablet containing a proprietary dry blend formulation of functional excipients to enhance permeability and/or solubility, including in any oral solid dosage forms, and/or (ii) the manufacture of drugs using such formulations. Such proprietary technology is generally described in Exhibit C of this Agreement.

"**Product**" means any drug product containing Drug in a formulation using or covered by the Licensed Technology.

"**Project Plan**" means that certain project plan attached hereto as Exhibit C of this Agreement and incorporated herein, as such plan may be amended or modified by the Parties in writing from time to time.

"**Proprietary Materials**" means any tangible chemical, biological or physical materials that are furnished by or on behalf of one Party to the other Party in connection with this Agreement, whether or not specifically designated as proprietary by the transferring Party. Proprietary Materials of Enteris shall include the Enteris DMF and all contents contained therein.

"**Recipient Party**" shall have the meaning set forth in Section 4.8.

"**Recipients**" shall have the meaning set forth in Section 4.1.

"**Regulatory Approval**" means (a) in the United States, approval by the FDA of an NDA or similar application for marketing approval, and satisfaction of all related applicable FDA registration and notification requirements, if any, or (b) in any other country in the Territory, approval by Regulatory Authorities (including pricing and reimbursement approvals) having jurisdiction over such country of a single application or set of applications comparable to an NDA and satisfaction of all related applicable regulatory and notification requirements required for the marketing and sale of pharmaceuticals in such country.

"**Regulatory Authority**" means any national, international, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity with authority over the distribution, importation, exportation, manufacture, production, use, storage, transport, clinical testing, pricing, sale or reimbursement of the Product in the Territory, including the FDA and the EMA.

"**Regulatory Filing**" means, collectively: (a) any IND, NDA, MAA, establishment license application, drug master file, application for designation as an "Orphan Product(s)" under the Orphan Drug Act, for "Fast Track" status under Section 506 of the FDCA (21 U.S.C. § 356), for "Breakthrough Therapy" status under Section 506 of the FDCA (21 U.S.C. §356), or for a Special Protocol Assessment under Section 505(b)(4)(B) and (C) of the FDCA (21 U.S.C. § 355(b)(4)(B)) and all other similar filings (including counterparts of any of the foregoing in any country or region in the Territory); (b) all supplements and amendments to any of the foregoing; and (c) all data and other information contained in, and correspondence relating to, any of the foregoing.

"**Royalty Buyout**" or "**Royalty Buyouts**" shall have the meaning set forth in Section 6.5(c)(ii).

"**Royalty Term**" shall have the meaning set forth in Section 6.5(a).

"**Securities Act**" shall have the meaning set forth in Section 6.5(c)(iii).

"**Significant Development Event**" means any of the following material Development events, a summary of which shall be included in any summary report: (a) any material interaction and/or written correspondence between Cara and any Regulatory Authority with respect to the Manufacture of a Product; (b) any material event with respect to any clinical trial involving the Manufacture of a Product; and (c) any material result obtained in the conduct of any clinical trial involving the Manufacture of a Product during the period covered by the Development report.

"**Stock Purchase Agreement**" means that certain common stock purchase agreement, in the form set forth in **Exhibit B** of this Agreement, that is entered into by the Parties concurrently with entry into this Agreement; for clarity, the Stock Purchase Agreement is not incorporated into or made part of this Agreement.

"**Sub-licensee**" means any Third Party to which Cara grants (directly or indirectly) a sublicense in accordance with Section 2.2.

"**Sublicense Agreement**" means any agreement by and between Cara and a Sub-licensee, and any agreement between any of Cara's Sub-licensees and a further Sub-licensee, and all additional downstream sublicense agreements thereafter, that are entered into in accordance with Section 2.2.

"**Successful Completion**" means the delivery of the meeting minutes from the FDA for the End of Phase 2 Meeting allowing for the continuation into Phase 3 clinical trials on Product.

"**Term**" shall have the meaning set forth in Section 8.1.

"**Territory**" means the United States ("U.S.") and the rest of world excluding Japan and South Korea.

"**Third Party**" means any Party other than Cara and Enteris and their respective Affiliates.

"**Transferring Party**" shall have the meaning set forth in Section 4.8.

"**Two Year Royalty Buyout**" shall have the meaning in Section 6.5(c)(ii).

"**VWAP**" shall have the meaning set forth in Section 6.1.

ARTICLE 2
LICENSE GRANT

2.1 Grant of License to Cara. Subject to the terms of this Agreement, Enteris hereby grants to Cara a non-exclusive, royalty-bearing license, including the right to grant sublicenses through multiple tiers as provided in Section 2.2, under the Licensed Technology, to Develop, Manufacture, and Commercialize Products in the Territory for use in the Field.

2.2 Right to Sublicense. Cara shall have the right to grant sublicenses through multiple tiers under the license granted to it under Section 2.1 to any of Cara's Affiliates and to any Third Parties (including the rights of Sub-licensees to grant further sublicenses) for the Development and Commercialization of Products in the Territory in the Field, including for Manufacture of Product by a CMO; provided that (i) Cara shall not be relieved of any of its obligations under this Agreement; (ii) Cara shall secure all appropriate covenants, obligations and rights from any such Sub-licensee, including licenses, assignment of intellectual property rights and confidentiality obligations, to ensure that such Sub-licensee is subject to, and complies with,

all of Cara's applicable covenants and obligations under this Agreement; (iii) Cara shall be responsible for the performance of its obligations under this Agreement and shall use Commercially Reasonable Efforts to enforce the obligations of each Sub-licensee under the relevant Sublicense Agreement, including the performance of activities required, the making of all payments due and the making of any reports under this Agreement with respect to sales of Product by such Sub-licensee, and such Sub-licensee's compliance with provisions of Sections 2.1, 2.6, 5.1, 5.4, 5.5, 5.7 and Article 4 of this Agreement; (iv) Cara shall require such Sub-licensee to retain such books and records, and Cara agrees that Cara will audit the books and records of any Sub-licensee, at Enteris' request and expense, in accordance with the provisions of Section 6.7; (v) Cara shall provide Enteris with a copy of any such Sublicense Agreement executed by Cara pursuant to this Section 2.2 within [***] after execution; provided, that, the financial terms and any other confidential terms of any such Sublicense Agreement may be redacted to the extent not relevant to the determination or enforcement of Enteris' rights under this Agreement; and (vi) Cara shall provide written notice to Enteris of such Sub-licensee within [***] after execution, but not in order to seek approval. All obligations of Cara under this Section 2.2 shall apply *mutatis mutandis* to all Sub-licensees of Cara that further sublicense their rights and obligations under this Agreement to further Sub-licensees, and Cara shall require each of its Sub-licensees to include appropriate provisions in such further sublicense.

2.3 Rights in Bankruptcy. All licenses and rights to licenses granted under or pursuant to this Agreement by Enteris to Cara are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code.

2.4 Disclosure of Technology. Enteris shall provide periodic written notice and disclosure to Cara of any and all Licensed Technology that is necessary or useful for the Manufacture, use or sale of the Product that is or comes under the Control of Enteris on or after the Effective Date and during the Term of the Agreement, except in the event that Cara exercises its Royalty Buyout, Enteris shall only provide notice to Cara under this Section 2.4 of any Licensed Technology that comes under the Control of Enteris after the Effective Date and on or prior to the date on which Enteris receives a payment from Cara in connection with the Royalty Buyout.

2.5 Retained Rights. Subject to the other terms of this Agreement, Enteris hereby retains the right to use and/or practice the Licensed Technology to develop, manufacture, or commercialize or have developed, manufactured, or commercialized any product (other than the Product) and for any and all uses either inside or outside of the Field and to otherwise exploit the Licensed Technology for any and all uses outside of the license grant.

2.6 Use of Licensed Technology. Cara hereby agrees that (a) it shall not use or practice the Licensed Technology for any purpose other than exercising its rights and performing its obligations under this Agreement; and (b) except for the rights expressly set forth in this Agreement, Cara is not granted any rights, title or interest in or to such Licensed Technology.

2.7 Negative Covenant. In order to preserve the economic value of the business deal in this Agreement for each Party, Enteris covenants that during the Term, it and its Affiliates shall not grant any third party generic manufacturer of pharmaceutical or drug products any license

or other rights (such as a covenant not to sue) under the Licensed Technology to Develop, Manufacture, or Commercialize any drug products containing the Drug in the Territory for use in the Field; provided that, the foregoing covenant shall automatically terminate, and this Section 2.7 shall thereafter be of no force and effect, if none of Cara or its Affiliates or Sub-licensees have launched a commercial Product by [***].

ARTICLE 3
DEVELOPMENT, REGULATORY AND COMMERCIALIZATION

3.1 Manufacture by Enteris. Enteris shall continue to perform its obligations under the Manufacturing Services Agreement in accordance with the terms thereof, including manufacture and supply requirements for Drug products for ongoing and (if applicable) future Phase 1 and Phase 2 clinical trials, until termination of such agreement. For clarity, the first sentence of Section 2.5 and the first sentence of Section 4.1(b) of the Manufacturing Services Agreement are hereby terminated.

3.2 Technology Transfer by Enteris.

(a) Enteris acknowledges that the transfer of all Licensed Technology existing as the Effective Date is critical to Cara's ability to exercise its rights and receive its benefits under this Agreement. Enteris hereby covenants that it shall complete the transfer of all such Licensed Technology, subject, however, to the cooperation, resources and efforts of Cara's CMO to fully and effectively receive such technology transfer, commencing on a date as reasonably specified by Cara, and Enteris shall use diligent, good faith efforts to complete such technology transfer, including achieving the Completion of Analytical Procedures Transfer and Completion of Manufacturing Processes Transfer, as soon as reasonably practicable thereafter. Cara shall cause its CMO to use diligent, good faith efforts to accept the technology transfer, and the Parties shall (and Cara shall cause its CMO to) work collaboratively and in good faith to conduct the full, accurate, and complete technology transfer under the Project Plan through the Completion of Analytical Procedures Transfer and Completion of Manufacturing Process Transfer.

