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

FORM 10-Q

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2020

OR

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

COMMISSION FILE NUMBER 001-36279

CARA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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

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

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

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

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

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

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

Large Accelerated Filer	☒	Accelerated Filer	☐
Non-Accelerated Filer	☐	Smaller Reporting Company	☐
		Emerging Growth Company	☐

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

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

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of August 6, 2020 was: 46,886,751.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2020

PART I –FINANCIAL INFORMATION

PART I
FINANCIAL INFORMATION

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

CARA THERAPEUTICS, INC.

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

	June 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 56,967	$ 18,305
Marketable securities	73,218	136,701
Income tax receivable	1,120	816
Other receivables	486	971
Prepaid expenses	10,124	8,863
Total current assets	141,915	165,656
Operating lease right-of-use asset	2,825	3,036
Marketable securities, non-current	22,861	63,159
Property and equipment, net	604	700
Restricted cash	408	408
Total assets	$ 168,613	$ 232,959
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 13,952	$ 19,665
Operating lease liability, current	1,006	967
Current portion of deferred revenue	9,768	22,262
Total current liabilities	24,726	42,894
Operating lease liability, non-current	2,959	3,352
Commitments and contingencies (Note 15)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at June 30, 2020 and December 31, 2019, zero shares issued and outstanding at June 30, 2020 and December 31, 2019	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at June 30, 2020 and December 31, 2019, 46,864,405 shares and 46,720,225 shares issued and outstanding at June 30, 2020 and December 31, 2019, respectively	47	47
Additional paid-in capital	594,963	587,223
Accumulated deficit	(454,717)	(400,727)
Accumulated other comprehensive income	635	170
Total stockholders' equity	140,928	186,713
Total liabilities and stockholders' equity	$ 168,613	$ 232,959

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Three Months Ended		Six Months Ended	
	June 30, 2020	June 30, 2019	June 30, 2020	June 30, 2019
Revenue:				
License and milestone fees	$ 5,099	$ 5,208	$ 13,120	$ 9,450
Clinical compound revenue	535	—	607	140
Total revenue	5,634	5,208	13,727	9,590
Operating expenses:				
Research and development	26,108	24,356	59,644	47,964
General and administrative	5,410	4,994	9,968	8,902
Total operating expenses	31,518	29,350	69,612	56,866
Operating loss	(25,884)	(24,142)	(55,885)	(47,276)
Other income, net	634	947	1,591	2,036
Loss before benefit from income taxes	(25,250)	(23,195)	(54,294)	(45,240)
Benefit from income taxes	182	235	304	320
Net loss	$ (25,068)	$ (22,960)	$ (53,990)	$ (44,920)
Net loss per share:				
Basic and Diluted	$ (0.54)	$ (0.58)	$ (1.15)	$ (1.13)
Weighted average shares:				
Basic and Diluted	46,799,703	39,818,162	46,762,327	39,685,954
Other comprehensive income, net of tax of $0:				
Change in unrealized gains (losses) on available-for-sale marketable securities	703	92	465	279
Total comprehensive loss	$ (24,365)	$ (22,868)	$ (53,525)	$ (44,641)

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

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2019	46,720,225	$ 47	$ 587,223	$ (400,727)	$ 170	$ 186,713
Stock-based compensation expense	—	—	2,846	—	—	2,846
Shares issued upon exercise of stock options	7,500	—	75	—	—	75
Net loss	—	—	—	(28,922)	—	(28,922)
Other comprehensive loss	—	—	—	—	(238)	(238)
Balance at March 31, 2020	46,727,725	$ 47	$ 590,144	$ (429,649)	$ (68)	$ 160,474
Stock-based compensation expense	—	—	2,993	—	—	2,993
Shares issued upon exercise of stock options	16,846	—	201	—	—	201
Shares issued upon vesting of restricted stock units	119,834	—	1,625	—	—	1,625
Net loss	—	—	—	(25,068)	—	(25,068)
Other comprehensive income	—	—	—	—	703	703
Balance at June 30, 2020	46,864,405	$ 47	$ 594,963	$ (454,717)	$ 635	$ 140,928

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Six Months Ended	
	June 30, 2020	June 30, 2019
Operating activities		
Net loss	$ (53,990)	$ (44,920)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	7,465	6,249
Depreciation and amortization	96	100
Amortization expense component of lease expense	325	293
Accretion of available-for-sale marketable securities, net	(34)	(803)
Realized gain on sale of available-for-sale marketable securities	(60)	—
Deferred revenue	(12,494)	(9,450)
Changes in operating assets and liabilities:		
Income tax receivable	(304)	(320)
Other receivables	485	321
Prepaid expenses	(1,261)	(2,609)
Accounts payable and accrued expenses	(5,713)	(856)
Operating lease liability	(470)	(427)
Net cash used in operating activities	(65,955)	(52,422)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	97,645	122,881
Proceeds from redemptions of available-for-sale marketable securities, at par	17,035	—
Proceeds from sale of available-for-sale marketable securities	10,677	—
Purchases of available-for-sale marketable securities	(21,016)	(71,236)
Purchases of property and equipment	—	(18)
Net cash provided by investing activities	104,341	51,627
Financing activities		
Proceeds from the exercise of stock options	276	4,208
Net cash provided by financing activities	276	4,208
Net increase in cash, cash equivalents and restricted cash	38,662	3,413
Cash, cash equivalents and restricted cash at beginning of period	18,713	15,850
Cash, cash equivalents and restricted cash at end of period	$ 57,375	$ 19,263
Noncash investing and financing activities		
Shares of common stock issued in exchange for consulting services	$ —	$ 197

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

1. Business

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

As of June 30, 2020, the Company had raised aggregate net proceeds of approximately $519,600 from several rounds of equity financing, including its initial public offering, or IPO, which closed in February 2014 and four follow-on public offerings of common stock, which closed in July 2019, July 2018, April 2017 and August 2015, respectively, and the issuance of convertible preferred stock and debt prior to the IPO. The Company had also received approximately $90,300 under its license agreements for CR845/difelikefalin, primarily with Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceutical Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and an earlier product candidate for which development efforts ceased in 2007. Additionally, in May 2018, the Company received net proceeds of $14,556 from the issuance and sale of 1,174,827 shares of the Company's common stock to Vifor (International) Ltd., or Vifor, in connection with the Company's license agreement with VFMCRP (see Note 10, *Collaboration and Licensing Agreements*).

As of June 30, 2020, the Company had unrestricted cash and cash equivalents and marketable securities of $153,046 and an accumulated deficit of $454,717. 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 $25,068 and $22,960 for the three months ended June 30, 2020 and 2019, respectively, and $53,990 and $44,920 for the six months ended June 30, 2020 and 2019, respectively, and had net cash used in operating activities of $65,955 and $52,422 for the six months ended June 30, 2020 and 2019, 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, 2019 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, 2019.

CARA THERAPEUTICS, INC.

