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 MARCH 31, 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

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.

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

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of May 2, 2019 was: 39,751,606.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED MARCH 31, 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)

	March 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 14,188	$ 15,081
Marketable securities	120,265	146,302
Income tax receivable	749	664
Other receivables	1,019	926
Prepaid expenses	7,577	4,805
Restricted cash, current	361	361
Total current assets	144,159	168,139
Operating lease right-of-use asset	3,492	—
Marketable securities, non-current	21,687	21,396
Property and equipment, net	841	880
Restricted cash	408	408
Total assets	$ 170,587	$ 190,823
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 13,310	$ 13,622
Operating lease liability, current	901	—
Current portion of deferred revenue	28,194	26,825
Total current liabilities	42,405	40,447
Operating lease liability, non-current	4,087	—
Deferred revenue, non-current	9,573	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 March 31, 2019 and December 31, 2018, zero shares issued and outstanding at March 31, 2019 and December 31, 2018	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at March 31, 2019 and December 31, 2018, 39,575,044 shares and 39,547,558 shares issued and outstanding at March 31, 2019 and December 31, 2018, respectively	39	39
Additional paid-in capital	430,724	428,059
Accumulated deficit	(316,314)	(294,354)
Accumulated other comprehensive income (loss)	73	(114)
Total stockholders' equity	114,522	133,630
Total liabilities and stockholders' equity	$ 170,587	$ 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	
	March 31, 2019	**March 31, 2018**
Revenue:		
License and milestone fees	$ 4,242	$ —
Clinical compound revenue	140	—
Total revenue	4,382	—
Operating expenses:		
Research and development	23,608	13,427
General and administrative	3,908	3,697
Total operating expenses	27,516	17,124
Operating loss	(23,134)	(17,124)
Other income	1,089	311
Loss before benefit from income taxes	(22,045)	(16,813)
Benefit from income taxes	85	46
Net loss	$ (21,960)	$ (16,767)
Net loss per share:		
Basic and Diluted	$ (0.56)	$ (0.51)
Weighted average shares:		
Basic and Diluted	39,552,277	32,681,661
Other comprehensive income (loss), net of tax of $0:		
Change in unrealized gains (losses) on available-for-sale marketable securities	187	(44)
Total comprehensive loss	$ (21,773)	$ (16,811)

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2017	32,662,255	$ 33	$ 307,158	$ (220,341)	$ (70)	$ 86,780
Stock-based compensation expense	—	—	1,871	—	—	1,871
Shares issued upon exercise of stock options	37,688	—	263	—	—	263
Net loss	—	—	—	(16,767)	—	(16,767)
Other comprehensive loss	—	—	—	—	(44)	(44)
Balance at March 31, 2018	32,699,943	$ 33	$ 309,292	$ (237,108)	$ (114)	$ 72,103

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2018	39,547,558	$ 39	$ 428,059	$ (294,354)	$ (114)	$ 133,630
Stock-based compensation expense	—	—	2,234	—	—	2,234
Shares issued upon exercise of stock options	17,291	—	234	—	—	234
Shares issued for consulting services	10,195	—	197	—	—	197
Net loss	—	—	—	(21,960)	—	(21,960)
Other comprehensive income	—	—	—	—	187	187
Balance at March 31, 2019	39,575,044	$ 39	$ 430,724	$ (316,314)	$ 73	$ 114,522

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Three Months Ended	
	March 31, 2019	**March 31, 2018**
Operating activities		
Net loss	$ (21,960)	$ (16,767)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	2,234	1,871
Depreciation and amortization	50	125
Amortization expense component of lease expense	145	—
Accretion of available-for-sale marketable securities	(478)	(217)
Realized loss on sale of available-for-sale marketable securities	—	15
Deferred rent costs	—	(61)
Deferred revenue	(4,242)	—
Changes in operating assets and liabilities:		
Income tax receivable	(85)	(46)
Other receivables	(93)	39
Prepaid expenses	(2,574)	(1,796)
Accounts payable and accrued expenses	(312)	(1,631)
Operating lease liability	(211)	—
Net cash used in operating activities	(27,526)	(18,468)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	79,295	26,650
Proceeds from sale of available-for-sale marketable securities	—	10,850
Purchases of available-for-sale marketable securities	(52,885)	(16,804)
Purchases of property and equipment	(11)	(2)
Net cash provided by investing activities	26,399	20,694
Financing activities		
Proceeds from the exercise of stock options	234	263
Net cash provided by financing activities	234	263
Net (decrease) increase in cash, cash equivalents and restricted cash	(893)	2,489
Cash, cash equivalents and restricted cash at beginning of period	15,850	10,157
Cash, cash equivalents and restricted cash at end of period	$ 14,957	$ 12,646
Noncash investing and financing activities		
Shares of common stock issued in exchange for consulting services (recorded as a prepaid expense)	$ 197	$ —

See Notes to Condensed Financial Statements.

1. Business

Cara Therapeutics, Inc., or the Company, is a clinical-stage biopharmaceutical corporation formed on July 2, 2004. The Company is focused on developing and commercializing new chemical entities with a primary focus on pruritus as well as pain 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, including conducting preclinical studies and clinical trials of CR845/difelikefalin-based product candidates and raising capital.