(b) The Parties agree that the fee for the work as set forth under Section I of the Project Plan as of the Effective Date (Completion of Analytical Procedures Transfer) is [***]. Prior to commencement of the transfer of the manufacturing process, fees for all work contemplated under Section II of the Project Plan (Transfer of Manufacturing Process) shall be proposed by Enteris and agreed to by Cara, and such fees shall be commercially reasonable and typical for similar technology transfer work. In the event that Cara reasonably determines that additional technology transfer work by Enteris – beyond the tasks generally set forth in the then-current Project Plan – are needed to enable the CMO successfully to complete manufacture of amounts of Product as specified in and in accordance with the criteria in Section II (Transfer of Manufacturing Process) of the Project Plan to achieve Completion of Manufacturing Process Transfer, then the Parties shall discuss and agree reasonably and in good faith on such additional work required to be conducted by the Parties (and, if applicable, any CMO selected by Cara) to satisfy all the

acceptance criteria in the Project Plan, and a timeline and budget for such work (with the Enteris fees for such additional Enteris work to be commercially reasonable and typical for similar technology transfer work), in each case in accordance with Section 3.2(c). Notwithstanding the foregoing, any additional work performed by Enteris in furtherance of the analytical procedures transfer under Section I of the initial Project Plan, but not set forth in Section I of the Project Plan as of the Effective Date, shall not be included in the [***] fee, and the fee for such additional work shall be commercially reasonable and typical for similar technology transfer work. All payments due under this Section 3.2 shall be paid upon Completion of the Analytical Procedures Transfer or Completion of the Manufacturing Process Transfer, as applicable.

(c) Cara shall request additional services to the Project Plan in writing, detailing the proposed changes to the services ("**Change of Scope**"). Within [***] of Enteris' receipt of such proposed Change of Scope, Enteris shall provide Cara with a cost and time estimate for performing the additional services as proposed, and the fees for such work, which costs and fees shall be commercially reasonable and typical for similar work. The Parties shall jointly review and discuss the proposed Change of Scope, costs, fees and time estimate reasonably and in good faith. Such additional services shall become part of the Project Plan upon execution by both Parties of the Change of Scope. Any disagreements with respect to the Change of Scope shall be subject to Section 11.1.

(d) For purposes of this Section 3.2, Cara shall ensure that any CMO of Cara is subject to confidentiality provisions comparable in scope to Article 4 with respect to the transfer by Enteris to Cara and its CMO of information and Know-how under Section 3.2. Enteris does not represent or warrant that the use of, or results from, the analytical procedures or manufacturing processes will satisfy the requirements of any Regulatory Authority at the time of submissions of any Regulatory Filings to any such Regulatory Authority.

3.3 Cara's Rights and Obligations.

(a) Except as provided in Section 3.1, Cara shall have the sole right and responsibility, at its sole cost and expense, and in its sole discretion, for the Development, Manufacture and Commercialization of Products for use in the Field and in the Territory.

(b) Cara shall have the sole right and responsibility, at its sole cost and expense, and in its sole discretion, during the Term to Develop, seek Regulatory Approval, and (if Regulatory Approval is achieved) Commercialize Products in the Field in the Territory and shall, in its sole discretion, commit such resources (including employees, consultants, contractors, facilities, funding, equipment and materials) as it determines are necessary or appropriate to conduct such Development and Commercialization activities.

(c) Cara shall provide Enteris with written reports describing in reasonable summary its Development activities and Commercialization activities with respect to the Products in the Territory and the results of such activities on an annual basis, with the first report being due [***] after the Effective Date, which reports shall include a reasonable

summary of: (a) all Development and Commercialization activities conducted with respect to the Product (including the status of any clinical trials) and any launch plans (including expected date of first commercial sales of Product); (b) the Regulatory Filings with respect to such Products that Cara or any of its Affiliates have filed, sought or obtained in the prior [***] period or reasonably expect to make, seek or attempt to obtain in the following [***] period in the Territory, and (c) any Significant Development Events applicable to the Product. The reports shall also include a summary of all material questions asked by any Regulatory Authority to Cara regarding the Licensed Technology and of Cara's responses thereto. For purposes of clarity, the obligation to provide summary reports hereunder does not affect or supersede any such reporting or disclosure obligations of Cara as set forth in the Manufacturing Services Agreement.

3.4 Regulatory Responsibility. Cara (and including its Affiliates and Sub-licensees) shall have the sole right and responsibility, at its and their sole discretion for (a) preparing, filing and maintaining all Regulatory Filings for Products in its own name in the Territory; provided that Enteris shall prepare, file and solely and exclusively own the Enteris DMF and all contents therein, and Cara shall have no ownership interest whatsoever in the Enteris DMF or the contents therein, and (b) reporting to Regulatory Authorities all adverse events and serious adverse events occurring in any clinical trials conducted by Cara related to any Products, to the extent required by Applicable Laws. Enteris agrees to provide Cara with all information contained in the Enteris DMF, and in any analogous regulatory filing or documents in any other jurisdiction, to facilitate Cara's Regulatory Filings in jurisdictions where the Enteris DMF is not recognized, subject to Section 4.8, it being understood that such information is deemed Proprietary Materials of Enteris.

3.5 Recalls. If any Regulatory Authority issues or requests a recall or takes similar action in connection with any Product in the Territory, or if Cara (or and its Affiliate or Sub-Licensee) reasonably believes that an event, incident or circumstance has occurred that may result in the need for a recall, market withdrawal or other corrective action regarding the Product, Cara shall promptly advise Enteris thereof by telephone or facsimile. Following such notification, Cara (or and its Affiliate or Sub-Licensee) shall decide and have control of whether to conduct a recall or market withdrawal (except in the event of a recall or market withdrawal mandated by a Regulatory Authority, in which case it shall be required) or to take other corrective action in any country and the manner in which any such recall, market withdrawal or corrective action shall be conducted; provided, that, Cara shall keep Enteris regularly informed regarding any such recall, market withdrawal or corrective action. All expenses incurred by Cara in connection with any such recall, market withdrawal or corrective action (including, without limitation, expenses for notification, destruction and return of the affected Product and any refund to customers of amounts paid for such Product) shall be the sole responsibility of Cara.

3.6 Safety Information. Each Party shall disclose to other Party any and all information of which that Party (or its Affiliate) becomes aware relating to any safety issues for formulations using or based on the Licensed Technology, which reasonably may impact the safety of Product, such disclosure to be made promptly after the Party becomes aware thereof.

3.7 Reference Rights. Cara (and its Affiliates and Sub-Licensees) shall have (i) the right of reference to the Enteris DMF and the information therein, and (ii) the right to reference the information contained in the Enteris DMF in all of Cara's (and its Affiliates and Sub-Licensees) Regulatory Filings in jurisdictions where the Enteris DMF is not recognized, in each case solely for the purpose of exercising, using and practicing the licenses and other rights granted to Cara pursuant to this Agreement, provided that Cara shall bear any expenses (including expenses of Enteris) in respect of exercising any such right of reference.

ARTICLE 4
CONFIDENTIALITY, PUBLICITY, PUBLICATIONS

4.1 Confidentiality. Each Party agrees that, during the Term and for a period of [***] thereafter, it and its Affiliates shall keep confidential and shall not publish or otherwise disclose to any Third Party and shall not use for any purpose other than to exercise its rights or perform its obligations under this Agreement or the Project Plan any Confidential Information furnished to it or its Affiliate by the other Party or its Affiliate pursuant to this Agreement or the Project Plan, except to the extent expressly authorized by this Agreement or the Project Plan, or as otherwise agreed to in writing by the Parties. Each Party shall further require its Affiliates, and its and their respective directors, officers, employees, agents, consultants, sublicensees, contractors, partners, acquirors, assignees, and distributors (collectively, "**Recipients**") who receive the other Party's Confidential Information to agree, in writing, to be bound by duties and obligations of confidentiality and non-use no less stringent than those contained in this Section 4.1. The foregoing confidentiality and non-use provisions will apply over any preceding obligations of confidentiality between Enteris and Cara, including those set forth in the Manufacturing Services Agreement. The foregoing confidentiality and non-use obligations do not apply to any particular portion of the disclosing Party's Confidential Information that the receiving Party can demonstrate by competent written proof:

(a) was already known to or otherwise in the possession of, the receiving Party, other than under an obligation of confidentiality, prior to the time of disclosure by the disclosing Party or its Affiliate, as evidenced by contemporaneous writing;

(b) was part of the public domain at the time of its disclosure to the receiving Party or any of its Recipients;

(c) became part of the public domain after its disclosure and other than through any act or omission of the receiving Party or any of its Recipients in breach of this Agreement;

(d) was disclosed to the receiving Party on a non-confidential basis by a Third Party who, to the receiving Party's knowledge after due inquiry, had a legal right to make such disclosure; or

(e) was independently discovered or developed by the receiving Party or its Affiliate without aid, application, reference to or use of the disclosing Party's Confidential

Information, as evidenced by a contemporaneous writing dated prior to the time of disclosure by the disclosing Party or its Affiliate.