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

Use of Estimates

The preparation of financial statements in conformity with GAAP requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities, and disclosure of contingent assets and liabilities, as of the date of the financial statements as well as the reported amounts of revenues and expenses during the reporting period. 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.

The ongoing COVID-19 pandemic has interrupted business operations across the globe. Estimates and assumptions about future events and their effects cannot be determined with certainty and therefore require the exercise of judgment. As of the date of issuance of these condensed financial statements, the Company is not aware of any specific event or circumstance that would require the Company to update its estimates, assumptions and judgments or revise the reported amounts of assets and liabilities or the disclosure of contingent assets and liabilities. These estimates, however, may change as new events occur and additional information is obtained, and are recognized in the condensed financial statements as soon as they become known.

Actual results could differ materially from the Company's estimates and assumptions.

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, 2019, except for the recent adoption of new accounting pronouncements as disclosed below.

Accounting Pronouncements Recently Adopted

On January 1, 2020, the Company adopted Accounting Standards Update, or 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 prior 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.

The Company deems certain of its investments to be marketable securities if the investment, or in the case of money market funds, the securities underlying the money market fund, meet the definition of a debt security in Accounting Standards Codification, or ASC, section 320-10-20. The Company considers its marketable securities to be available-for-sale, which are its only financial instruments that are within the scope of ASU 2016-13 as of June 30, 2020. The Company's investments in marketable securities, including U.S. Treasury securities, U.S. government agency obligations, corporate bonds, commercial paper and municipal bonds, are highly rated by Moody's and S&P and have maturities primarily of less than one year but no longer than two years. Accordingly, credit risk associated with the Company's available-for-sale debt security portfolio is mitigated.

ASU 2016-13 modifies the prior other-than-temporary impairment model for available-for-sale debt securities by requiring (1) estimating expected credit losses (the portion of the amortized cost basis of a financial asset that the

CARA THERAPEUTICS, INC.

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

Company does not expect to collect) 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 was previously prohibited. In April and November 2019, respectively, codification improvements were issued to help clarify and correct certain portions of ASU 2016-13.

The Company reviews each of its available-for-sale marketable securities for unrealized losses (declines in fair value below its amortized cost basis) at each balance sheet date presented in its financial statements and whenever events or changes in circumstances indicate that the amortized cost basis of an asset may not be recoverable. In accordance with the adoption of ASU 2016-13, the Company is required to determine whether any portion of the unrealized loss for any available-for-sale debt security is due to a credit loss, and if so, to measure the amount of the credit loss.

The Company will rely on both qualitative and quantitative factors to determine whether the unrealized loss for each available-for-sale debt security at any balance sheet date is due to a credit loss.

Qualitative factors may include a credit downgrade, severity of the decline in fair value below amortized cost and other adverse conditions related specifically to the security, as well as the intent to sell the security, or whether the Company will more likely than not be required to sell the security before recovery of its amortized cost basis. The Company's assessment of whether a security is impaired could change in the future due to new developments or changes in assumptions related to any particular security. If material qualitative factors indicate that a credit loss has occurred, the Company will determine the magnitude of that credit loss using a discounted cash flow model or other quantitative method.

If the Company intends to sell the security or it is more likely than not that the Company will be forced to sell the security before recovery of the amortized cost of the security, the entire unrealized loss is deemed to be a credit loss, which is recognized in net income (loss). Otherwise, the portion of the unrealized loss that is due to a credit loss will be recorded as an Allowance for Credit Loss, which will offset the balance of Marketable Securities on the Condensed Balance Sheets and as credit loss expense within other income, net on the Condensed Statements of Comprehensive Loss. The portion of the unrealized loss that is not due to a credit loss as well as all unrealized gains will be recorded in Accumulated Other Comprehensive Income (Loss), or AOCI, net of taxes, on the Condensed Balance Sheets. There was no cumulative effect adjustment as a result of the adoption of ASU 2016-13 on January 1, 2020 (see Note 3, *Available-for-Sale Marketable Securities*, and Note 5, *Fair Value Measurements)*.

Accrued interest receivables are excluded from the Company's amortized cost bases for its available-for-sale marketable securities and are included within Other Receivables on the Company's Condensed Balance Sheets. The Company's policy is to not measure an allowance for credit losses on accrued interest receivable balances at each reporting period since it elects to write off uncollectible accrued interest receivable balances as credit loss expense in a timely manner, which is by maturity date for all categories of its debt securities.

On January 1, 2020, the Company adopted ASU 2019-08, *Compensation – Stock Compensation (Topic 718) and Revenue from Contracts with Customers (Topic 606)*, or ASU 2019-08, which requires the Company to measure and classify share-based payment awards granted to a customer by applying the guidance in Topic 718. The amount recorded as a reduction to the transaction price is required to be measured on the basis of the grant-date fair value of the share-based payment award in accordance with Topic 718. The grant date is the date at which a grantor (supplier) and a grantee (customer) reach a mutual understanding of the key terms and conditions of a share-based payment award. The classification and subsequent measurement of the award are subject to the guidance in Topic 718 unless the share-based payment award is subsequently modified and the grantee is no longer a customer. The adoption of ASU 2019-08 did not

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
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(unaudited)

have a material effect on its results of operations, financial position or cash flows since the Company has not historically granted share-based payment awards to customers.

On January 1, 2020, the Company adopted 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. The adoption of ASU 2018-18 did 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*).

On January 1, 2020, the Company adopted 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. Upon adoption of ASU 2018-13, the Company did not have any assets or liabilities that are included in Level 3 fair value measurements and no retrospective treatment was applicable. As a result, the adoption of ASU 2018-13 did not have a material effect on its results of operations, financial position or cash flows.

Accounting Pronouncements Not Yet Adopted

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740)*, or ASU 2019-12, which removes specific exceptions to the general principles in Topic 740. ASU 2019-12 eliminates the need for an organization to analyze whether the following apply in a given period: (1) exception to the incremental approach for intra-period tax allocation; (2) exceptions to accounting for basis differences when there are ownership changes in foreign investments; and (3) exception to the general methodology for calculating income taxes in an interim period when a year-to-date loss exceeds the anticipated loss. ASU 2019-12 also simplifies the accounting for income taxes for: (i) franchise taxes that are partially based on income; (ii) transactions with a government that result in a step up in the tax basis of goodwill; (iii) separate financial statements of legal entities that are not subject to tax; and (iv) enacted changes in tax laws in interim periods. The amendments in ASU 2019-12 are effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020. Early adoption of the amendments is permitted. An entity that elects to early adopt the amendments in an interim period should reflect any adjustments as of the beginning of the annual period that includes that interim period and must adopt all the amendments in the same period. The amendments in ASU 2019-12 related to separate financial statements of legal entities that are not subject to tax should be applied on a retrospective basis for all periods presented. The amendments related to changes in ownership of foreign equity method investments or foreign subsidiaries should be applied on a modified retrospective basis through a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption. The amendments related to franchise taxes that are partially based on income should be applied on either a retrospective basis for all periods presented or a modified retrospective basis through a cumulative-effect adjustment to retained earnings as of the beginning of the fiscal year of adoption. All other amendments should be applied on a prospective basis. As such, the Company expects to adopt ASU 2019-12 on January 1, 2021 and is currently evaluating the effect it will have on its results of operations, financial position and cash flows.