As of March 31, 2019, the Company had raised aggregate net proceeds of approximately $383,200 from several rounds of equity financing, including its initial public offering, or IPO, which closed in February 2014 and three follow-on public offerings of common stock, which closed in July 2018, April 2017 and August 2015, and the issuance of convertible preferred stock and debt prior to the IPO. The Company had also received $88,900 under its license agreements for CR845/difelikefalin, primarily with Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceutical Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and an earlier product candidate for which development efforts ceased in 2007. Additionally, in May 2018, the Company received net proceeds of $14,556 from the issuance and sale of 1,174,827 shares of the Company's common stock to Vifor (International) Ltd., or Vifor, in connection with the Company's license agreement with VFMCRP (see Note 10, *Collaboration and Licensing Agreements*).

As of March 31, 2019, the Company had unrestricted cash and cash equivalents and marketable securities of $156,140 and an accumulated deficit of $316,314. 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 $21,960 and $16,767 for the three months ended March 31, 2019 and 2018, respectively, and had net cash used in operating activities of $27,526 and $18,468 for the three months ended March 31, 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.

Use of Estimates

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

Significant Accounting Policies

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

Accounting Pronouncements Recently Adopted

Leases

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

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

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

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

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

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

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

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

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

Other Accounting Pronouncements Recently Adopted

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

Accounting Pronouncements Not Yet Adopted

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

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

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

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, cash flows or footnote disclosures.

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. ASU 2016-13 will be effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. As such, the Company expects to adopt ASU 2016-13 on January 1, 2020 and is currently evaluating the effect it will have on its results of operations, financial position and cash flows.

3. Available-for-Sale Marketable Securities

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

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

As of March 31, 2019

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 15,921	$ 16	$ —	$ 15,937
U.S. government agency obligations	12,440	7	—	12,447
Corporate bonds	69,914	56	(10)	69,960
Commercial paper	38,104	6	(2)	38,108
Municipal bonds	5,500	—	—	5,500
Total available-for-sale marketable securities	$ 141,879	$ 85	$ (12)	$ 141,952

As of December 31, 2018

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

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

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

The Company classifies its marketable debt securities based on their contractual maturity dates. As of March 31, 2019, the Company's marketable debt securities mature at various dates through March 2021. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows.

	As of March 31, 2019		As of December 31, 2018	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 120,201	$ 120,265	$ 146,363	146,302
One year to two years	21,678	21,687	21,449	21,396
Total	$ 141,879	$ 141,952	$ 167,812	$ 167,698

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

As of March 31, 2019

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Corporate bonds	$ 14,761	$ (10)	$ —	$ —	$ 14,761	$ (10)
Commercial paper	15,884	(2)	—	—	15,884	(2)
Total	$ 30,645	$ (12)	$ —	$ —	$ 30,645	$ (12)

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 March 31, 2019 and December 31, 2018, the Company held a total of 18 out of 73 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 March 31, 2019 and December 31, 2018. The Company does not intend to sell these debt securities before maturity and the Company believes it is not more likely than not that it will be required to sell these securities before the recovery of their amortized cost basis, which may be maturity.

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

4. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss), or AOCI, net of tax, from unrealized gains (losses) on available-for-sale marketable securities, the Company's only component of AOCI, for the three months ended March 31, 2019 and March 31, 2018.

	Total Accumulated Other Comprehensive Income (Loss)
Balance, December 31, 2018	$ (114)
Other comprehensive income before reclassifications	187
Amount reclassified from accumulated other comprehensive income	—
Net current period other comprehensive income	187
Balance, March 31, 2019	$ 73
Balance, December 31, 2017	$ (70)
Other comprehensive loss before reclassifications	(59)
Amount reclassified from accumulated other comprehensive loss	15
Net current period other comprehensive loss	(44)
Balance, March 31, 2018	$ (114)

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

Component of AOCI	Three Months Ended March 31, 2019	Three Months Ended March 31, 2018	Affected Line Item in the Statements of Operations
Unrealized gains (losses) on available-for-sale marketable securities			
Realized gains (losses) on sale of securities	$ —	$ (15)	Other income
	—	—	Benefit from income taxes
	$ —	$ (15)	

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

5. Fair Value Measurements

As of March 31, 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.

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

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 March 31, 2019 or December 31, 2018.

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

Fair value measurement as of March 31, 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	$ 14,188	$ 14,188	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	15,937	—	15,937	—
U.S. government agency obligations	12,447	—	12,447	—
Corporate bonds	69,960	—	69,960	—
Commercial paper	38,108	—	38,108	—
Municipal bonds	5,500	—	5,500	—
Restricted cash:				
Commercial money market account	769	769	—	—
Total financial assets	$ 156,909	$ 14,957	$ 141,952	$ —

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

Fair value measurement as of December 31, 2018:

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

There were no purchases, sales or maturities of Level 3 financial assets and no unrealized gains or losses related to Level 3 available-for-sale marketable securities for the three months ended March 31, 2019. There were no transfers of financial assets between Levels 1, 2, or 3 classifications during the three months ended March 31, 2019.

6. Restricted Cash

The Company is required to maintain a stand-by letter of credit as a security deposit under its lease for its office space in Stamford, Connecticut (refer to Note 15, *Commitments and Contingencies: Leases*). The fair value of the letter of credit approximates its contract value. The Company's bank requires the Company to maintain a restricted cash balance to serve as collateral for the letter of credit issued to the landlord by the bank. As of March 31, 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 is required to remain at $769 through May 19, 2019 and may, upon request from the Company, thereafter be reduced to $408 through the end of the lease term in November 2023. The reduction in the balance of the letter of credit for the Stamford Lease is contingent upon the Company not being in default of any provisions of that lease prior to the request for the reduction. As of March 31, 2019 and December 31, 2018, the Company had $361 of restricted cash related to the Stamford Lease in current assets and $408 in long-term assets, respectively.