4.2 Authorized Disclosure. Notwithstanding the obligations set forth in Section 4.1, a Party or its Affiliate may disclose the other Party's Confidential Information and the terms of this Agreement to the extent:

(a) such disclosure is reasonably necessary (i) for the filing or prosecuting of Patent Rights as contemplated by this Agreement; (ii) to comply with the requirements of Regulatory Authorities with respect to obtaining and maintaining Regulatory Approval of a Product or submission of information to tax or other Governmental Authorities; (iii) for prosecuting or defending litigation as contemplated by this Agreement; or (iv) complying with Applicable Law;

(b) such disclosure is reasonably necessary to its officers, directors, employees, agents, consultants, contractors, licensees, sublicensees, attorneys, accountants, sources of debt or equity financing, insurers or licensors who need to know such information in order for such Party to perform its obligations or exercise its rights under this Agreement, and to potential acquirers, merger partners, strategic partners, or sources of debt or equity financing, and their professional advisors, for use in diligence and related activities in the proposed transaction(s); provided that in each case, the disclosees are bound by written obligations of confidentiality and non-use, or by equivalent professional ethical obligations, no less stringent than those of this Agreement with a reasonable duration based on customary terms;

(c) such disclosure is reasonably necessary to any bona fide potential or actual investor, acquiror, merger partner or other financial or commercial partner for the sole purpose of evaluating an actual or potential investment, acquisition or other business relationship; provided that, in each case, the disclosees are bound by written obligations of confidentiality and non-use no less stringent than to those of this Agreement with a reasonable duration based on customary terms, and further provided that in the case of any such disclosure of Confidential Information to any actual or potential competitor of either Party, all competitively sensitive information (including, for the avoidance of doubt, all financial information) herein shall be redacted until, subject to Applicable Laws, the execution of a definitive agreement with such actual or potential competitor to implement a transaction with the receiving Party is imminent; or

(d) such disclosure is reasonably necessary to comply with Applicable Laws, including regulations promulgated by applicable security exchanges, court order, administrative subpoena or other order.

(e) Notwithstanding the foregoing, if a Party or its Affiliate is required to make a disclosure of the other Party's Confidential Information pursuant to Section 4.2(a)(iii)-(iv) or 4.2(d), then such Party shall (i) promptly notify the other Party of such required disclosure, (ii) give the other Party an opportunity to seek confidential treatment and, upon the other Party's request, such Party and its Affiliates shall use reasonable efforts to obtain,

or to assist the other Party in obtaining, a protective order preventing or limiting the required disclosure and (iii) if the other Party is unsuccessful in its efforts pursuant to subsection (ii), disclose only that portion of the Confidential Information that such Party is legally required to disclose.

4.3 Employees and Consultants. Enteris and Cara each hereby represents that all of its employees and consultants, and all of the employees and consultants of its Affiliates, who have access to Confidential Information of the other Party are or will, prior to having such access, be bound by written obligations to maintain such Confidential Information in confidence. Each Party agrees to use, and to cause its Affiliates to use, Commercially Reasonable Efforts to enforce such obligations and to prohibit its employees and consultants from using such information except as expressly permitted hereunder. Recipient party will be liable to the other for any disclosure or misuse by its employees of Confidential Information of the disclosing Party.

4.4 Publicity. The Parties shall, upon the execution of this Agreement, issue a joint press release with respect to this Agreement in a form mutually agreeable by both Parties, and each Party may make subsequent public disclosure of the contents of such press release without further approval of the other Party. After release of such press release, if either Party or its Affiliate desires to make a public announcement concerning the existence or terms of this Agreement, or any clinical or regulatory announcements, early notification of such public announcement by the proposing Party shall be given in writing to the other Party at least [***] before the proposed disclosure date and a draft of such public announcement shall be sent to the commenting Party for its review and comment at least [***] before the proposed disclosure date, but subject to Section 4.5. Under no circumstances shall any competitively sensitive information contained in this Agreement (including all financial information, including total value of this Agreement) be disclosed, except as otherwise provided in Section 4.5.

4.5 Public Filings. The Parties acknowledge that either or both Parties may be obligated to file under Applicable Laws a copy of this Agreement with the U.S. Securities and Exchange Commission or other Governmental Authorities. Each Party shall be entitled to make such a required filing, provided that it requests confidential treatment of the commercial terms and sensitive technical terms hereof and thereof to the extent such confidential treatment is reasonably available to such Party. In the event of any such filing, each Party will provide the other Party with a copy of this Agreement marked to show provisions for which such Party intends to seek confidential treatment and shall reasonably consider and incorporate the other Party's reasonable comments thereon to the extent consistent with the legal requirements, with respect to the filing Party, governing disclosure of material agreements and material information that must be publicly filed. Further, each Party acknowledges that the other Party, or its successor, may be required by Applicable Laws to make public disclosure of events or results of activities under this Agreement, and that such disclosures may be made, if required by such Applicable Laws, prior to the expiration of the notice periods in Section 4.4., *provided that* a Party (or successor) shall not, in any such public disclosure, disclose any of the other Party's Confidential Information, unless such Party is required by Applicable Law to make such a public disclosure of such particular information. In such event, such Party shall submit the proposed disclosure in writing to the other Party as far in advance as reasonably practicable so as to provide a reasonable opportunity to comment thereon, and such Party required to make the disclosure shall consider all comments from such other Party

in good faith, and shall in any event only disclose such information of the other Party as is required by Applicable Law to be disclosed publicly in such manner.

4.6 Publications and Presentations. Except for disclosures permitted pursuant to Section 4.4 or Section 4.5, if a Party wishes to make a publication relating to activities conducted under this Agreement or the results of such activities hereunder, and such publication would disclose Confidential Information of the other Party, (a) it shall deliver to the other Party a copy of any such proposed written publication or an outline of a proposed oral disclosure at least [***] prior to submission for publication or presentation, (b) the reviewing Party shall have the right to require a delay of up to [***] in publication or presentation in order to enable patent applications to be filed protecting such reviewing Party's rights in potentially patentable inventions that are owned by such Party and that would be publicly disclosed by the publication of the information in such publication, and (c) such reviewing Party shall have the right to prohibit disclosure of any of its Confidential Information in any such proposed publication or presentation. In any such publication or presentation by a Party, the other Party's contribution shall be duly recognized, in accordance with customary industry standards. For clarity, Cara is free to make publications about its (and its Affiliates' and Sub-licensees') activities under this Agreement, and results of such activities, without review by Enteris, provided that such publications do not disclose Confidential Information of Enteris. Further, Enteris covenants that it and its Affiliates shall not publish (or permit publication of) any non-public information relating to Cara's (and its Affiliate's and Sub-licensee's) activities under this Agreement, or the results of such activities, without the prior written consent of Cara, such consent not to be unreasonably withheld.

4.7 Permitted Publications. Notwithstanding Sections 4.4 through 4.6, either Party may include in a public disclosure or in a scientific or medical publication or representation, without prior delivery to or approval by the other Party, any information which has previously been included in a public disclosure or scientific or medical publication that has been approved or otherwise made pursuant to Section 4.4 or 4.5 or reviewed pursuant to Section 4.6 or published or publicly disclosed by the other Party. A Party relying on this Section 4.7 shall bear the burden of establishing that information has previously been included in a public disclosure or scientific or medical publication that has been approved pursuant to Section 4.4 or 4.5 or reviewed pursuant to Section 4.6 or published or publicly disclosed by the other Party. For clarity, Cara (and its Affiliates and Sub-licensees) retain the full rights to publish clinical and other data and results relating to Drug or Product without consent of or comment by Enteris, provided that such publications do not disclose Enteris Confidential Information. Cara and Enteris each may further disclose or publish that Cara and Enteris are parties to this Agreement and the general scope of the rights granted hereunder, but excluding any financial terms or the total value of the Agreement.

4.8 Use of Proprietary Materials. From time to time during the Term, one Party (the "**Transferring Party**") may supply the other Party (the "**Recipient Party**") with Proprietary Materials of the Transferring Party for use in the Manufacture or Development of a Product. In connection therewith, each Recipient Party hereby agrees that: (a) it shall not use such Proprietary Materials for any purpose other than exercising its rights or performing its obligations hereunder; (b) it shall use such Proprietary Materials only in compliance with all Applicable Laws; (c) it shall not transfer any such Proprietary Materials to any Third Party without the prior written consent of the Transferring Party, except for (i) the transfer of Products for use in clinical trials or

(ii) in a transaction expressly permitted hereby (such as transfer by Cara to its CMO); (d) the Recipient Party shall not acquire any right of ownership or title in or to such Proprietary Materials as a result of such supply by the Transferring Party; and (e) upon the expiration or termination of this Agreement, the Recipient Party shall, if and as instructed by the Transferring Party, either destroy or return any such Proprietary Materials that are not the subject of the grant of a continuing license under this Agreement.

ARTICLE 5
INTELLECTUAL PROPERTY RIGHTS

5.1 Enteris Rights. Enteris shall own all rights, title, and interest on a worldwide basis in and to the Licensed Patent Rights and Licensed Know-how, including any Improvements (including any Patent Rights claiming or covering such Improvements) regardless of inventorship, used to formulate, develop or otherwise exploit the Drug or Product, and Enteris retains all rights to prosecute and maintain the Licensed Patent Rights at its sole discretion and sole expense. Cara shall cooperate with and assist Enteris in all reasonable respects, at Enteris' expense, in connection with Enteris' preparation, filing, prosecution (including review and comments regarding responses to office actions and/or official actions from worldwide patent offices) and maintenance of such Licensed Patent Rights, including by obtaining assignments to reflect chain of title consistent with the terms of this Agreement, gaining United States patent term extensions, supplementary protection certificates and any other extensions that are now or become available in the future wherever applicable to such Licensed Patent Rights.

5.2 Cara Rights. Cara shall own all rights, title, and interest on a worldwide basis in and to any Inventions, other than Improvements, including any Patent Rights claiming or covering any such Invention, and Cara shall retain all rights to prosecute and maintain such Patent Rights in its sole discretion and sole expense. Further, and notwithstanding the foregoing, Cara shall own the overall formulation of the Product, *provided that* Enteris shall retain ownership of all Licensed Technology that claims or is incorporated in such formulation. Notwithstanding the foregoing, Cara acknowledges that a license shall be required with respect to any formulation to the extent that the formulation uses or practices issued patents or Confidential Information of Enteris in the Licensed Technology (excluding any Confidential Information that is subject to any of the exceptions in subsections 4.1(a)-(e)).