CARA THERAPEUTICS, INC.

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

3. Available-for-Sale Marketable Securities

As of June 30, 2020 and December 31, 2019, the Company's available-for-sale marketable securities consisted of debt securities issued by the U.S. Treasury, U.S. government-sponsored entities and investment grade institutions as well as municipal bonds.

The following tables summarize the Company's available-for-sale marketable securities by major type of security as of June 30, 2020 and December 31, 2019:

As of June 30, 2020

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 13,070	$ 180	$ —	$ 13,250
U.S. government agency obligations	3,499	18	—	3,517
Corporate bonds	62,077	416	(3)	62,490
Commercial paper	13,298	24	—	13,322
Municipal bonds	3,500	—	—	3,500
Total available-for-sale marketable securities	$ 95,444	$ 638	$ (3)	$ 96,079

As of December 31, 2019

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 16,052	$ 31	$ (2)	$ 16,081
U.S. government agency obligations	25,803	14	(1)	25,816
Corporate bonds	115,788	125	(23)	115,890
Commercial paper	38,547	27	(1)	38,573
Municipal bonds	3,500	—	—	3,500
Total available-for-sale marketable securities	$ 199,690	$ 197	$ (27)	$ 199,860

The following tables summarize the fair value and gross unrealized losses of the Company's available-for-sale marketable securities by investment category and disaggregated by the length of time that individual debt securities have been in a continuous unrealized loss position.

As of June 30, 2020

	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	$ 5,507	$ (3)	$ —	$ —	$ 5,507	$ (3)
Total	$ 5,507	$ (3)	$ —	$ —	$ 5,507	$ (3)

CARA THERAPEUTICS, INC.

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

As of December 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
U.S. Treasury securities	$ 3,185	$ (2)	$ —	$ —	$ 3,185	$ (2)
U.S. government agency obligations	2,400	(1)	—	—	2,400	(1)
Corporate bonds	28,895	(23)	—	—	28,895	(23)
Commercial paper	4,264	(1)	—	—	4,264	(1)
Total	$ 38,744	$ (27)	$ —	$ —	$ 38,744	$ (27)

As of June 30, 2020 and December 31, 2019, respectively, no allowance for credit losses were recognized on the Company's available-for-sale debt securities as no portion of the unrealized losses associated with those securities were due to credit losses. The information that the Company considered in reaching the conclusion that an allowance for credit losses was not necessary for the following categories of securities is as follows:

As of June 30, 2020 and December 31, 2019, the Company held a total of 2 out of 42 positions and 16 out of 81 positions, respectively, that were in an unrealized loss position, none of which had been in an unrealized loss position for 12 months or greater. Unrealized losses individually and in aggregate were not considered to be material for each respective period. 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.

Corporate bonds. The unrealized losses on the Company's investments in corporate bonds relate to increased volatility and reduced liquidity in the investment grade corporate debt market due to the ongoing COVID-19 pandemic. The credit ratings of the corporate bonds in the Company's portfolio have not been downgraded below investment grade status as a result of the pandemic. The Company expects to recover the entire amortized cost bases of those securities as the pandemic subsides and markets normalize. The Company does not intend to sell its investments in corporate bonds, and it is not more likely than not that the Company will be required to sell those investments, before recovery of their amortized cost bases. As of June 30, 2020, the Company held 2 out of 28 positions in an unrealized loss position for its corporate bonds.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of June 30, 2020, the Company's marketable debt securities mature at various dates through December 2021. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows.

	As of June 30, 2020		As of December 31, 2019	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 72,845	$ 73,218	$ 136,565	$ 136,701
One year to two years	22,599	22,861	63,125	63,159
Total	$ 95,444	$ 96,079	$ 199,690	$ 199,860

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. Other income includes interest and dividends, accretion/amortization of discounts/premiums, realized gains and losses on sales of securities and credit loss expense due to declines in the fair value of securities, if any. The cost of securities sold is based on the specific identification method.

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During the three and six months ended June 30, 2020, the Company sold certain shares of its available-for-sale debt securities with a total fair value of $10,677. The sales of shares of available-for-sale debt securities resulted in a realized gain of $60 for the three and six months ended June 30, 2020. There were no sales of available-for-sale marketable securities during the three and six months ended June 30, 2019.

As of June 30, 2020 and December 31, 2019, accrued interest receivables on our available-for-sale debt securities were $401 and $971, respectively.

4. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in AOCI, net of tax, from unrealized gains (losses) on available-for-sale marketable securities, the Company's only component of AOCI, for the six months ended June 30, 2020 and June 30, 2019.

	Total Accumulated Other Comprehensive Income (Loss)
Balance, December 31, 2019	$ 170
Other comprehensive income before reclassifications	525
Amount reclassified from accumulated other comprehensive income	(60)
Net current period other comprehensive income	465
Balance, June 30, 2020	$ 635
Balance, December 31, 2018	$ (114)
Other comprehensive income before reclassifications	279
Amount reclassified from accumulated other comprehensive income	—
Net current period other comprehensive income	279
Balance, June 30, 2019	$ 165

Amounts reclassified out of AOCI into net loss are determined by specific identification. The reclassifications out of AOCI and into net loss were as follows:

Component of AOCI	Three Months Ended June 30, 2020	Three Months Ended June 30, 2019	Six Months Ended June 30, 2020	Six Months Ended June 30, 2019	Affected Line Item in the Statements of Operations
Unrealized gains (losses) on available-for- sale marketable securities					
Realized gains on sale of securities	$ 60	$ —	$ 60	$ —	Other income, net
	—	—	—	—	Benefit from income taxes
	$ 60	$ —	$ 60	$ —	

5. Fair Value Measurements

As of June 30, 2020 and December 31, 2019, 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

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fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services, as described below.

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

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

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

Valuation Techniques - Level 2 Inputs

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

The Company validates the prices provided by its third-party pricing services by reviewing their pricing methods, obtaining market values from other pricing sources and comparing them to the share prices presented by the third-party pricing services. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by its third-party pricing services as of June 30, 2020 or December 31, 2019.

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The following tables summarize the Company's financial assets measured at fair value on a recurring basis as of June 30, 2020 and December 31, 2019.