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

	March 31, 2019	December 31, 2018
Cash and cash equivalents	$ 14,188	$ 15,081
Restricted cash, current assets	361	361
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 14,957	$ 15,850

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

7. Prepaid expenses

As of March 31, 2019, prepaid expenses were $7,577, consisting of $6,121 of prepaid R&D clinical costs, $920 of prepaid insurance and $536 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:

	March 31, 2019	December 31, 2018
Accounts payable	$ 4,943	$ 4,371
Accrued research projects	6,446	6,079
Accrued professional fees	721	802
Accrued compensation and benefits	1,200	2,370
Accrued other	—	—
Total	$ 13,310	$ 13,622

9. Stockholders' Equity

In order to fund future operations, including planned clinical trials, the Company filed a shelf registration statement on Form S-3 (File No. 333-230333), which the Securities and Exchange Commission, or SEC, declared effective on April 4, 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 this 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.

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

10. Collaboration and Licensing Agreements

Vifor Fresenius Medical Care Renal Pharma Ltd.

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

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

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

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

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

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

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

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

Maruishi Pharmaceutical Co., Ltd.

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

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

During the three months ended March 31, 2019, the Company recognized clinical compound revenue of $140 from the sale of clinical compound to Maruishi and as a result, the Company incurred R&D expense of $126 during the respective period. There were no clinical compound sales to Maruishi during the three months ended March 31, 2018.

Chong Kun Dang Pharmaceutical Corporation

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

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

11. Revenue Recognition

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

Contract balances

As of March 31, 2019, the Company had deferred revenue, current of $28,194 and deferred revenue, non-current of $9,573 related to the performance obligations from the VFMCRP Agreement and had no balances of receivables or other assets related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of March 31, 2019. As of December 31, 2018, the Company had deferred revenue, current of $26,825 and deferred revenue, non-current of $15,184 related to the performance obligations from the VFMCRP Agreement and no balances of receivables or other assets related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of December 31, 2018.

Performance obligations

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

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

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

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

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

Transaction price allocated to the remaining performance obligations

At inception of the VFMCRP Agreement, the entire transaction price of $55,444 was allocated to the one combined performance obligation, as described above. For the three months ended March 31, 2019, $4,242 was recognized as license and milestone fees revenue based on the percentage of R&D services that were completed during the period. As of March 31, 2019, $17,677 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 March 31, 2019, there were no remaining performance obligations under either the Maruishi Agreement or the CKDP Agreement, although the Company is eligible to receive milestone payments and sales royalties in the future.

Significant judgments

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

5. Determination of the timing of revenue recognition for contracts

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

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

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

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

Similarly, under the VFMCRP Agreement, revenue related to the single distinct performance obligation, which includes both granting of the license and performance of the R&D services, will be recognized as the R&D services are performed, based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation. The Company expects that the remaining amount of the transaction price that was allocated to the combined performance obligation of $37,767 at March 31, 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 months ended March 31, 2019 and 2018, no milestone events were probable of occurrence or achieved.

Sublicense payments

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

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

Sales-based Royalty Payments

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

a. The subsequent sale or usage occurs.

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

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

12. Net Loss Per Share

The Company computes basic net income (loss) per share by dividing net income (loss) by the weighted-average number of shares of common stock outstanding. Diluted net income per share includes the potential dilutive effect of common stock equivalents as if such securities were exercised during the period, when the effect is dilutive. Common stock equivalents may include outstanding stock options or restricted stock units, which are included using the treasury stock method when dilutive. For the three months ended March 31, 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 March 31,	
	2019	2018
Basic:		
Weighted average common shares outstanding	39,552,277	32,681,661
Diluted:		
Weighted average common shares outstanding - Basic	39,552,277	32,681,661
Common stock options*	—	—
Denominator for diluted net loss per share	39,552,277	32,681,661

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

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

	Three Months Ended March 31,	
	2019	2018
Net loss	$ (21,960)	$ (16,767)
Weighted-average common shares outstanding:		
Basic and Diluted	39,552,277	32,681,661
Net loss per share, Basic and Diluted	$ (0.56)	$ (0.51)

As of March 31, 2019 and 2018, 4,925,641 and 3,932,992 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, 215,000 restricted stock units granted during the three months ended March 31, 2019 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.

Restricted Stock Units

During the three months ended March 31, 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. Vesting of the restricted stock units will be contingent on the achievement of certain performance targets, subject to the recipient's continuous service through the vesting events. The Company has determined that the probability of achievement of the performance targets cannot be determined until they are achieved, and accordingly, the Company intends to recognize compensation expense associated with these awards when, and to the extent, the restricted stock units vest in accordance with achievement of the performance targets. As of March 31, 2019, none of the restricted stock units had vested and, consequently, no compensation expense has been recognized.