5.3 Notice; Inventorship. Cara hereby agrees to promptly notify Enteris of the conception or reduction to practice of any Improvements made by or on behalf of Cara and to promptly execute any documents that may be necessary to perfect Enteris' ownership and rights in and to any such Improvements. In case of a dispute between the Parties over whether any particular Invention is an Improvement, such dispute shall be resolved according to U.S. patent law pursuant to Article 11, with an arbitration (if conducted) by patent counsel mutually selected by the Parties who (and whose firm) is not at the time of the Dispute, and was not at any time during the [***] prior to such Dispute, performing services for either of the Parties. Expenses of the patent counsel shall be shared equally by the Parties. With respect to any Inventions that are Improvements, Cara, its Affiliates and Sub-licensees, and their respective employees,

subcontractors and contractors, and agents, shall assign, and do hereby irrevocably and perpetually assign, to Enteris, all worldwide rights, title and interest in and to all such Improvements (including all Patent Rights or other intellectual property rights relating thereto).

5.4 Third Party Infringement.

(a) Notice. If either Party becomes aware of any suspected infringement or misappropriation of any Licensed Technology that cover the Development, Manufacture or Commercialization of the Product anywhere in the Territory (each, an "**Infringement**"), that Party shall promptly notify the other Party within [***] and provide it with all details of such Infringement of which it is aware, excluding privileged information (each, an "**Infringement Notice**").

(b) Enteris Right to Enforce. Enteris shall have the first right, but not the obligation, to address such Infringement in the Territory that involves such Licensed Technology by taking reasonable steps, which may include the institution of legal proceedings or other action, and to compromise or settle such Infringement (each, an "**Infringement Response**"); provided, that: (A) Enteris shall keep Cara fully informed about such Infringement Response and Cara shall provide, at Enteris' expense all reasonable cooperation to Enteris in connection with such Infringement Response; (B) Enteris shall not take any position with respect to, or compromise or settle, any such Infringement in any way that is reasonably likely to directly and adversely affect the scope, validity or enforceability of any such Licensed Technology, without the prior consent of Cara, which consent shall not be unreasonably withheld, conditioned or delayed; and (C) if Enteris does not intend to prosecute or defend an Infringement, or ceases to diligently pursue an Infringement Response with respect to such an Infringement, it shall inform Cara in such a manner that such Infringement Response will not be prejudiced and Section 5.4(c) shall apply. [***]

(c) Cara's Right to Enforce. If (A) Enteris informs Cara in writing that it does not intend to prosecute any Infringement Response with respect to any such Infringement, (B) within [***] after the receipt of notice of any such Infringement, Enteris has not commenced to take any Infringement Response with respect thereto, or (C) if Enteris does not diligently pursue any such Infringement Response, then, unless Enteris provides Cara with a commercially reasonable justification for its delay of such Infringement Response, and *provided* that such delay will not adversely affect the scope, validity or enforceability of the Licensed Technology subject to the Infringement and will not materially affect Cara's Commercialization of Product, Cara shall have the right, at its own expense, upon written notice to Enteris to take appropriate action to address such Infringement, including by initiating an Infringement Response or taking over prosecution of any legal proceedings initiated by Enteris. In that event, Cara shall keep Enteris fully informed about such Infringement Response and shall consult with Enteris before taking any major steps during the conduct of that Infringement Response. Enteris shall provide reasonable cooperation to Cara in connection with that Infringement Response. Cara shall not take any position with respect to, or compromise or settle, such Infringement in any way that is reasonably likely

to directly and adversely affect the scope, validity or enforceability of such Licensed Technology. [***]

(d) Right to Representation. Each Party shall have the right to participate and be represented by counsel that it selects, in any Infringement Response instituted under Section 5.4(b) or 5.4(c) by the other Party. If a Party with the right to initiate an Infringement Response under Section 5.4 to eliminate an Infringement lacks standing to do so and the other Party has standing to initiate such action, then the Party with the right to initiate an action under Section 5.4 may name the other Party as plaintiff in such action or may require the Party with standing to initiate such Infringement Response at the expense of the other Party.

(e) Cooperation. In any Infringement Response instituted under this Section 5.4, the Parties shall cooperate with and assist each other in all reasonable respects. Upon the reasonable request of the Party instituting that Infringement Response, the other Party shall join such Infringement Response and shall be represented using counsel of its own choice, at the requesting Party's expense.

(f) Allocation of Recoveries. Any settlements, damages or monetary awards ("**Recovery**") recovered by either Party pursuant to any Infringement Response shall, after reimbursing the Parties for their reasonable out-of-pocket expenses in making such recovery (which amounts shall be allocated pro rata if insufficient to cover the totality of such expenses), [***].

5.5 Defense of Claims. If any action, suit or proceeding is brought against either Party or any Affiliate of either Party alleging the infringement of the Know-how or Patent Rights of a Third Party by reason of the Development, Manufacture or Commercialization of any Product, such Party shall notify the other Party within [***] of the earlier of (a) receipt of service of process in such action, suit or proceeding, or (b) the date such Party becomes aware that such action, suit or proceeding has been instituted, and the Parties shall meet as soon as possible to discuss the overall strategy for defense of such matter. Except as otherwise agreed in writing by the Parties, the Party alleged to have infringed, or whose Affiliate or Sub-licensee is alleged to have infringed, shall have the obligation to defend such action, suit or proceeding at its sole expense, and in its sole discretion; the other Party shall have the right to separate counsel at its own expense in any such action, suit or proceeding, *provided that* its intellectual property rights are actually at issue in the action or proceeding, and that it shall not interfere or compromise the defending Party's defense of such action. In any such action or proceeding, the Parties shall cooperate with each other in all reasonable respects in the defense of any such action, suit or proceeding. All such expenses with respect to any such action, suit or proceeding in the Territory shall be borne solely by the Party defending such action, suit or proceeding. Each Party shall promptly furnish the other Party with a copy of each communication relating to the alleged infringement that is received by such Party including all material documents filed in any related litigations as to such infringement that are reasonably needed by the other Party, but excluding confidential or privileged communications or documents.

5.6 Patent Term Extension. The Parties shall cooperate with each other in obtaining patent term extensions or supplemental protection certificates or their equivalents in any country in the Territory where applicable to Licensed Patent Rights. Such cooperation shall include diligently and timely conferring and coordinating with respect to such matters to ensure compliance with applicable filing deadlines, and agreeing on procedures to be followed by the Parties to ensure such compliance. In the event that elections with respect to obtaining such patent term extension are to be made, Enteris shall have the right to make the election with respect to Licensed Patent Rights.

5.7 Patent Marking. Cara agrees to mark, and to cause its Affiliates and Sub-licensees to mark, Products sold in the U.S. with all applicable U.S. patent numbers in issued Patent Rights that claim the Product (or its manufacture), and to mark Products shipped to or sold in other countries, in each case to comply with the patent laws and practices of the countries of manufacture, use and sale. Such marking may be on the packaging for the Products, if permitted by Applicable Laws.

ARTICLE 6
CONSIDERATION

6.1 Upfront Fee. In consideration of the grant by Enteris to Cara of the license in Section 2.1, Cara shall pay Enteris or Enteris' designees (as contemplated by the Stock Purchase Agreement) a non-refundable, non-creditable upfront fee in an aggregate amount equal to eight million dollars ($8,000,000), fifty percent (50%) of which shall be payable by transfer of immediately available funds, within five (5) days of execution of this Agreement, in accordance with the wire transfer instructions set forth in **Exhibit A**, attached hereto and incorporated herein, and the invoice provided in writing by Enteris to Cara prior to the Effective Date, and the other fifty percent (50%) of which shall be paid in Cara stock issued by Cara to Enteris, or its designee, pursuant to the terms of the Stock Purchase Agreement.

6.2 Milestone Payments. Cara shall make the following non-refundable, non-creditable one-time payments to Enteris within [***] after the first achievement of each of the following milestone events with respect to Cara's first Product (or Products, cumulatively, in the case of sales milestones) (whether such milestone is achieved by Cara or its Affiliate or Sub-licensee) utilizing the Licensed Technology, regardless of indication:

	Milestone Event	**Payment ($ U.S. Dollars)**
Milestone #1	[***]	$[***]
Milestone #2	[***]*	$[***]

Milestone #3	[***]	$[***]
Milestone #4	[***]	$[***]
Milestone #5	[***]	$[***]
Milestone #6	[***]	$[***]
Milestone #7	[***]	$[***]

***[***]**

6.3 [***]

6.4 Notice and Payment of Milestones. Cara shall provide Enteris with prompt written notice, in any event within [***] thereafter, upon Cara's knowledge of the occurrence of each milestone event set forth in Section 6.2. If Enteris believes any such milestone event has occurred and has not received a written notice of same from Cara, it shall so notify Cara and shall provide to Cara documentation or other information that support its belief. Any dispute under this Section 6.4 that relates to whether or not a milestone event has occurred shall be resolved by discussion and, if needed, arbitration in accordance with Article 11. If Cara determines that there is a reasonable likelihood of a particular milestone event being achieved on or about a particular date, Cara shall use reasonable efforts to provide advance notice thereof to Enteris, which notice shall be provided solely for Enteris' planning purposes and shall not be construed as a representation, warranty or covenant by Cara that such milestone event will occur when anticipated, or at all. Each milestone payment under Section 6.2 shall only be payable once, and, for clarity, the total amount of milestones payable under Section 6.2 shall not exceed $[***].

6.5 Payment of Royalties; Accounting and Records.

(a) Payment of Royalties. Cara shall pay Enteris a tiered royalty on the applicable amount of Net Sales of Products in each Calendar Year (or partial Calendar Year) at the following rates:

Aggregate Amount of Net Sales in a Calendar Year for All Products in All Indications	**Royalty Rate (%)**
Amount of annual Net Sales [***]	[***]%
Amount of annual Net Sales [***]	[***]%

[***]

(b) Royalty Reductions. For sales of Product in countries where there is no valid claim in an issued patent in the Licensed Patent Rights that covers the Product, royalties for such Product in such country will be paid on Net Sales of such Product in such country at [***] of the royalty rate otherwise applicable to such Net Sales in the above schedule.

(c) Royalty Buyout.

(i) On or before the first (1st) anniversary of the Effective Date, Cara shall have the right, but not the obligation, to terminate its obligation to pay any royalties by paying to Enteris or Enteris' designees (as contemplated by the Stock Purchase Agreement) the sum of [***] payable in cash (the "**One Year Royalty Buyout**").