Fair value measurement as of June 30, 2020:

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	$ 56,967	$ 56,967	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	13,250	—	13,250	—
U.S. government agency obligations	3,517	—	3,517	—
Corporate bonds	62,490	—	62,490	—
Commercial paper	13,322	—	13,322	—
Municipal bonds	3,500	—	3,500	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 153,454	$ 57,375	$ 96,079	$ —

Fair value measurement as of December 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	$ 18,305	$ 18,305	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	16,081	—	16,081	—
U.S. government agency obligations	25,816	—	25,816	—
Corporate bonds	115,890	—	115,890	—
Commercial paper	38,573	—	38,573	—
Municipal bonds	3,500	—	3,500	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 218,573	$ 18,713	$ 199,860	$ —

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 during the three and six months ended June 30, 2020 and 2019, respectively. There were no transfers of financial assets into or out of Level 3 classification during the three and six months ended June 30, 2020 and 2019, respectively.

6. Restricted Cash

The Company is required to maintain a stand-by letter of credit as a security deposit under its leases for its office space in Stamford, Connecticut (refer to Note 15, *Commitments and Contingencies: Leases*). The fair value of the letter of credit approximates its contract value. The Company's bank requires the Company to maintain a restricted cash

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balance to serve as collateral for the letter of credit issued to the landlord by the bank. As of June 30, 2020, the restricted cash balance for the Stamford Lease was invested in a commercial money market account.

As of June 30, 2020 and December 31, 2019, the Company had $408 of restricted cash related to the Stamford Lease in long-term assets.

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

	June 30, 2020	December 31, 2019
Cash and cash equivalents	$ 56,967	$ 18,305
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 57,375	$ 18,713

7. Prepaid expenses

As of June 30, 2020, prepaid expenses were $10,124, consisting of $8,499 of prepaid R&D clinical costs, $1,170 of prepaid insurance and $455 of other prepaid costs. As of December 31, 2019, prepaid expenses were $8,863, consisting of $8,498 of prepaid R&D clinical costs, $181 of prepaid insurance, and $184 of other prepaid costs.

8. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	June 30, 2020	December 31, 2019
Accounts payable	$ 4,828	$ 9,100
Accrued research projects	5,864	6,637
Accrued professional fees	706	635
Accrued compensation and benefits	2,554	3,293
Total	$ 13,952	$ 19,665

9. Stockholders' Equity

In June 2020, as a result of the completion of the one-year vesting period, an aggregate of 24,000 restricted stock units of members of the Board of Directors vested and were settled in shares of the Company's common stock (see Note 13, *Stock-Based Compensation*).

In April and June 2020, as a result of the achievement of certain performance targets, an aggregate of 95,834 restricted stock units of various executive officers vested and were settled in shares of the Company's common stock (see Note 13, *Stock-Based Compensation*).

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

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On March 20, 2019, or the Effective Date, the Company entered into a consulting agreement with an existing stockholder. In accordance with the agreement, the stockholder provided various consulting services to the Company in exchange for 10,195 unregistered shares of the Company's common stock. The closing price of the Company's common stock on the Effective Date was $19.37 per share. The services provided by the consultant were performed during the six-month period following the Effective Date. The Company recorded a prepaid expense of $197 with a corresponding offset to Additional Paid-In Capital during the six months ended June 30, 2019. The Company amortized the entire amount of the prepaid expense on a straight-line basis as stock compensation expense within general and administrative expense over the six-month period in 2019 as services were performed. During the three and six months ended June 30, 2019, $99 of stock-based compensation expense was recognized as stock compensation expense in the Condensed Statement of Comprehensive Loss, all of which was related to G&A expense.

10. Collaboration and Licensing Agreements

Vifor Fresenius Medical Care Renal Pharma Ltd.

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

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

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

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

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The Company retains the rights to make and have made the Licensed Product in the Territory for commercial sale by VFMCRP in the Field in or outside the Territory and for supply of Licensed Product to VFMCRP under the terms of a supply agreement, or the VFMCRP Supply Agreement, which was executed in May 2020. The supply price is the Company's cost of goods sold, as calculated under U.S. GAAP, plus an agreed upon margin. The VFMCRP Supply Agreement will co-terminate with the VFMCRP Agreement.

The VFMCRP Supply Agreement is accounted for as a customer option that is not a material right because the selling price of the Licensed Product under the VFMCRP Supply Agreement is the Company's cost of goods sold plus an agreed upon margin, which is commensurate with the "cost of goods sold plus" model that the Company would charge other parties under similar agreements (the standalone selling price) and not at a discount. Therefore, the sale of clinical compound to VFMCRP is not a performance obligation under the VFMCRP Agreement but rather the VFMCRP Supply Agreement is a separate agreement from the VFMCRP Agreement. The only performance obligation under the VFMCRP Supply Agreement is the delivery of the Licensed Product to VFMCRP for commercialization. Revenue from the sale of the Licensed Product to VFMCRP will be recognized as clinical compound revenue in the Company's Condensed Statements of Comprehensive Loss as sales of the Licensed Product occur. During the three and six months ended June 30, 2020, the Company recognized clinical compound revenue of $88 from the sale of clinical compound to VFMCRP and as a result, the Company incurred R&D expense of $79 during these respective periods.

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

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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 June 30, 2020, the Company recognized clinical compound revenue of $447 from the sale of clinical compound to Maruishi and as a result, the Company incurred R&D expense of $403 during this period. There were no sales of clinical compound to Maruishi during the three months ended June 30, 2019. During the six months ended June 30, 2020 and 2019, the Company recognized clinical compound revenue of $519 and $140, respectively, from the sale of clinical compound to Maruishi, and as a result, the Company incurred R&D expense of $467 and $126, respectively, during these periods.

Chong Kun Dang Pharmaceutical Corporation

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

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

11. Revenue Recognition

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

Contract balances

As of June 30, 2020, the Company had deferred revenue, current of $9,768 related to the performance obligations from the VFMCRP Agreement and had no balances of receivables, other assets or deferred revenue, non-current related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of June 30, 2020. As of December 31, 2019, the Company had deferred revenue, current of $22,262 related to the performance obligations from the VFMCRP Agreement and had no balances of

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receivables, other assets or deferred revenue, non-current related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of December 31, 2019.

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. The Company's only performance obligation under the VFMCRP Supply Agreement is to deliver CR845/difelikefalin injection to VFMCRP in accordance with the receipt of purchase orders.

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

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

Transaction price allocated to the remaining performance obligations

At inception of the VFMCRP Agreement, the entire transaction price of $55,444 was allocated to the one combined performance obligation, as described above. For the three and six months ended June 30, 2020, $4,473 and $12,494, respectively, were recognized as license and milestone fees revenue based on the percentage of R&D services that were completed during the period. As of June 30, 2020, $45,676 of the $55,444 has been recognized as license and milestone fees revenue based on the percentage of R&D services that has been completed since the inception of the VFMCRP Agreement. As of June 30, 2020, 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.

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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

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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

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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.

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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 $9,768 at June 30, 2020 will be recognized in the second half of 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).