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

Stock Options

Under the 2014 Plan, the Company granted 957,000 and 596,000 stock options during the three months ended March 31, 2019 and 2018, respectively. The fair values of stock options granted during the three months ended March 31, 2019 and 2018 were estimated as of the dates of grant using the Black-Scholes option pricing model with the following assumptions:

	Three Months Ended March 31,	
	2019	2018
Risk-free interest rate	2.54% - 2.62%	2.51% - 2.71%
Expected volatility	74.29% - 75.19%	85.9%
Expected dividend yield	0%	0%
Expected life of employee options (in years)	6.25	6.25
Expected life of non-employee options (in years)	—	—

The weighted-average grant date fair value per share of options granted to employees, non-employee members of the Company's Board of Directors for their Board service and non-employee consultants during the three months ended March 31, 2019 and 2018 was $10.83 and $10.43, 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 March 31, 2018 are as follows:

	January 1, 2019	March 31, 2018
Risk-free interest rate	2.59% - 2.62%	1.82% - 2.70%
Expected volatility	58.9% - 84.6%	78.2% - 101.0%
Expected dividend yield	0%	0%
Expected life of non-employee options (in years)	0.81 - 8.19	0.50 - 8.94

During the three months ended March 31, 2019 and 2018, the Company recognized compensation expense in the accompanying Condensed Statements of Comprehensive Loss relating to stock options, as follows:

	Three Months Ended March 31,	
	2019	2018
Research and development	$ 1,082	$ 649
General and administrative	1,152	1,222
Total stock option expense	$ 2,234	$ 1,871

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 three months ended March 31, 2019 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2018	4,004,422	$ 13.34
Granted	957,000	16.06
Exercised	(17,291)	13.52
Forfeited	(18,490)	16.55
Outstanding, March 31, 2019	4,925,641	$ 13.86
Options exercisable, March 31, 2019	2,134,424	

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 three months ended March 31, 2019 and 2018.

14. Income Taxes

For the three months ended March 31, 2019 and 2018, pre-tax losses were $22,045 and $16,813, respectively. The Company recognized a full tax valuation allowance against its deferred tax assets as of March 31, 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 $85 and $46 for the three months ended March 31, 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 March 31, 2019 and December 31, 2018, the Company did not have any foreign subsidiaries and the international aspects of the Act are not applicable for the respective periods.

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

15. Commitments and Contingencies

Leases

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

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

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

Total rent expense under the Stamford Lease was $246 for the three months ended March 31, 2018.

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

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

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

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

Under ASC 842, lease expense is recognized on a straight-line basis over the lease term. As a result, $234 of operating lease cost, or lease expense, was recognized in the Company's Condensed Statements of Comprehensive Loss for the three months ended March 31, 2019, consisting of $164 relating to R&D lease expense and $70 relating to G&A lease expense.

Other information related to the Stamford Lease was as follows:

	Three Months Ended March 31, 2019
Cash paid for amounts included in the measurement of lease liability:	
Operating cash outflows from operating lease	$ (300)
ROU assets obtained in exchange for new operating lease liabilities	$ 3,636
Remaining lease term-operating lease	4.7 years
Discount rate - operating lease	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 March 31, 2019, were as follows:

Year Ending December 31,	
2019 (Excluding the three months ended March 31, 2019)	$ 915
2020	1,239
2021	1,264
2022	1,288
2023	1,164
Total future minimum lease payments, undiscounted	5,870
Less imputed interest	(882)
Total	$ 4,988
Operating lease liability reported as of March 31, 2019:	
Operating lease liability-current	$ 901
Operating lease liability - non-current	4,087
Total	$ 4,988

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

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

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

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

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

Introduction

We are a clinical-stage biopharmaceutical company focused on developing and commercializing new chemical entities with a primary focus on pruritus as well as pain by selectively targeting peripheral kappa opioid receptors. We are developing a novel and proprietary class of product candidates, led by KORSUVA (CR845/difelikefalin), a first-in-class kappa opioid receptor agonist that targets the body’s peripheral nervous system, as well as certain immune cells.

In 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, and is currently being investigated in Phase 3 trials in hemodialysis patients with 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

In order to fund our future operations, including our planned clinical trials, we filed a shelf registration statement on Form S-3 (File No. 333-230333), which the Securities and Exchange Commission, or SEC, declared effective on April 4, 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.

Our Product Candidates

Our product candidate, CR845/difelikefalin, is a new chemical entity, which is designed to selectively stimulate kappa, rather than mu, and delta opioid receptors outside of the central nervous system, or CNS. CR845/difelikefalin has been designed with specific chemical characteristics to restrict its entry into the CNS and further limit its mechanism of action to kappa opioid receptors in the peripheral nervous system and on immune cells. In addition to the side effects associated with activation of mu opioid receptors in the CNS, activation of kappa receptors in the CNS is also known to result in some undesirable effects, including dysphoria. CR845/difelikefalin is designed to specifically target kappa receptors located on peripheral nervous system and certain immune cells that results in modulation of pain signals as well as relief from pruritus or itch associated with certain chronic diseases. Since CR845/difelikefalin is designed to modulate 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, rapid 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 diseases such as AD as well as moderate-to-severe pain due to the following attributes:

- novel, peripherally-acting, kappa opioid receptor 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 chronic pain or pruritus 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 Chronic Kidney Disease-Hemodialysis	• KALM-1 (U.S.) and KALM-2 (Global) Phase 3 efficacy trials ongoing. KALM-1: enrollment completed • Phase 3 safety trials ongoing • Phase 2 adaptive trial completed and data reported • 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	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus Chronic Liver Disease (CLD)	• Phase 1 safety and PK trial completed • Phase 2 initiation expected in Q2 2019	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Atopic Dermatitis (AD)	• Phase 2 efficacy trial to be initiated around mid-year 2019 • Phase 1 safety and PK trial in healthy volunteers completed	Cara (Worldwide, other than South Korea); CKDP (South Korea)
Pain	CR845/difelikefalin Injection	Acute Post-Operative Pain	• Adaptive Phase 2/3 trial completed; Top-line data released	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral CR845/difelikefalin	Chronic Pain	• Phase 2b osteoarthritis, or OA, clinical 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)

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

CKD-associated pruritus, or CKD-aP, also known as uremic pruritus, is an intractable systemic itch condition with high prevalence in patients with CKD for which there are no approved therapeutics in the United States or Europe.