(ii) After the first (1st) anniversary of the Effective Date but on or before the second (2nd) anniversary of the Effective Date, Cara shall have the right, but not the obligation, to terminate its obligation to pay any royalties by paying to Enteris or Enteris' designees (as contemplated by the Stock Purchase Agreement) the sum of [***] payable in cash (the "**Two Year Royalty Buyout**", collectively with the One Year Royalty Buyout, the "**Royalty Buyouts**", and each a "**Royalty Buyout**").

(iii) If either (x) Cara is a "well-known seasoned issuer," as such term is defined in Rule 405 promulgated under the Securities Act of 1933, as amended (the "Securities Act"), as of the date of the exercise of the Royalty Buyout, or (y) (i) the staff of the Division of Corporation Finance of the U.S. Securities and Exchange Commission has issued to Cara a no-action letter regarding the commencement of the holding period under Rule 144(d) promulgated under the Securities Act for such shares of Cara stock as are otherwise issuable at the election of Cara as partial payment of the Royalty Buyout as permitted under this Section 6.5(c)(iii), and such no-action letter permits tacking of such holding period back to the date of this Agreement, and (ii) sufficient time has passed since the date of this Agreement (and all other requirements under Rule 144 are met) to permit the holders of the stock to be issued by Cara in relation to the Royalty Buyout to sell all such shares on the date of Cara's exercise of such option in compliance with Rule 144 under the Securities Act without any restrictions, then Cara shall have the option, but not the

obligation, to pay fifty percent (50%) of the Royalty Buyout amount by issuing Cara stock to Enteris or its designee pursuant to the Stock Purchase Agreement.

(iv) In order to exercise a Royalty Buyout, Cara shall notify Enteris and, if the option to partially pay in Cara stock as permitted by Section 6.5(c)(iii) above is exercised by Cara, EBP Holdco LLC and any designees of Enteris and EBP Holdco LLC, in writing that it is paying the Royalty Buyout and shall pay such Royalty Buyout within [***] of such notice. For avoidance of doubt, upon Enteris' receipt of the Royalty Buyout under this Section 6.5(c), no royalties shall thereafter be due to Enteris under this Agreement and the Royalty Term (and the provisions of this Section 6.5) shall end immediately. For the avoidance of doubt, the expiration of the Royalty Term, including due to payment of a Royalty Buyout, shall not affect Cara's obligation to pay Enteris milestones pursuant to Section 6.2 of this Agreement, including milestone events based on [***]. In the event that Cara provides Enteris with a notice that it is exercising the Royalty Buyout but no payment is received by Enteris within the [***] period (other than solely due to an issue with Enteris or its bank), then the Royalty Buyout is deemed to not have been exercised. Such failure to pay the Royalty Buyout amount within that [***] period is not subject to cure.

6.6 Payment Dates and Reports. Cara shall make all royalty payments due hereunder within [***] after the end of each Calendar Quarter in which the sale of such Product shall occur. Cara shall provide, within [***] after each Calendar Quarter in which a sale of such Product shall occur, a report showing: (a) the Net Sales of each Product by type of Product and country in the Territory; (b) an itemization of the deductions permitted to determine Net Sales; (c) a calculation of the amount of royalty due to Enteris, if applicable; and (d) [***]. Payment of all milestone events due hereunder, including the milestones on [***], shall be made in accordance with Section 6.2. The Parties agree that, notwithstanding anything to the contrary in the Manufacturing Services Agreement, Cara has and shall have no further obligation under Section 4.1(b) of the Services Agreement to pay any additional License Access Fees (as defined in the Manufacturing Services Agreement), and any such obligation going forward is hereby terminated.

6.7 Records; Audit Rights. Cara and its Affiliates and Sub-licensees shall keep and maintain, for [***] from the date of (x) each payment of royalties under this Agreement and (y) each milestone owed, complete and accurate records of gross sales and Net Sales by Cara and its Affiliates and Sub-licensees, in sufficient detail to allow royalties and milestones on Net Sales to be determined accurately. All such records required to be maintained under this Section 6.7 shall include the information contained in the reports required under Section 6.6. Enteris shall have the right for a period of [***] after receiving any such payments to appoint at its expense an independent certified public accountant reasonably acceptable to Cara to audit such records of Cara, or its Affiliates, to verify that the amount of any such payment was correctly determined. Cara and its Affiliates shall each make its records available for audit by such independent certified public accountant during regular business hours at such place or places where such records are customarily kept, upon [***] written notice from Enteris. Such audit right shall not be exercised by Enteris more than once in any Calendar Year or more than once with respect to sales of a particular Product in a particular period or with respect to an individual milestone. All records

made available for audit shall be deemed to be Confidential Information of Cara. The results of each audit, if any, shall be binding on both Parties absent manifest error. In the event there was an underpayment by Cara under this Agreement, Cara shall promptly (but in any event no later than [***] after Cara's receipt of the report so concluding) make payment to Enteris of any shortfall together with interest as provided in Section 6.8 from the date such payment was due to the date paid in full. Enteris shall bear the full cost of such audit unless such audit discloses a variance to the detriment of Enteris of five percent 5% or more from the amount of the original payment calculation in which case Cara shall bear all reasonable cost of the performance of such audit.

6.8 Overdue Payments. All payments not made by Cara to Enteris when due under this Agreement shall bear interest at a rate equal at [***] (as quoted in *The Wall Street Journal* or its successor on the day after the payment is due) calculated from the due date to the date paid in full. Any such overdue payment shall, when made, be accompanied by, and credited first to, all interest so accrued.

6.9 Payments; Withholding Tax.

(a) Payments in Dollars. All payments made by Cara under this Section shall be made by wire transfer from a banking institution in United States Dollars in accordance with instructions given in writing from time to time by the other Party.

(b) Withholding Taxes. If Applicable Laws require withholding of income or other taxes imposed upon any payments made by Cara to Enteris under this Agreement, Cara shall (i) make such withholding payments as may be required, (ii) subtract such withholding payments from such payments, (iii) submit appropriate proof of payment of the withholding taxes to Enteris within a reasonable period of time, and (iv) promptly provide Enteris with all official receipts with respect thereto. Cara shall render Enteris reasonable assistance in order to allow Enteris to obtain the benefit of any present or future treaty against double taxation which may apply to such payments.

6.10 Foreign Currency Exchange. If, in any Calendar Quarter, Net Sales are made in any currency other than United States Dollars, such Net Sales shall be converted into United States Dollars by applying the exchange rate conversion consistently used by Cara in its audited consolidated accounts making use of a publicly available foreign exchange rate source.

6.11 Cara Obligations. Cara shall be solely responsible for all amounts it owes to any Third Party in connection with the Development, Manufacture, or Commercialization of Products in the Field in the Territory.

ARTICLE 7
REPRESENTATIONS AND WARRANTIES; COVENANTS; LIABILITY

7.1 Mutual. Enteris and Cara each represents and warrants to the other Party, as of the Effective Date, as follows:

(a) It is a corporation or company duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver and perform this Agreement.

(b) The execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action and will not violate (a) such Party's certificate of incorporation or bylaws, (b) any agreement, instrument or contractual obligation to which such Party is bound in any material respect, (c) any requirement of any Applicable Laws, or (d) any order, writ, judgment, injunction, decree, determination or award of any court or governmental agency presently in effect applicable to such Party.

(c) This Agreement is a legal, valid and binding obligation of such Party, enforceable against it in accordance with its terms and conditions, subject to all bankruptcy and other debtor laws and protections and to equitable principles.

(d) It is not under any obligation, contractual or otherwise, to any other person or entity that conflicts with or is inconsistent in any respect with the terms of this Agreement or that would impede the diligent and complete fulfillment of its obligations hereunder.

(e) Such Party has never been, and is not currently, a Debarred Entity. Each of the Parties further warrants and represents that no Debarred Entity has performed or rendered, any services or assistance on its behalf relating to activities contemplated or rights granted pursuant to this Agreement. Each Party certifies and covenants that it shall not use, in any capacity, a Debarred Entity in the performance of this Agreement. "**Debarred Entity**" for purposed of this Section 7.1(e) means a corporation, partnership or association that has been debarred by the FDA pursuant to 21 U.S.C. §335a (a) or (b) from submitting or assisting in the submission of any abbreviated drug application, or an employee, partner, shareholder, member, subsidiary or affiliate of a Debarred Entity.

7.2 By Cara. Cara represents, warrants, and covenants to Enteris that:

(a) All of its activities and the activities of its Affiliates and its Sub-licensees, related to its use and practice of the Licensed Technology and all Development, Manufacture and Commercialization of the Products pursuant to this Agreement, shall to its knowledge comply in all material respects with all Applicable Laws.

(b) Cara, its Affiliates, and to its knowledge its Sub-licensees, shall not encumber, with liens, mortgages, or security interests, the Licensed Technology, except as otherwise expressly permitted in this Agreement.

7.3 By Enteris.

(a) Enteris owns or has license rights to all the Licensed Technology existing as of the Effective Date. Enteris is entitled to grant the licenses specified in this Agreement. The Licensed Patent Rights existing as of the Effective Date constitute all of the Patent

Rights owned by or licensed to Enteris or its Affiliate as of the Effective Date that are necessary or reasonably useful to Develop, Manufacture, sell and otherwise Commercialize the Product. The Licensed Know-how existing as of the Effective Date constitute all of the Licensed Know-how owned by or licensed to Enteris or its Affiliate as of the Effective Date that are necessary or reasonably useful to Develop, Manufacture, sell and otherwise Commercialize the Product.