In May 2020, the criteria for revenue recognition for a milestone event set forth in the CKDP Agreement was achieved, and the Company recorded $626 (net of South Korean taxes) as license and milestone fees revenue in its Condensed Statements of Comprehensive Loss for the three and six months ended June 30, 2020. There were no contract assets or receivables related to this milestone payment from CKDP as the payment was received during the three months ended June 30, 2020. During the three and six months ended June 30, 2019, 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.

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Sales-based Royalty Payments

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

a. The subsequent sale or usage occurs.

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

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

12. Net Loss Per Share

The Company computes basic net income (loss) per share by dividing net income (loss) by the weighted-average number of shares of common stock outstanding. Diluted net income per share includes the potential dilutive effect of common stock equivalents as if such securities were exercised during the period, when the effect is dilutive. Common stock equivalents may include outstanding stock options or restricted stock units, which are included using the treasury stock method when dilutive. For the three and six months ended June 30, 2020 and 2019, the Company excluded the effects of potentially dilutive shares that were outstanding during those respective periods from the denominator as their inclusion would be anti-dilutive due to the Company's net losses during those periods.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Basic:				
Weighted average common shares outstanding	46,799,703	39,818,162	46,762,327	39,685,954
Diluted:				
Weighted average common shares outstanding - Basic	46,799,703	39,818,162	46,762,327	39,685,954
Common stock options*	—	—	—	—
Denominator for diluted net loss per share	46,799,703	39,818,162	46,762,327	39,685,954

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

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Net loss	$ (25,068)	$ (22,960)	$ (53,990)	$ (44,920)
Weighted-average common shares outstanding:				
Basic and Diluted	46,799,703	39,818,162	46,762,327	39,685,954
Net loss per share, Basic and Diluted	$ (0.54)	$ (0.58)	$ (1.15)	$ (1.13)

As of June 30, 2020 and 2019, 4,964,766 and 4,705,722 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, 236,000 unvested restricted stock units issued to executive officers that were outstanding at June 30, 2020 were also not included in the computation of diluted net loss per share because to do so would have been anti-dilutive. The 36,000 restricted stock units granted in June 2020 to the non-employee members of the Board of Directors were also not included in the computation of diluted net loss per share because to do so would have been anti-dilutive (see Note 13, *Stock-Based Compensation*).

13. Stock-Based Compensation

2019 Inducement Plan

On October 30, 2019, the Company's Board of Directors adopted the 2019 Inducement Plan, or the 2019 Plan, which is a non-stockholder approved stock plan adopted pursuant to the "inducement exception" provided under Nasdaq Listing Rule 5635(c)(4), or Rule 5635, for the purpose of awarding (i) non-statutory stock options, (ii) restricted stock awards, (iii) restricted stock unit awards, (iv) other stock awards (collectively, the Inducement Awards) to new employees of the Company, as inducement material to such new employees entering into employment with the Company. On November 20, 2019, the Company filed a Registration Statement on Form S-8 with the SEC covering the offering of up to 300,000 shares of its common stock, par value $0.001, pursuant to the Company's 2019 Plan. Initial grants of Inducement Awards made to employees 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.

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 new members of the Company's Board of Directors vest over a period of three years in equal quarterly 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

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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, 2020, the aggregate number of shares of common stock that may be issued pursuant to Stock Awards under the 2014 Plan automatically increased from 6,086,907 to 7,488,513. 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

Pursuant to the Company's non-employee director compensation policy, an aggregate of 36,000 restricted stock units were granted to non-employee directors on June 4, 2020, the date of the Company's 2020 Annual Meeting of Stockholders, under the 2014 Plan with a grant date fair value of $15.62 per share. The restricted stock units will vest on the earlier of (i) June 4, 2021 and (ii) immediately prior to the Company's next Annual Meeting of Stockholders following the grant date, subject to the recipient's continued service through such date. As a result, the Company will recognize compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the three and six months ended June 30, 2020, $40 of stock compensation expense relating to these restricted stock units was recognized in the Condensed Statements of Comprehensive Loss, all of which related to G&A expense. None of the 36,000 restricted stock units vested and were settled in shares of the Company's common stock as of June 30, 2020.

In February 2020, the Compensation Committee of the Company's Board of Directors approved and granted a total of 138,000 restricted stock units to executive officers under the 2014 Plan with a grant date fair value of $16.36 per share. Vesting of the restricted stock units is contingent on the achievement of certain performance targets related to the results of ongoing clinical trials, NDA filing and FDA approval as well as the recipient's continuous service through each performance target. At the date of grant, the Company concluded that the probability of achievement of the performance targets could not be determined until the various milestones were probable of being achieved, and accordingly, the Company did not recognize any compensation expense during the three and six months ended June 30, 2020. Recognition of compensation expense associated with these awards begins when, and to the extent, the performance criteria have been achieved and therefore, the restricted stock units are earned and vesting has occurred.

Additionally in February 2020, the Compensation Committee of the Company's Board of Directors also approved and granted a total of 98,000 time-based restricted stock units to executive officers under the 2014 Plan with a grant date fair value of $16.36 per share. The restricted stock units vest in three equal installments annually from the date of the grant. As a result, the Company recognizes compensation expense associated with these restricted stock units ratably over the three-year vesting period following the grant date. For the three months ended June 30, 2020, the Company recognized $142 of stock compensation expense in the Condensed Statement of Comprehensive Loss, consisting of $47 relating to R&D expense and $95 relating to G&A expense. For the six months ended June 30, 2020, the Company recognized $186 of stock compensation expense in the Condensed Statement of Comprehensive Loss, consisting of $61 relating to R&D expense and $125 relating to G&A expense. None of the 98,000 restricted stock units vested or were settled in shares of the Company's common stock as of June 30, 2020.

Pursuant to the terms of the Company's non-employee director compensation policy, an aggregate of 24,000 restricted stock units were granted to non-employee directors on June 4, 2019, the date of the Company's 2019 Annual

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Meeting of Stockholders, under the 2014 Plan with a grant date fair value of $20.47 per share. The restricted stock units vested on the earlier of (i) June 4, 2020 and (ii) immediately prior to the Company's next Annual Meeting of Stockholders following the grant date, subject to the recipient's continued service through such date. As a result, the Company recognized compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the three and six months ended June 30, 2020, $82 and $205, respectively, of stock compensation expense relating to these restricted stock units was recognized in the Condensed Statements of Comprehensive Loss, all of which related to G&A expense. For the three and six months ended June 30, 2019, the Company recognized $41 of stock compensation expense relating to the Board of Directors' restricted stock units in the Condensed Statements of Comprehensive Loss, all of which related to G&A expense. All 24,000 restricted stock units vested and were settled in shares of the Company's common stock as of June 30, 2020.