In the first quarter of 2018, we initiated the first pivotal Phase 3 efficacy trial of KORSUVA (CR845/difelikefalin) injection (with a 52-week open label extension phase) in the United States for the treatment of CKD-aP in patients undergoing hemodialysis. The enrollment in this study is now complete and we expect top-line data for the randomized part of the study in the second quarter of 2019. In August 2018, we initiated the second pivotal Phase 3 efficacy trial (with a 52-week open label extension phase) of KORSUVA (CR845/difelikefalin) injection that is expected to enroll patients in the United States and multiple countries outside the United States. In addition to these trials, we are also conducting 52-week and 12-week Phase 3 open label safety studies of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP.

In June 2017, the FDA granted breakthrough therapy designation for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe uremic 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). The primary efficacy endpoint is the proportion of patients 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. Secondary endpoints of the Phase 3 trial include assessment of itch-related quality of life changes measured using self-assessment 5-D Itch and Skindex-10 scales, as well as the proportion of patients achieving at least 4-point improvement from baseline in weekly mean of the daily 24-hour worst itching NRS score at week 12 and patient global impression of change. In January 2019, we announced the completion of enrollment in the KALM-1 Phase 3 trial after a pre-specified interim conditional power analysis conducted by the Independent Data Monitoring Committee, or IDMC, that recommended no adjustment to the original trial size. Over 350 hemodialysis patients with CKD-aP have been randomized across approximately 60 clinical sites in the United States and we expect to report top-line data in the second quarter of 2019.

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

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

In the second quarter of 2017, we initiated a 52-week Phase 3 safety trial that is expected to enroll up to 300 hemodialysis patients with CKD-aP, including those who have completed prior Phase 2 trials of KORSUVA (CR845/difelikefalin) injection as well as patients who have not been previously exposed to CR845/difelikefalin. This open-label trial is evaluating the long-term safety of KORSUVA (CR845/ difelikefalin) injection at the dose of 0.5mcg/kg. Currently, approximately 150 patients have completed at least six months of treatment (approximately 40% of these patients have completed one year of treatment).

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

The design and dose selection for our Phase 3 trials are based on results of the previously completed Phase 2 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP in consultation with the FDA as part of our End of Phase 2 meeting with the FDA that was held in September 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 uremic 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 uremic 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 assessed using the Skindex-10 scale, 5-D itch scale, sleep disturbance subscale and others. 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.

Phase 2 Efficacy Trial in Dialysis Patients

In 2014, we conducted a Phase 2 randomized, double-blind, placebo-controlled proof-of-concept trial (Part B), which measured the efficacy of KORSUVA (CR845/difelikefalin) injection at the dose of 1.0 mcg/kg compared to placebo in reducing the intensity of itch in 65 dialysis patients with uremic pruritus over a two-week dosing period, who had baseline "worst itching" scores of greater than 40 mm on a visual analog scale, or VAS ranging from 0 to 100 mm. In July 2015, we reported positive top-line efficacy results from this trial, in which we observed that KORSUVA (CR845/difelikefalin) injection demonstrated statistically significant reduction in worst itch intensity as measured by VAS, the primary endpoint of the trial, as well as statistically significant improvement in quality of life measures such as Skindex-10, the trial's secondary endpoint**.** The overall safety and tolerability profile was favorable. The dose of the Phase 2 study was informed by the Phase 1 safety and pharmacokinetic, or PK, trial (Part A) that was conducted in subjects undergoing hemodialysis at doses ranging from 0.5 mcg/kg to 2.5 mcg/kg after each dialysis session up to three times per week.

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 dose levels (0.25 mg, 0.5 mg and 1 mg, once daily) 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 analysis 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 Numeric Rating Scale, or 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. We expect top-line data from this trial in the second half 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 trial was 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 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 (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 was generally well tolerated with no unexpected safety signals reported. We expect to initiate a Phase 2 trial in chronic liver disease patients with moderate-to-severe pruritus in the second quarter of 2019.

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.

Around mid-year 2019, we expect to initiate a multi-dose Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of moderate-to-severe pruritus associated with AD. Additional details of the clinical trial will be discussed at the time of initiation of the trial.

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.

Phase 1 Safety and PK and Phase 2 Acute Pain Clinical Trials (Post-Surgery) of CR845/Difelikefalin Injection

Previously, in three different randomized, double-blind, placebo-controlled Phase 2 clinical trials, CR845/difelikefalin injection has been shown to be well tolerated and demonstrated efficacy of pain relief. Two of these trials were conducted in patients undergoing laparoscopic hysterectomy, a soft tissue surgical procedure, and a third trial was in patients undergoing bunionectomy, a hard tissue surgical procedure. Intravenous administration of CR845/difelikefalin resulted in statistically significant reductions in pain intensity, as measured by the sum of pain intensity difference. In addition, in both surgical models, CR845/difelikefalin injection exhibited an ability to decrease the opioid-related adverse events, or AEs, of nausea and vomiting associated with current therapies, along with no evidence of drug-related respiratory depression.