(b) To Enteris' knowledge, there is no actual or threatened infringement of the Licensed Technology in the Field by any Third Party;

(c) To Enteris' knowledge, the Licensed Patent Rights existing as of the Effective Date are subsisting and are not invalid or unenforceable, in whole or in part. As of the Effective Date, there are no claims, judgments, or settlements against, or amounts with respect thereto owed by, Enteris or any of its Affiliates relating to the Licensed Patent Rights that would have a material adverse effect on the license rights granted to Cara under this Agreement or on Cara's ability to use or practice such license rights;

(d) As of the Effective Date, no claim or litigation has been brought against Enteris or, to Enteris' knowledge, against any Third Party or, to Enteris' knowledge, threatened, alleging that (A) the Licensed Patent Rights are invalid or unenforceable; or (B) the Licensed Patent Rights or the licensing or exploiting of such Licensed Patent Rights violates, infringes, or other conflicts or interferes with any intellectual property or proprietary right of any Third Party, nor is there any reasonable basis for any such claim; or (C) the Licensed Know-how has been misappropriated; or (D) the Licensed Know-how or the licensing or exploiting of such Licensed Know-how violates, misappropriates, or otherwise conflicts or interferes with any intellectual property or proprietary right of any Third Party;

(e) The practice or use of the Licensed Technology (including in the Manufacture or Commercialization of Products) does not, and to the knowledge of Enteris shall not, result in any payment obligation by Cara (of any royalty, milestone payment or other license fee), other than the payments due to Enteris under this Agreement, to any Third Party;

(f) Neither Enteris, nor any of its Affiliates, has granted any mortgage, pledge, claim, security interest, encumbrance, lien, or other charge of any kind (collectively, "**liens**" and each a "**lien**") on any of the Licensed Technology anywhere in the Territory, and the Licensed Patents and Licensed Know-how are free and clear of all liens in the Territory; except with respect to (i) any such liens on the Licensed Technology that are junior in priority to the rights of a licensee in ordinary course of business, or (ii) liens on revenue received under this Agreement.

(g) Within [***] of the Effective Date of this Agreement, Enteris shall have provided to Cara all material documentation, data, and information under its control requested by Cara relating to the Licensed Know-how and the use thereof in formulations, including all material safety information. All information and data provided by or on

behalf of Enteris to Cara as set forth in this Section 7.3(g) in contemplation of this Agreement or the transactions contemplated hereby is, to Enteris' knowledge, true, accurate and complete in all material respects, and Enteris shall not knowingly fail to disclose any material information or data in Enteris' (or its Affiliate's) control that could be reasonably expected to cause the Enteris information or data that has been disclosed to Cara to be misleading in any material respect.

7.4 Warranty Disclaimer. EXCEPT FOR THE EXPRESS WARRANTIES PROVIDED IN THIS AGREEMENT, NEITHER PARTY MAKES ANY WARRANTY, EXPRESS OR IMPLIED, WITH RESPECT TO ANY KNOW-HOW, PATENT RIGHTS OR OTHER SUBJECT MATTER OF THIS AGREEMENT, AND EACH PARTY HEREBY DISCLAIMS ALL SUCH OTHER WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT.

7.5 Indemnification; Insurance.

(a) Cara shall indemnify, defend and hold harmless Enteris and its Affiliates, and their respective directors, officers, employees and agents, and their respective successors, heirs and assigns (collectively, the "**Enteris Indemnitees**"), against all liabilities, damages, losses and expenses (including reasonable attorneys' fees and expenses of litigation) (collectively, "**Losses**") incurred by or imposed upon the Enteris Indemnitees, or any of them, as a direct result of claims, suits, actions, demands or proceedings ("**Claims**") brought by a Third Party against Enteris Indemnitees, including, personal injury and product liability claims (collectively, "**Enteris Indemnity Claims**"), to the extent arising out of (i) the Development, Manufacture and/or Commercialization of any Product by Cara or any of its Affiliates, Sub-licensees and/or agents in the Territory, including warranty claims or Product recalls; (ii) any breach of this Agreement by Cara or any of its Affiliates, Sub-licensees or agents; (iii) any tort claims for the death, personal injury, or illness of any person or claims relating to any damage to any property related in any way to the rights granted under this Agreement or activities conducted by or on behalf of Cara, its Affiliates or Sub-licensees and their respective directors, officers, employees and agents, in connection with this Agreement; except, in each case, to the extent such Claim or Loss is caused by a breach by Enteris of its representations, warranties, covenants or obligations in this Agreement, or the gross negligence or willful misconduct of any Enteris Indemnitee; or (iv) the gross negligence or willful misconduct of any Cara Indemnitee, or agent of Cara; *but excluding* any Enteris Indemnity Claim or Losses to the extent that Enteris has an obligation to indemnify Cara Indemnitees pursuant to Section 7.5(b), as to which Claim or Losses each Party shall indemnify the other to the extent of their respective liability for such Losses.

(b) Enteris shall indemnify, defend and hold harmless Cara, its Affiliates and Sub-licensees, and their respective directors, officers, employees and agents, and their respective successors, heirs and assigns (collectively, the "**Cara Indemnitees**"), against all Losses incurred by or imposed upon the Cara Indemnitees, or any of them, as a direct result of claims, suits, actions, demands or proceedings brought by a Third Party against

Cara Indemnitees, including personal injury and product liability claims (collectively, "**Cara Indemnity Claims**") to the extent arising out of (i) any breach of this Agreement by Enteris or any of its Affiliates or agents, except, in each case, to the extent such Claim is caused by a breach by Cara of its representations, warranties, covenants or obligations in this Agreement, or the gross negligence or willful misconduct of any Cara Indemnitee; or (ii) the gross negligence or willful misconduct of any Enteris Indemnitee; or (iii) infringement or violation of Third Party intellectual property rights to the extent due to the use or practice of the Licensed Technology; *but excluding* any Cara Indemnity Claim or Losses to the extent that Cara has an obligation to indemnify any Enteris Indemnitees pursuant to Section 7.5(a) as to which Claims or Losses each Party shall indemnify the other to the extent of their respective liability for such Losses.

(c) Upon receipt of notice of any Loss, or of any claim, suits, action, demand or proceeding, that may give rise to a right of indemnity from the other Party hereto, the Party seeking indemnification (the "**Indemnified Party**"), either on behalf of itself or, as applicable, for a member of its group entitled to such indemnity (an "**Indemnified Member**"), shall give prompt written notice to the other Party (the "**Indemnifying Party**") of the Loss (or related claim, action, or allegation) for which indemnification is sought (a "**Claim**"). Provided that the Indemnifying Party is not contesting its obligation to indemnify as to the noticed Claim under this Article 7, the Indemnified Party (and the Indemnified Member, as applicable) shall permit the Indemnifying Party to control any the defense of such Claim and any litigation relating to such Claim and all related Losses and the disposition of such Claim and Losses. The Indemnifying Party shall (i) act reasonably and in good faith with respect to all matters relating to the settlement or disposition of such Claim and all related Losses as the settlement or disposition relates to such Indemnified Party and (ii) not settle or otherwise resolve such Claim and related Losses in a way that would adversely impact the Indemnified Party (or the Indemnified Member, as applicable) without the prior written consent of such Indemnified Party (which consent shall not be unreasonably withheld, conditioned or delayed). Each Indemnified Party (and all applicable Indemnified Members) shall cooperate with the Indemnifying Party in its defense of any such Claim and related Losses in all reasonable respects and shall have the right to be present in person or through counsel at all legal proceedings with respect to such Claim and Loss. If the Indemnifying Party does not assume and conduct the defense of the Claim and Loss as provided above, (a) the Indemnified Party may defend against, consent to the entry of any reasonable judgment, or enter into any reasonable settlement with respect to such Loss in any manner the Indemnified Party may deem reasonably appropriate (and the Indemnified Party need not consult with, or obtain any consent from, the Indemnifying Party in connection therewith), and (b) the Indemnifying Party shall remain responsible to indemnify the Indemnified Party as provided in this Article 7.

(d) Limited Liability. EXCEPT FOR LIABILITY ARISING FROM A PARTY'S BREACH OF CONFIDENTIALITY OBLIGATIONS HEREUNDER, NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY OR ANY OF ITS AFFILIATES FOR ANY SPECIAL, PUNITIVE, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, INCLUDING LOST PROFITS OR LOST REVENUES, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH

DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 7.5(d) IS INTENDED TO OR SHALL LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER SECTION 7.5(a) OR 7.5(b).

(e) Cara shall procure and maintain insurance, including product liability insurance, or shall self-insure, in each case in a manner adequate to cover its obligations under this Agreement and consistent with normal business practices of prudent companies similarly situated at all times during the Term and for a period of [***] thereafter. Such insurance shall provide that the policy is primary and not in excess or contributory with regard to other insurance Enteris may have. Cara shall provide Enteris with written evidence of such insurance or self-insurance upon request. Cara shall provide Enteris with written notice at least [***] prior to the cancellation, non-renewal or material change in such insurance.

7.6 The terms of this Article 7 shall survive termination of this Agreement for whatever reason.

ARTICLE 8
TERM AND TERMINATION

8.1 Term. This Agreement shall commence on the Effective Date, and shall continue in full force and effect until the earlier of (i) the expiration of the Agreement upon the expiration or termination of all payment obligations under this Agreement with respect to the last Product in all countries in the Territory, or (ii) the termination of this Agreement by either Party pursuant to Sections 8.3 through 8.5, inclusive (the "**Term**").

8.2 Expiration of Term. Upon expiry of the Term pursuant to clause (i) of Section 8.1, all rights and licenses granted to Cara under this Agreement in respect of Products shall become fully paid-up and irrevocable with respect to all countries in the Territory.

8.3 Termination for Material Breach. A Party may terminate this Agreement by notice in writing to the other Party if such other Party materially breaches its obligations under the Agreement, and does not cure such breach, in accordance with the following: In the case of such material breach, the non-breaching Party may provide the breaching Party with a written notice specifying in reasonable detail the nature of the material breach, and stating its intention to terminate this Agreement if such breach is not cured. If the material breach is not cured within sixty (60) days (or thirty (30) days with respect to a material breach of a payment obligation) after the receipt of such notice, the non-breaching Party shall be entitled, without prejudice to any of its other rights under this Agreement, and in addition to any other remedies available to it by law or in equity, to terminate this Agreement by providing written notice to the other Party, such notice to be provided no later than [***] after the end of the cure period (and subject to Article 11).