In March 2019, the Compensation Committee of the Company's Board of Directors approved and granted a total of 215,000 restricted stock units to executive officers under the 2014 Plan with a grant date fair value of $16.10 per share. Vesting of the restricted stock units was contingent on the achievement of certain performance targets related to the results of ongoing clinical trials, subject to the recipient's continuous service through the vesting events. At the date of grant, the Company concluded that the probability of achievement of the performance targets could not be determined until the milestones were probable of being achieved, and accordingly, the Company would recognize compensation expense associated with these awards when, and to the extent, the restricted stock units vested in accordance with achievement of the performance targets. In May 2019, performance targets relating to an aggregate of 74,166 restricted stock units had been achieved and thus such restricted stock units vested and the awards were settled in shares of common stock. In December 2019, performance targets relating to 36,666 restricted stock units had been achieved and thus such restricted stock units vested and the awards were settled in shares of common stock. Also in December 2019, 8,334 restricted stock units were forfeited. In April and June 2020, performance targets relating to 65,834 and 30,000 restricted stock units, respectively, had been achieved and thus such restricted stock units vested and the awards were settled in shares of common stock. As a result, no restricted stock units remain unvested as of June 30, 2020. During the three and six months ended June 30, 2020, the Company recognized $1,543 of stock compensation expense relating to the vesting of these restricted stock units in the Condensed Statements of Comprehensive Loss, consisting of $1,087 relating to R&D expense and $456 relating to G&A expense. During the three and six months ended June 30, 2019, $1,194 of stock compensation expense relating to the vesting of these restricted stock units was recognized in the Condensed Statements of Comprehensive Loss, consisting of $590 relating to G&A expense and $604 relating to R&D expense.

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Stock Options

Under the 2014 Plan, the Company granted 147,000 and 241,000 stock options during the three months ended June 30, 2020 and 2019, respectively, and 820,350 and 1,198,000 stock options during the six months ended June 30, 2020 and 2019, respectively. No stock options were granted under the 2019 Inducement Plan during the three and six months ended June 30, 2020. The fair values of stock options granted during the three and six months ended June 30, 2020 and 2019 were estimated as of the dates of grant using the Black-Scholes option pricing model with the following assumptions:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Risk-free interest rate	0.42% - 0.54%	1.95% - 2.36%	0.42% - 1.57%	1.95% - 2.62%
Expected volatility	73.73% - 74.80%	73.06% - 73.78%	73.72% - 74.80%	73.06% - 75.19%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee options (in years)	6.25	6.25	6.25	6.25
Expected life of non-employee options (in years)	—	—	—	—

The weighted-average grant date fair value per share of options granted to employees and non-employee members of the Company's Board of Directors for their Board service during the three months ended June 30, 2020 and 2019 was $10.23 and $13.07, respectively, and during the six months ended June 30, 2020 and 2019 was $10.53 and $11.28, respectively. No options were granted to non-employee consultants during the three and six months ended June 30, 2020 and 2019.

On January 1, 2019, the Company used the Black-Scholes option valuation model to remeasure the fair value of all outstanding unvested options that had been granted to non-employee consultants in accordance with ASU 2018-07, *Compensation – Stock Compensation (Topic 718), Improvements to Non-employee Share-Based Payment Accounting*. The range of assumptions used by the Company on January 1, 2019 were as follows:

	January 1, 2019
Risk-free interest rate	2.59% - 2.62%
Expected volatility	58.9% - 84.6%
Expected dividend yield	0%
Expected life of non-employee options (in years)	0.81 - 8.19

During the three and six months ended June 30, 2020 and 2019, the Company recognized compensation expense relating to stock options as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Research and development	$ 1,670	$ 1,326	$ 3,279	$ 2,408
General and administrative	1,142	1,355	2,212	2,507
Total stock option expense	$ 2,812	$ 2,681	$ 5,491	$ 4,915

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The following were excluded from the table above as they are not related to stock options: compensation expense for (i) the vesting of executives' restricted stock units for $1,133 in R&D expense and $551 in G&A expense for the three months ended June 30, 2020, and $1,147 in R&D expense and $581 in G&A expense for the six months ended June 30, 2020; (ii) the vesting of executives' restricted stock units for $604 in R&D expense and $590 in G&A expense for the three and six months ended June 30, 2019; (iii) compensation expense relating to the Board of Directors' restricted stock units for $122 and $245 in G&A expense for the three and six months ended June 30, 2020, respectively; (iv) compensation expense relating to the Board of Directors' restricted stock units for $41 in G&A expense for the three and six months ended June 30, 2019; and (v) the issuance of common stock relating to the consulting agreement for $99 in G&A expense for the three and six months ended June 30, 2019.

A summary of stock option award activity related to employees, non-employee members of the Company's Board of Directors and non-employee consultants as of and for the six months ended June 30, 2020 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2019	4,450,517	$ 14.73
Granted	820,350	16.04
Exercised	(24,346)	11.34
Expired	(167,964)	13.85
Forfeited	(113,791)	16.21
Outstanding, June 30, 2020	4,964,766	$ 14.96
Options exercisable, June 30, 2020	2,756,734	

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 and six months ended June 30, 2020 and 2019.

14. Income Taxes

For the three months ended June 30, 2020 and 2019, pre-tax losses were $25,250 and $23,195, respectively, and for the six months ended June 30, 2020 and 2019, pre-tax losses were $54,294 and $45,240, respectively. The Company recognized a full tax valuation allowance against its deferred tax assets as of June 30, 2020 and December 31, 2019. 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 $182 and $235 for the three months ended June 30, 2020 and 2019, respectively, and $304 and $320 for the six months ended June 30, 2020 and 2019, 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 June 30, 2020 and December 31, 2019, the Company did not have any foreign subsidiaries and the international aspects of the Tax Cuts and Jobs Act are not applicable for the respective periods.

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15. Commitments and Contingencies

License Agreement with Enteris Biopharma, Inc.

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

As consideration for the licensed rights under the Enteris License Agreement, the Company paid an upfront fee equal to $8,000, consisting of $4,000 in cash and $4,000 in shares of the Company's common stock pursuant to the Purchase Agreement with Enteris, or the Purchase Agreement.

The Company is also obligated, pursuant to the Enteris License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. Until the second anniversary of the entry into the Enteris License Agreement, the Company has the right, but not the obligation, to terminate its obligation to pay any royalties under the Enteris License Agreement in exchange for a lump sum payment in cash, or the Royalty Buyout. Subject to certain conditions, the Company may elect to pay 50% of the lump sum due under the Royalty Buyout in shares of the Company's common stock pursuant to the Purchase Agreement. During the three and six months ended June 30, 2020, no milestone payments or royalties were paid to Enteris by the Company.

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

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

Manufacturing Agreement

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

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The MSA has an initial term ending December 31, 2023, and will automatically renew after the initial term for successive terms of two years each if there is a Product Agreement in effect, unless either party gives notice of its intention to terminate the MSA at least 18 months prior to the end of the then current term.

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

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

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

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 December 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. As of the Commencement Date, the Stamford Lease landlord had made tenant improvements of $1,094 to the leased premises which was included in Property and equipment, net.

CARA THERAPEUTICS, INC.