The safety profile of CR845/difelikefalin injection has been demonstrated in multiple studies. CR845/difelikefalin injection was observed to be generally well tolerated in all of these clinical trials. The most common treatment-emergent adverse events, or TEAEs, across evaluated populations in acute pain trials were transient facial tingling or numbness, dizziness and fatigue. In addition, a transient increase in urine output in the absence of electrolyte loss, otherwise known as aquaresis, was also observed, which in some subjects in acute pain trials was accompanied by asymptomatic elevations in plasma sodium that were generally considered to be clinically unimportant. No clinically significant changes in electrocardiogram characteristics have been observed in any of these studies. Importantly, there appeared to be no cases of dysphoria/hallucinations typically observed with prior-generation CNS-active kappa agonists.

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 IV 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 percent.

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.

Oral CR845/Difelikefalin for Treatment of Osteoarthritis

We also investigated an oral version of CR845/difelikefalin, or Oral CR845/difelikefalin for pain relief, which we believe could be used to provide pain relief to patients with acute or chronic pain in an outpatient setting and also as an I.V.-to-oral transition, or step-down, therapy for hospital patients being prepared for discharge.

Phase 2b Trial of Oral CR845/Difelikefalin

In the third quarter of 2016 we initiated a Phase 2b trial with Oral CR845/difelikefalin, which was designed to evaluate three tablet strengths (1.0 mg, 2.5 mg and 5.0 mg), dosed twice-daily over an eight-week treatment period in 476 patients with OA of the knee or hip experiencing moderate-to-severe pain across the United States. The primary efficacy endpoint was the change from baseline at week eight, with respect to the weekly mean of the daily pain intensity score using an NRS score. Secondary endpoints included overall Patient Global Assessment, or PGA, score, and overall improvement in Western Ontario and McMaster Osteoarthritis Index, or WOMAC, scores, two commonly used patient-reported outcome measures, as well as mean reduction in rescue medication.

In June 2017, we announced top-line results from the Phase 2b trial. The results of the primary efficacy analysis of change from baseline in pain intensity NRS score comparing Oral CR845/difelikefalin (all doses) vs. placebo were not statistically significant across all patients (OA of the knee or hip). However, patients with OA of the hip maintained on the 5.0 mg dose to the end of the eight-week treatment period exhibited a statistically significant 39% reduction in mean joint pain score versus placebo (p=0.043); although this effect did not reach statistical significance in a combined analysis of all patients with OA of the knee or hip maintained on the 5.0 mg dose (p=0.111). For patients maintained on the 5.0 mg dose, there was a statistically significant increase in the proportion of patients whose OA pain was "very much improved" or "much improved" as indicated by PGA score in both the total patient group (p <0.005 vs. placebo) and in patients with primary OA of the hip (p<0.006 vs. placebo). The reduction in pain score in the 5.0 mg dose group in hip patients was accompanied by a reduction in mean rescue medication of 41% at week eight versus placebo. Patients maintained on the 1.0 mg and 2.5 mg tablet strengths did not exhibit significant reductions in mean joint pain scores compared to placebo. All tablet strengths were generally well tolerated with no drug-related serious adverse events. For the 5.0 mg dose, the most common adverse events reported at the >5 percent incidence level were dizziness (8%), headache (6%), dry mouth (6%) and constipation (12%). There were no clinically significant changes in serum sodium levels observed during the eight-week treatment period for any dose group.

In 2015, we completed a Phase 2a trial of Oral CR845/difelikefalin in 80 patients with OA of the knee or hip with moderate-to-severe pain evaluating four tablet strengths (0.25 mg, 0.5 mg, 1.0 mg and 5.0 mg) administered twice a day over a two-week treatment period. We reported data that showed dose related reduction in mean joint pain score and that all four tablet strengths were observed to be generally well tolerated with no unexpected safety signals reported.

We do not intend to develop Oral CR845/difelikefalin in pain associated with OA on our own and will likely seek one or more potential partner(s) for further development of Oral CR845/difelikefalin in this indication.

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 Months Ended March 31, 2019 and 2018

Revenue

	Three Months Ended March 31,		
	2019	2018	% change
	Dollar amounts in thousands		
License and milestone fees revenue	$ 4,242	$ —	100%
Clinical compound revenue	140	—	100%
Total revenue	$ 4,382	$ —	100%

License and milestone fees revenue

License and milestone fees revenue of $4.2 million for the three months ended March 31, 2019 was related to license fees earned by us during the period in connection with the VFMCRP Agreement. There was no license and milestone fees revenue for the three months ended March 31, 2018 (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 three months ended March 31, 2019 included $140 thousand from the sale of clinical compound to Maruishi. There was no clinical compound revenue for the three months ended March 31, 2018.

Research and Development Expense

	Three Months Ended March 31,		
	2019	2018	% change
	Dollar amounts in thousands		
Direct clinical trial costs	$ 17,741	$ 9,348	90%
Consultant services in support of clinical trials	1,258	542	132%
Stock-based compensation	1,082	649	67%
Depreciation and amortization	28	105	-74%
Other R&D operating expenses	3,499	2,783	26%
Total R&D expense	$ 23,608	$ 13,427	76%

For the three months ended March 31, 2019 compared to the three months ended March 31, 2018, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $13.3 million, mainly from activities related to the two Phase 3 efficacy trials of I.V. KORSUVA (CR845/difelikefalin) in CKD patients undergoing hemodialysis, the Phase 3 long-term (52-week) safety study of I.V. KORSUVA (CR845/difelikefalin) in hemodialysis patients with CKD-aP, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients, the Phase 3 (12-week) safety study in hemodialysis patients with CKD-aP and the Phase 2 efficacy trial for CLD-aP. Those costs were partially offset by a decrease of $4.4 million, mainly from the Phase 2/3 I.V. CR845/difelikefalin adaptive clinical trial in post-operative pain and the Phase 1 safety and PK trial of multiple doses of Oral KORSUVA (CR845/difelikefalin) in non-hemodialysis CKD patients, all of which are complete and no longer ongoing. The increase in stock-based compensation expense relates primarily to an increase in the number of options outstanding. The increase in other R&D operating expenses was primarily the result of an increase in payroll and related costs associated with R&D personnel.