8.4 Termination for Challenge Enteris shall have the right to terminate this Agreement upon written notice to Cara, if all the following criteria are met: (a) Cara or any of its

Affiliates formally Challenges the validity of any Licensed Patent Rights or Assists a Third Party in initiating a Challenge of any Licensed Patent Rights, and (b) Enteris provides Cara written notice that it intends to terminate this Agreement as a result of such Challenge by Cara (or its Affiliate), or of such Assist by Cara of a Third Party Challenge. Such termination by Enteris shall become effective thirty (30) days after notice of termination to Cara (but subject to Article 11), unless Cara has withdrawn such Challenge of such Licensed Patent Rights or ceased providing such Assist to the Third Party (as applicable). The notice provided by Enteris must provide the details of Enteris' belief that Cara has initiated, or has Assisted in the initiation of, such a Challenge. If a Sub-licensee of Cara, or a Sub-licensee of Cara's Sub-licensee, initiates a Challenge of any Licensed Patent Rights, then Cara shall, upon written notice from Enteris, terminate such sublicense or direct Cara's Sub-licensee to do so, unless such Sub-licensee has ceased such Challenge within thirty (30) days of such written notice.

8.5 Without Cause Termination. Cara may terminate this Agreement for any reason or no reason: (a) prior to receipt of first Regulatory Approval for a Product in the United States for any indication upon thirty (30) days prior written notice to Enteris or (b) on or after receipt of first Regulatory Approval for a Product in the United States for any indication upon sixty (60) days prior written notice to Enteris.

8.6 Consequences of Termination. Upon early termination of this Agreement pursuant to clause (ii) of Section 8.1 for any reason (but not upon expiration of the Term pursuant to clause (i) of Section 8.1), in addition to any remedies available to a Party at law or in equity, the following provisions shall apply, as applicable:

(a) all licenses and rights granted by Enteris to Cara pursuant to this Agreement, including the licenses and rights granted to Cara under Section 2.1 shall terminate as of the effective date of termination;

(b) Cara shall not use or practice any issued Licensed Patent Rights or, to the extent consisting of Enteris Confidential Information, any Licensed Know-how that, in each case, are incorporated into any Product for any purpose;

(c) Cara shall cease all Commercialization and Development activities with respect to the Products (except as otherwise provided in this Section) and shall diligently wind down, according to good clinical practice, any clinical trials of such Product(s) that are ongoing at the time of notice of such termination or expiration, to the extent any such activities would use or practice issued claims in the Licensed Patent Rights, or Enteris Confidential Information or Licensed Know-how that is not subject to the exceptions in subclauses (a) – (e) of Section 4.1;

(d) all reference rights granted by Enteris to Cara under this Agreement shall cease, including Cara's right to reference the Enteris DMF, the contents therein, and any set of documents referencing the Enteris DMF, in any Regulatory Filings, and (1) such Regulatory Filings referencing the Enteris DMF or the contents therein shall immediately be withdrawn with appropriate notification to the Regulatory Authority, and (2) all copies (in any form, including electronic) of documents referencing the Enteris DMF which have

been provided to Third Parties shall be sequestered until the applicable retention period of the Regulatory Authority expires and shall thereafter be promptly destroyed; and

(e) each Party shall cease use of, and promptly return, all Confidential Information of the other Party that are not subject to a continuing license hereunder; provided, that, each Party may retain one (1) copy of the Confidential Information of the other Party in its archives solely for the purpose of establishing the contents thereof and ensuring compliance with its obligations hereunder.

(f) Except in the event Enteris terminates this Agreement pursuant to this Article 8, Cara and its Affiliates and Sub-licensees shall be entitled, during the [***] period following such termination, to continue to sell any commercial inventory of such terminated Product(s) so long as Cara pays to Enteris the amounts applicable to said subsequent sales in accordance with the terms and conditions set forth in this Agreement. Any drug substance, clinical supplies and finished forms of such terminated Product(s) remaining following such [***] period shall be destroyed.

8.7 **Survival** Termination or expiration of this Agreement for any reason shall be without prejudice to: (a) any obligations of the Parties that arose or accrued prior to the effective date of such termination; (b) the survival of rights specifically stated in this Agreement to survive; (c) the rights and obligations of the Parties provided in Article 1, Article 4, Article 5, Article 10, Article 11, Article 13, Sections 3.5, 3.63.6, 6.5, 6.7, 6.8, 6.9, 6.10, 6.11, 7.5, 8.2, 8.6, 8.7, 12.1-12.8 (including all other Sections referenced in any such Section), all of which shall survive such termination except as provided in this Article 8; and (d) any other rights or remedies provided at law or equity which either Party may otherwise have.

ARTICLE 9
ASSIGNMENT; SUCCESSORS AND ASSIGNS

9.1 Neither Party shall be entitled to assign, transfer, charge or in any way make over the benefit and/or the burden of this Agreement without the prior written consent of the other, which consent shall not be unreasonably withheld, conditioned or delayed, except that (a) each Party shall be entitled without the prior written consent of the other Party to assign this Agreement and the rights, obligations and interests thereunder to (i) an Affiliate, provided that the assigning Party shall remain liable and responsible to the non-assigning Party for the performance and observance of all such duties and obligations by such Affiliate, or (ii) its successor in interest in connection with a sale, merger, or acquisition of all or substantially all of the assets of its business to which this Agreement relates and (b) Enteris shall be entitled without the prior written consent of Cara to (i) pledge, grant a security interest, lien or charge in, or other encumbrance upon, any of its rights or interests in this Agreement (and may assign this Agreement or the rights hereunder, in whole or in part in connection with any of the foregoing), including without limitation pursuant to the terms of any secured indebtedness (and any amendment, restatement, replacement or refinancing thereof) and any related documents, and (ii) assign all or a portion of its rights and interests to receive any payments pursuant to Article 6 to its current or former shareholders, provided, however, in such event, Cara shall, in accordance with Article 6, continue to make such payments directly to Enteris (who shall receive such payments on behalf of, and as agent for, such

current or former shareholders, to the extent of the payment rights and interests so assigned). Any attempted assignment in violation of this Article 9 shall be null and void.

9.2 The terms and conditions of this Agreement shall be binding on and inure to the benefits of permitted successors and assigns of each Party.

ARTICLE 10
GOVERNING LAW

10.1 This Agreement shall be construed, governed and interpreted in accordance with the laws of the State of New York without regard to the application of its principles of conflict of law.

ARTICLE 11
DISPUTE RESOLUTION; ARBITRATION

11.1 Dispute Resolution. If a dispute or issues arises between the Parties regarding any matter under this Agreement, including interpretation of a provision of the Agreement or performance or breach of an obligation hereunder, (a "Dispute") then on notice from either Party detailing such Dispute, the senior executive officers of each Party shall promptly meet and discuss and seek to resolve, reasonably and in good faith, such Dispute, for a period of up to [***] from the date of receipt of such notice. Any resolution by the Parties of such a Dispute shall be set forth in writing acknowledged by the Parties. Neither Party shall initiate any court or other legal proceeding to resolve or enforce its rights as to, any Dispute except as provide in this Article 11.

11.2 Arbitration of Unresolved Disputes. For any Dispute that is not resolved by the Parties pursuant to Section 11.1 above, such Dispute shall be resolved, at the election of either Party, by binding arbitration before a panel of three (3) neutral, fully independent arbitrators in accordance with the rules of the American Arbitration Association ("**AAA**") in effect at the time the proceeding is initiated, by such Party providing written notice of the arbitration, such notice setting forth in detail the Dispute to be resolved. In any such arbitration, the following procedures shall apply:

(a) The panel will be comprised of one arbitrator chosen by Cara, one by Enteris and the third, who shall act as the chairman of the panel, by the two co-arbitrators. If either Party fails or both Parties fail to choose an arbitrator or arbitrators within [***] after receiving notice of commencement of arbitration or if the two arbitrators fail to choose a third arbitrator within [***] after their appointment, then either or both Parties shall immediately request that the AAA select the remaining number of arbitrators to be selected, which arbitrator(s) shall have the requisite scientific background, experience and expertise. All such arbitrators must have no current or prior relationship with or to either Party and all its respective Affiliates, be neutral and unbiased as to the subject matter of the Dispute, and have significant experience in the creation and interpretation of license agreements similar to this Agreement. The place of arbitration shall be New York, New York. The language of the arbitration shall be English.

(b) Either Party may apply to the arbitrators for interim injunctive relief until the arbitration decision is rendered or the Dispute is otherwise resolved. Either Party also may, without waiving any right or remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect the rights or property of that Party pending resolution of the Dispute pursuant to this Section 11.2. The arbitrators shall have no authority to award punitive or any other type of damages not measured by a Party's compensatory damages.

(c) The award of the arbitrators shall be final and binding on the parties (except for those remedies expressly set forth in this Agreement). Judgment on the award rendered by the arbitrators may be entered in any court having jurisdiction thereof. Notwithstanding anything in this Section 11.2 to the contrary, each Party shall have the right to institute judicial proceedings against the other Party or anyone acting by, through or under such other Party, in order to enforce the instituting Party's rights hereunder through specific performance, injunction or similar equitable relief.

(d) Each Party shall bear its own costs and expenses and attorneys' fees in connection with any such arbitration; provided, that, the arbitrators shall be authorized to determine whether a Party is the prevailing Party, and if so, to award to the prevailing Party reimbursement for its reasonable attorneys' fees, costs and expenses (including, for example, expert witness fees and expenses, photocopy charges and travel expenses).

(e) Unless otherwise agreed by the parties, Disputes relating to patents and non-disclosure, non-use and maintenance of Confidential Information shall not be subject to arbitration, and shall be submitted to a court of competent jurisdiction.

(f) The arbitration shall be confidential. Except to the extent necessary to confirm an award or decision or as may be required by Applicable Laws, neither Party nor any arbitrator may disclose the existence or results of any arbitration without the prior written consent of both parties. In no event shall any arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the Dispute would be barred by the applicable New York statute of limitations.