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

On January 1, 2019, the Company adopted ASC 842: Leases, or ASC 842. 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 upon adoption.

Under ASC 842, lease expense is recognized on a straight-line basis over the lease term. As a result, $236 and $470 of operating lease cost, or lease expense, was recognized in the Company's Condensed Statements of Comprehensive Loss for the three and six months ended June 30, 2020, respectively, consisting of $165 relating to R&D lease expense and $71 relating to G&A lease expense for the three month period, and $329 relating to R&D lease expense and $141 relating to G&A lease expense for the six month period. For the three and six months ended June 30, 2019, $234 and $469, respectively, of operating lease cost, or lease expense, was recognized in the Company's Condensed Statements of Comprehensive Loss, consisting of $164 relating to R&D lease expense and $70 relating to G&A lease expense for the three month period, and $328 relating to R&D lease expense and $141 relating to G&A lease expense for the six month period.

In June 2020, the Company entered into an amendment to the Stamford Lease to add additional office space, or the Lease Amendment. The term of the Lease Amendment begins when renovation of the additional space is complete and the Company takes possession of the additional space (expected by the end of 2020), or the Amendment Commencement Date, and ends on December 31, 2023. The Lease Amendment is also renewable for one five-year term, although this renewable period is not included as part of the lease term as defined in ASC 842 since it is not reasonably certain that the Company will exercise that option. The Lease Amendment contains both a lease and non-lease component which are accounted for separately. The Company allocates the consideration to the lease and non-lease component on a relative standalone price basis. The rent for the Lease Amendment is at market rate as of the signing of the Lease Amendment. The Lease Amendment requires monthly lease payments, including rent escalations, during the lease term. The Company will begin paying rent for the Lease Amendment on the Amendment Commencement Date.

The Company will account for the terms and conditions of the Lease Amendment as a lease modification, as defined in ASC 842, because it grants an additional right-of-use to an underlying asset (the new additional space). Under ASC 842, a lease modification can result in either a new lease that is accounted for separately from the original lease or as a single modified lease. The Lease Amendment is accounted for separately from the original Stamford Lease because the Lease Amendment grants the right-of-use to additional space and the price of the additional right-of-use is commensurate with its standalone price as no discounts were provided to the Company. Furthermore, there were no material changes to the original Stamford Lease.

As of the Amendment Commencement Date, the Company will determine and record the lease liability for the Lease Amendment as the sum of the present value of the future minimum lease payments over the term for the new lease (which is expected to approximate $2,000). Since the Lease Amendment does not provide an implicit interest rate, the Company will use an incremental borrowing rate of 7%, which is based on the rate that the Company could obtain in the market for a fully collateralized loan equal to the term of the Lease Amendment. The Company will also record a ROU

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asset equal to the amount of the lease liability, as no lease incentives were identified in the Lease Amendment. During the term of the Lease Amendment, interest expense will be calculated using the effective interest method and the ROU asset will be amortized on a straight-line basis over the lease term, and both will be recorded as lease expense in the Company's Condensed Statements of Comprehensive Loss.

Other information related to the Stamford Lease was as follows (information related to the Lease Amendment is not included until the Amendment Commencement Date):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Cash paid for amounts included in the measurement of lease liability:				
Operating cash outflows relating to operating lease	$ 309	$ 302	$ 615	$ 603
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ —	$ —	$ 3,636
Remaining lease term - operating lease (years)	3.5	4.4	3.5	4.4
Discount rate - operating lease	7.0 %	7.0 %	7.0 %	7.0 %

Future minimum lease payments under non-cancellable operating leases, as well as a reconciliation of these undiscounted cash flows to the operating lease liability as of June 30, 2020, were as follows (information related to the Lease Amendment is not included until the Amendment Commencement Date):

Year Ending December 31,	
2020 (Excluding the six months ended June 30, 2020)	$ 625
2021	1,264
2022	1,288
2023	1,311
2024	—
Total future minimum lease payments, undiscounted	4,488
Less imputed interest	(523)
Total	$ 3,965
Operating lease liability reported as of June 30, 2020:	
Operating lease liability - current	$ 1,006
Operating lease liability - non-current	2,959
Total	$ 3,965

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 timing of our regulatory submissions for KORSUVA™ (CR845/difelikefalin) injection in chronic kidney disease associated pruritus, or CKD-aP;
- the success and timing of our clinical trials and reporting of our results from these trials, including our clinical trial programs for KORSUVA (CR845/difelikefalin) injection in CKD-aP, and for Oral KORSUVA (CR845/difelikefalin) in CKD-aP, chronic liver disease associated pruritus, or CLD-aP, and pruritus associated with atopic dermatitis, or AD;
- our plans to develop and commercialize KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) and any future 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;
- the potential regulatory development pathway for KORSUVA (CR845/difelikefalin) injection in CKD-aP and CR845/difelikefalin injection in acute post-operative setting;
- the rate and degree of market acceptance of any approved products;
- our ability to obtain and maintain regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- the anticipated commercial launch of our lead product candidate, KORSUVA (CR845/difelikefalin) injection;
- the anticipated use of Enteris's Peptelligence® technology to develop, manufacture and commercialize Oral KORSUVA (CR845/difelikefalin);
- the potential of future scheduling of KORSUVA (CR845/difelikefalin) injection by the United States Drug Enforcement Administration, or DEA, if regulatory approval is received;

- the performance of our current and future collaborators and licensees, including Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceuticals Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, as well as sub-licensees, including Kissei Pharmaceutical Co. Ltd., or Kissei, and our ability to maintain such collaborations;
- our ability to establish additional collaborations for our product candidates;
- the continued service of our key scientific or management personnel;
- our ability to establish commercialization and marketing capabilities;
- regulatory developments in the United States and foreign countries;
- 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;
- the performance of third-party manufacturers and clinical research organizations, or CROs; and
- the potential effects of the ongoing COVID-19 pandemic on our business, operations and clinical development and regulatory timelines and plans.

You should refer to Part II Item 1A. “Risk Factors” of this Quarterly Report on Form 10-Q 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, 2019.

Introduction

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

In our KALM™-1 and KALM-2 Phase 3 trials and two Phase 2 trials, KORSUVA (CR845/difelikefalin) injection (intravenous formulation) has demonstrated statistically significant reductions in itch intensity and concomitant improvement in pruritus-related quality of life measures in hemodialysis patients with moderate-to-severe CKD-aP. 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 were incorporated and 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 and the sale of clinical compound.

Recent Developments

COVID-19 Update

The extent of the impact of the ongoing COVID-19 pandemic on our business, operations and clinical development and regulatory timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, partners, CROs, third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. The timing of our anticipated submission of our New Drug Application, or NDA, to the FDA for KORSUVA (CR845/difelikefalin) injection has not been affected, and we are still on track to submit our NDA in the fourth quarter of 2020. The COVID-19 pandemic, however, has affected, and may in the future affect, the initiation of certain trial sites and patient enrollment for our ongoing Phase 2 clinical trials of Oral KORSUVA (CR845/difelikefalin) for moderate-to-severe pruritus in patients with AD and for the treatment of pruritus in patients with hepatic impairment due to primary biliary cholangitis, or PBC. While we currently do not expect any significant delays in our clinical development or commercial timelines, the ultimate impact of the evolving COVID-19 pandemic remains difficult to predict.