The following table summarizes our R&D expenses by programs for the three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,		
	2019	2018	% change
	Dollar amounts in thousands		
External research and development expenses:			
I.V. CR845 - Pruritus	$ 13,890	$ 3,671	278%
I.V. CR845 - Pain	199	3,269	-94%
Oral CR845 - Pruritus	4,899	2,246	118%
Oral CR845 - Pain	10	703	-99%
Internal research and development expenses	4,610	3,538	30%
Total research and development expenses	$ 23,608	$ 13,427	76%

General and Administrative Expenses

	Three Months Ended March 31,		
	2019	2018	% change
	Dollar amounts in thousands		
Professional fees and public/investor relations	$ 929	$ 593	57%
Stock-based compensation	1,152	1,222	-6%
Depreciation and amortization	22	20	12%
Other G&A operating expenses	1,805	1,862	-3%
Total G&A expense	$ 3,908	$ 3,697	6%

For the three months ended March 31, 2019 compared to the three months ended March 31, 2018, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs, legal fees and accounting fees. Stock-based compensation, depreciation and amortization and other G&A operating expenses remained relatively consistent between the respective periods.

Other Income

	Three Months Ended March 31,		
	2019	2018	% change
	Dollar amounts in thousands		
Other Income	$ 1,089	$ 311	250%

During the three months ended March 31, 2019 compared to the three months ended March 31, 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 March 31, 2019 and 2018, pre-tax losses were $22.0 million and $16.8 million, respectively, and we recognized a benefit from income taxes of $85 thousand and $46 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 March 31, 2019 and December 31, 2018.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception and through March 31, 2019, we have raised an aggregate of approximately $486.6 million to fund our operations, including (1) net proceeds of $309.8 million from the sale of shares of our common stock in four public offerings, including our initial public offering; (2) proceeds of $73.3 million from the sale of shares of our convertible preferred stock and from debt financings prior to our initial public offering; (3) payments of $88.9 million under our license agreements, primarily with VFMCRP, Maruishi, CKDP and an earlier product candidate for which development efforts ceased in 2007; and (4) net proceeds of $14.6 million from the purchase of our common stock in relation to the license agreement with VFMCRP (see Note 10 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

In order to fund our future operations, including our planned clinical trials, we filed a shelf registration statement on Form S-3 (File No. 333-230333), which the Securities and Exchange Commission, or SEC, declared effective on April 4, 2019. The shelf registration statement provides for aggregate offerings of up to $300.0 million of common stock, preferred stock, debt securities, warrants or any combination thereof. The securities registered under this shelf registration statement include unsold securities that had been registered under our previous shelf registration statement (File No. 333-216657) that was declared effective on March 24, 2017.

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

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

We intend to use the net proceeds from this most recent underwritten offering to fund our clinical and research development activities, including the completion of our Phase 3 programs and submission of a new drug application to the FDA for KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in hemodialysis patients, the advancement of Oral KORSUVA (CR845/difelikefalin) through Phase 2 trials for the treatment of CKD-aP in Stage III-V patients and CLD patients, the expansion of our Oral KORSUVA program into atopic dermatitis and the exploration of further development of CR845/difelikefalin injection in the post-operative setting after consultation with the FDA, 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. We believe that the use of a shelf registration statement provides us with the flexibility to raise additional capital to finance our operations as needed.

As of March 31, 2019, we had $156.1 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 fourth quarter of 2020, 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 March 31, 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 March 31, 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 for the completion by us in the United States of a Phase 3 trial of CR845/difelikefalin in uremic pruritus. If achieved, this milestone will result in a payment of $750 thousand, before South Korean withholding tax, being due to us.

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 $22.0 million and $16.8 million for the three months ended March 31, 2019 and 2018, respectively. As of March 31, 2019, we had an accumulated deficit of $316.3 million. We expect to continue to incur significant expenses and operating and net losses in the near future. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials, the receipt of additional milestone payments, if any, under our licensing and collaborations with VFMCRP, Maruishi and CKDP, the receipt of payments under any future collaborations and/or licensing agreements we may enter into, and our expenditures on other R&D activities.

We anticipate that our expenses will increase as we:

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

- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development and potential future commercialization efforts.