(g) In the event of a Dispute involving the alleged breach of this Agreement (including whether a Party has satisfied its diligence obligations hereunder), (i) the running of the time periods as to which a Party must cure a breach of this Agreement shall be tolled during the period the breach that is the subject matter of the Dispute is being arbitrated, and (ii) if the arbitrators render a decision that a breach of this Agreement has occurred, the arbitrators shall have no authority to modify the right of the non-breaching Party to terminate this Agreement in accordance with Section 8.3. Any disputed performance or suspended performance, pending the resolution of a Dispute that the arbitrators determine to be required to be performed by a Party, shall be completed within a reasonable time period following the final decision of the arbitrators.

(h) Any monetary payment to be made by a Party pursuant to a decision of the arbitrators shall be made in U.S. dollars, free of any tax or other deduction.

ARTICLE 12
MISCELLANEOUS

12.1 Amendment and Modification. This Agreement may only be amended, modified, or supplemented by an agreement in writing signed by each Party hereto.

12.2 Headings. Section and subsection headings are inserted for convenience of reference only and do not form a part of this Agreement.

12.3 Counterparts. This Agreement may be executed simultaneously in two or more counterparts, each of which shall be deemed an original and both of which, together, shall constitute a single agreement. Each Party may execute this Agreement by facsimile transmission or in Adobe™ Portable Document Format ("PDF") sent by electronic mail. In addition, facsimile or PDF signatures of authorized signatories of any Party will be deemed to be original signatures and will be valid and binding, and delivery of a facsimile or PDF signature by any Party will constitute due execution and delivery of this Agreement. This Agreement may be amended, modified, superseded or canceled, and any of the terms of this Agreement may be waived, only by a written instrument executed by each Party or, in the case of waiver, by the Party or parties waiving compliance. The delay or failure of either Party at any time or times to require performance or to exercise any right arising out of any provisions shall in no manner affect the rights at a later time to enforce the same.

12.4 Waiver. Any waiver by a Party of a particular provision or right shall be in writing, shall be as to a particular matter and, if applicable, for a particular period of time and shall be signed by such Party. No single or partial exercise of any right, power or privilege will preclude any other or further exercise of such right, power or privilege or the exercise of any other right, power or privilege. No waiver by either Party of any condition or of the breach of any term contained in this Agreement, whether by conduct, or otherwise, in any one or more instances, shall be deemed to be, or considered as, a further or continuing waiver of any such condition or of the breach of such term or any other term of this Agreement. Except as otherwise expressly set forth in this Agreement, all rights and remedies available to a Party, whether under this Agreement or afforded by Applicable Law or otherwise, will be cumulative and not in the alternative to any other rights or remedies that may be available to such Party.

12.5 No Third Party Beneficiaries. Except as set forth in Sections 7.5(a) and 7.5(b) and in Article 9, no Third Party (including employees of either Party) shall have or acquire any rights by reason of this Agreement.

12.6 Independent Relationship. The Parties understand and agree that the relationship between the Parties to this Agreement is purely contractual and is limited to the activities, rights and obligations as set forth in this Agreement. Nothing in this Agreement shall be construed (a) to create or imply a general partnership between the parties, (b) to make either Party the agent of the other for any purpose, (c) to alter, amend, supersede or vitiate any other arrangements between the Parties with respect to any subject matter not covered hereunder, (d) to give either Party the right to bind the other, (e) to create any duties or obligations between the

parties except as expressly set forth herein, or (f) to grant any direct or implied licenses or any other rights other than as expressly set forth herein.

12.7 Interpretation. The Parties acknowledge and agree that: (a) each Party and its counsel reviewed and negotiated the terms and provisions of this Agreement and have contributed to its revision; and (b) the rules of construction to the effect that any ambiguities are resolved against the drafting Party shall not be employed in the interpretation of this Agreement. In addition, unless a context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders, the word "or" is used in the inclusive sense (and/or) and the word "including" is used without limitation and means "including without limitation". Unless otherwise specified, references in this Agreement to any Section shall include all Sections, subsections and paragraphs in such Section, references to any Section shall include all subsections and paragraphs in such Section, and references in this Agreement to any subsection shall include all paragraphs in such subsection. The words "herein," "hereof" and "hereunder" and other words of similar import refer to this Agreement as a whole and not to any particular Section or other subdivision. All references to days in this Agreement shall mean calendar days, unless otherwise specified. Unless the context requires otherwise, (i) any definition of or reference to any agreement, instrument or other document herein will be construed as referring to such agreement, instrument or other document as from time to time amended, supplemented or otherwise modified (subject to any restrictions on such amendments, supplements or modifications set forth herein or therein), (ii) any reference to any Applicable Laws herein will be construed as referring to such Applicable Laws as from time to time enacted, repealed or amended, (iii) any reference herein to any person will be construed to include the person's successors and permitted assigns, (iv) any reference herein to the words "mutually agree" or "mutual written agreement" will not impose any obligation on either Party to agree to any terms relating thereto or to engage in discussions relating to such terms except as such Party may determine in such Party's sole discretion, (v) all references herein to Sections or Exhibits will be construed to refer to Sections and Exhibits to this Agreement, (vi) except as otherwise expressly provided herein all references to "$" or "dollars" refer to the lawful money of the U.S., and (vii) the words "copy" and "copies" and words of similar import when used in this Agreement include, to the extent available, electronic copies, files or databases containing the information, files, items, documents or materials to which such words apply. This Agreement has been prepared in the English language and the English language shall control its interpretation. In addition, all notices required or permitted to be given hereunder, and all written, electronic, oral or other communications between the parties regarding this Agreement shall be in the English language.

12.8 Entire Agreement; Severability. This Agreement and the Stock Purchase Agreement set forth the entire agreements between the Parties with respect to the subject matter of this Agreement and of such Stock Purchase Agreement and supersede all other agreements and understandings between the Parties with respect to such subject matter. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties with respect to the subject matter of this Agreement other than as are set forth in this Agreement and any other documents delivered pursuant hereto or thereto. If any provision of this Agreement is or becomes invalid or is ruled invalid by any court of competent jurisdiction or is deemed unenforceable, it is the intention of the parties that the remainder of the Agreement shall not be affected.

12.9 Delay Due to Force Majeure. A Party shall not be liable for failure of or delay in performing any of its obligations set forth in this Agreement, and shall not be deemed in breach of such obligations, if such failure or delay is due to a Force Majeure. In the event of such Force Majeure, the Party affected shall use Commercially Reasonable Efforts to cure or overcome the same and resume performance of its obligations hereunder. Notice of a Party's failure or delay in performance due to Force Majeure must be given to the other Party within thirty (30) days after the affected Party becomes aware of its occurrence. All delivery dates under this Agreement that have been affected by Force Majeure shall be tolled for the duration of such Force Majeure. If a Force Majeure persists for more than ninety (90) days, then the Parties will discuss in good faith the reasonable modification of the Parties' respective obligations under this Agreement in order to mitigate the delays caused by such Force Majeure and the impacts of such delays.

12.10 Further Assurances. Each of Enteris and Cara, upon the reasonable request of the other Party, whether before or after the Effective Date, will do, execute, acknowledge, and deliver or cause to be done, executed, acknowledged or delivered all such further reasonable acts, deeds, documents, assignments, transfers, conveyances, powers of attorney, instruments and assurances as may be reasonably necessary to effect complete consummation of the transactions contemplated by this Agreement, and to do all such other reasonable acts, as may be necessary or reasonably needed in order to carry out the purposes and intent of this Agreement. The Parties agree to execute and deliver such other reasonable documents, certificates, agreements and other writings and to take such other reasonable actions as may be reasonably necessary in order to consummate or implement expeditiously the transactions contemplated by this Agreement.

12.11 Expenses. Each of the Parties will bear its own direct and indirect expenses incurred in connection with the negotiation and preparation of this Agreement and, except as set forth in this Agreement, the performance of the obligations contemplated hereby and thereby.

ARTICLE 13
NOTICE

13.1 Any notice or other documents to be given under this Agreement shall be in writing and shall be deemed to have been duly given if sent by registered post, courier, facsimile or other electronic media to a Party or delivered in person to a Party at the address or facsimile number set out below for such Party or such other address as the Party may from time to time designate by written notice to the other(s):

Address of Enteris:

Enteris Biopharma, Inc., 83 Fulton St., Boonton, NJ 07005, USA
Facsimile: [***]
E-mail: [***]
For the attention of the President & CFO

Address of Cara:

Cara Therapeutics, Inc.
4 Stamford Plaza
107 Elm Street, 9th Floor
Stamford, CT 06902

Facsimile: [***]
E-mail: [***]
For the attention of: Chief Executive Officer

With a copy to:

Cara Therapeutics, Inc.
4 Stamford Plaza
107 Elm Street, 9th Floor
Stamford, CT 06902

Facsimile: [***]
E-mail: [***]
For the attention of: General Counsel

13.2 Any such notice or other document shall be deemed to have been received by the addressee seven (7) working days following the date of dispatch of the notice or other document by post or, where the notice or other document is sent by hand or is given by facsimile or other electronic media or transmission, simultaneously with the transmission or delivery.

IN WITNESS WHEREOF, the hands of the duly authorized representatives of the Parties have caused this License Agreement to be executed effective as of the Effective Date.

Signed for and on behalf of

/s/ Brian Zietsman

ENTERIS BIOPHARMA, INC.

NAME Brian Zietsman
TITLE President & CFO

Signed for and on behalf of
CARA THERAPEUTICS, INC.

/s/ Derek Chalmers

NAME Derek Chalmers
TITLE CEO

EXHIBIT A

Wire Instructions

EXHIBIT B

Form Stock Purchase Agreement

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.

EXHIBIT C

Project Plan
Transfer of Analytical Procedures and Manufacturing Process

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: November 5, 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: November 5, 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 September 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: November 5, 2019

/s/ MANI MOHINDRU
Name: Mani Mohindru, Ph.D.
Title: Chief Financial Officer
Date: November 5, 2019