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

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

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

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

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

Outlook

Based on timing expectations and projected costs for our current clinical development plans, which include completing our Phase 3 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients suffering from moderate-to-severe CKD-aP to enable an NDA submission, and conducting Phase 1 and Phase 2 trials of Oral (CR845/difelikefalin) in patients with CKD-aP, CLD-aP and certain dermatologic conditions such as pruritus associated with AD, we expect that our existing cash and cash equivalents and available-for-sale marketable securities as of March 31, 2019 will be sufficient for us to fund our currently anticipated operating expenses and capital expenditures into the fourth quarter of 2020, 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 March 31, 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 three months ended March 31, 2019 and 2018:

	Three Months Ended March 31,	
	2019	2018
	Dollar amounts in thousands	
Net cash used in operating activities	$ (27,526)	$ (18,468)
Net cash provided by investing activities	26,399	20,694
Net cash provided by financing activities	234	263
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (893)	$ 2,489

Net cash used in operating activities

Net cash used in operating activities for the three months ended March 31, 2019 consisted primarily of a net loss of $22.0 million, a $3.3 million cash outflow from net changes in operating assets and liabilities and a $2.3 million cash outflow from net non-cash charges. The net change in operating assets and liabilities primarily consisted of a cash outflow of $2.6 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs, a cash outflow of $0.3 million from a decrease in accounts payable and accrued expenses, and a cash outflow of $0.2 million from operating lease liability relating to lease payments made for the Stamford Lease as a result of our adoption of ASC 842: *Leases*. Net non-cash charges primarily consisted of a decrease of $4.2 million in deferred revenue associated with our VFMCRP Agreement and $0.5 million related to accretion of available-for-sale securities, partially offset by stock-based compensation expense of $2.2 million.

Net cash used in operating activities for the three months ended March 31, 2018 consisted primarily of a net loss of $16.8 million and a $3.4 million outflow from net changes in operating assets and liabilities, partially offset by a $1.7 million cash inflow from net non-cash charges. The net change in operating assets and liabilities primarily consisted of a cash outflow of $1.8 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs, and a cash outflow of $1.6 million from a decrease in accounts payable and accrued expenses. Net non-cash charges primarily consisted of stock-based compensation expense of $1.9 million.

Net cash provided by investing activities

Net cash provided by investing activities was $26.4 million for the three months ended March 31, 2019, which primarily included cash inflows of $79.3 million from maturities of available-for-sale marketable securities, partially offset by cash outflows of $52.9 million for the purchase of available-for-sale marketable securities.

Net cash provided by investing activities was $20.7 million for the three months ended March 31, 2018, which primarily included cash inflows of $26.7 million from maturities of available-for-sale marketable securities and $10.9 million from the sale of available-for-sale marketable securities, partially offset by cash outflows of $16.8 million for the purchase of available-for-sale marketable securities.

Net cash provided by financing activities

Net cash provided by financing activities for the three months ended March 31, 2019 and 2018, consisted of proceeds of $234 thousand and $263 thousand, respectively, received from the exercise of stock options.

Significant Contractual Obligations and Commitments

Contractual obligations and commitments as of March 31, 2019 consisted of an operating lease obligation in connection with our operating facility in Stamford, Connecticut. See Note 15 of Notes to Condensed Financial Statements, *Commitments and Contingencies: Leases*, in this Quarterly Report on Form 10-Q.

Recent Accounting Pronouncements

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

Off-Balance Sheet Arrangements

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

Discussion of Critical Accounting Policies

The preparation of financial statements in conformity with GAAP requires us to use judgment in making certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities and the reported amounts of revenues and expenses in our condensed financial statements and accompanying notes. Critical accounting policies are those that are most important to the portrayal of our financial condition and results of operations and require difficult, subjective and complex judgments by management in order to make estimates about the effect of matters that are inherently uncertain. During the three months ended March 31, 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 March 31, 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 March 31, 2019, we had invested $142.0 million of our cash reserves in such marketable securities. Those marketable securities include $142.0 million of investment grade debt instruments with a yield of approximately 2.65% and maturities through March 2021. As of December 31, 2018, we had invested $167.7 million of our cash reserves in such marketable securities. Those marketable securities included $167.7 million of investment grade debt instruments with a yield of approximately 2.64% and maturities through November 2020.

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

Duration is a sensitivity measure that can be used to approximate the change in the fair value of a security that will result from a change in interest rates. Applying the duration model, a hypothetical 1% increase in interest rates as of March 31, 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 March 31, 2019. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of March 31, 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 three months ended March 31, 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 March 31, 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 three months ended March 31, 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.***

On March 20, 2019, or the Effective Date, we issued 10,195 shares of our common stock pursuant to a consulting agreement with an existing stockholder, in consideration for consulting services to be performed by the consultant during the six-month period following the Effective Date. These shares were issued in reliance upon the exemption from the registration requirements of the Securities Act of 1933, as amended, or the Securities Act, set forth under Section 4(a)(2) of the Securities Act relating to sales by an issuer not involving any public offering. The consultant represented that it is an accredited investor and that it is acquiring the shares for investment purposes only and not with a view to any resale, distribution or other disposition of such securities in violation of the United States federal securities laws.

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)
31.1 †	Certification of Chief Executive Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
31.2 †	Certification of Chief Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
32.1 †*	Certifications of Chief Executive Officer and Chief Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101 †	Interactive Data File
101.CAL †	XBRL Taxonomy Extension Calculation Linkbase.
101.INS †	XBRL Instance Document.
101.LAB †	XBRL Taxonomy Extension Label Linkbase.
101.PRE †	XBRL Taxonomy Extension Presentation Linkbase.
101.SCH †	XBRL Taxonomy Extension Schema Linkbase.
101.DEF †	XBRL Definition Linkbase Document.

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

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

† Filed herewith.

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

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: May 7, 2019

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

Date: May 7, 2019

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

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: May 7, 2019

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

EXHIBIT 31.2

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

I, Mani Mohindru, certify that:

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

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 7, 2019

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

EXHIBIT 32.1

CERTIFICATIONS OF
CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
OF CARA THERAPEUTICS, INC.
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906 OF THE
SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended March 31, 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: May 7, 2019

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