To the extent possible, we are conducting business as usual, with necessary or advisable modifications to employee travel and employee work locations. We are continuing to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees, partners and other third-parties with

whom we do business. The extent to which the ongoing and evolving COVID-19 pandemic may affect our business, operations and clinical development and regulatory timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain.

Dr. Susan Shiff Appointed to Board of Directors

In June 2020, we increased the size of our Board of Directors, or the Board, and appointed Susan Shiff, Ph.D., M.B.A. to serve as a member of our Board with a term expiring at our 2021 Annual Meeting of Stockholders. Dr. Shiff was also appointed to serve as a member of the Compensation Committee and the Nominating and Corporate Governance Committee of the Board. There is no arrangement or understanding between Dr. Shiff and any other person pursuant to which she was selected as a director, and there is no family relationship between Dr. Shiff and any of our other directors or executive officers.

Our Product Candidate

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

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

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

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

Program	Product Candidate	Primary Indication	Status	Commercialization Rights
Pruritus	KORSUVA (CR845/difelikefalin) Injection	Pruritus CKD - Hemodialysis	• KALM-2 (Global) Phase 3 pivotal trial completed; top-line data reported • KALM-1 pivotal trial completed; top-line data reported • Phase 3 safety trials complete • 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 trial completed; top-line data reported	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus CLD - PBC	• Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus Atopic Dermatitis	• KARE Phase 2 efficacy trial ongoing; interim assessment complete – target enrollment increased to 410 patients	Cara (Worldwide, other than South Korea); CKDP (South Korea)
Post-Op Setting	CR845/difelikefalin Injection	Acute Post-Operative Pain/PONV	• Adaptive Phase 2/3 trial completed; top-line data reported	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)

CKD-aP is an intractable systemic itch condition with high prevalence for which there are no approved therapeutics in the United States or Europe. Based on the results from our efficacy and safety trials highlighted below, we expect to submit an NDA to the FDA for KORSUVA (CR845/difelikefalin) injection in the fourth quarter of 2020, and expect our partner, VFMCRP, to submit a Marketing Authorisation Application, or MAA, to the European Medicines Agency, or EMA, shortly thereafter.

In April 2020, we announced positive top-line results from our KALM-2 pivotal Phase 3 trial of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with moderate-to-severe CKD-aP. The trial met the primary and key secondary endpoints after 12 weeks of treatment. The open label extension phase of this trial is also complete.

The study met the primary efficacy endpoint with 54% of the patients receiving 0.5 mcg/ kg of KORSUVA (CR845/difelikefalin) injection versus 42% of patients receiving placebo achieving at least a three-point improvement from baseline with respect to the weekly mean of the daily 24-hour worst itching intensity numeric rating scale, or NRS, score at week 12 (p= 0.02). The study also met the key secondary endpoint with 41% of patients receiving KORSUVA (CR845/difelikefalin) injection achieving a four-point or greater improvement from baseline in the weekly mean of the daily 24-hour worst itching NRS score at week 12 versus 28% for patients receiving placebo (p= 0.01). In this trial, KORSUVA (CR845/difelikefalin) injection was generally well-tolerated with a safety profile consistent with that seen in KALM-1 and the KORSUVA clinical program in patients with CKD-aP. Overall, the incidence of adverse effects, or AEs, and serious AEs were similar across both KORSUVA (CR845/difelikefalin) injection and placebo groups. The most common treatment emergent AEs reported in greater than 5% of patients were diarrhea (8.1% KORSUVA vs 5.5% placebo), falling (6.8% KORSUVA vs 5.1% placebo), vomiting (6.4% KORSUVA vs 5.9% placebo), nausea (6.4% KORSUVA vs 4.2% placebo) and dizziness (5.5% KORSUVA vs 5.1% placebo).

In May 2019, we announced positive results from the double blinded phase of our KALM-1 pivotal Phase 3 efficacy trial (KALM-1) of KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in patients undergoing hemodialysis. The trial met the primary and all secondary endpoints after 12 weeks of treatment. The open label extension phase of this trial is also complete.

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

Currently, more than 1,500 total patient exposures have been achieved across our clinical trials in hemodialysis patients, with more than 700 patients completing at least six months of treatment and more than 400 patients completing one year of treatment.

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

In December 2019, we announced top-line data from our Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in stage III - V (moderate-to-severe) CKD patients. The Phase 2, multicenter, randomized, double-blind, placebo-controlled 12-week trial is designed to evaluate the safety and efficacy of three tablet strengths (0.25 mg, 0.5 mg and 1 mg, once daily administration) of Oral KORSUVA (CR845/difelikefalin) versus placebo in approximately 240 stage III - V (moderate to severe) CKD patients with moderate-to-severe pruritus. The primary efficacy endpoint was the change from baseline in the weekly mean of the daily 24-hour worst itching 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 itching NRS score at week 12.

Patients treated with the 1.0 mg tablet strength of Oral KORSUVA (CR845/difelikefalin) achieved the primary endpoint of statistically significant reduction in weekly mean of the daily worst itching NRS scores vs. placebo after the 12-week treatment period (-4.4 KORSUVA vs. -3.3 placebo, p=0.018). The treatment was statistically significant after two weeks of treatment and sustained through the 12-week treatment period. Regarding secondary endpoints, the proportion of patients on 1.0 mg tablet strength achieving a 3 point or greater improvement from baseline in the weekly mean of the daily worst itching NRS score at week 12 was 72% vs. 58% for placebo but did not achieve statistical significance. Furthermore, patients on 1.0 mg tablet strength showed positive improvements vs. placebo in itch quality of life endpoints as measured using self-assessment Skindex-10 and 5-D Itch scales but did not achieve statistical significance. Oral KORSUVA (CR845/difelikefalin) was generally well-tolerated with a safety profile consistent with that seen in earlier KORSUVA clinical trials. Overall, the incidence of treatment AEs were similar across KORSUVA and placebo groups. The most common AEs reported in >5% of patients in the 1.0 mg KORSUVA group vs. placebo were dizziness (7.5% KORSUVA vs. 0% placebo), fall (6% KORSUVA vs. 0% placebo), diarrhea (6% KORSUVA vs. 1.5% placebo) and constipation (6% KORSUVA vs. 3% placebo).

We intend to initiate the safety portion of a Phase 3 program for Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in stage III - V (moderate-to-severe) CKD in the fourth quarter of 2020, and expect to conduct an End of Phase 2 Meeting with the FDA in the first quarter of 2021.

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

Pruritus is a common and serious symptom in patients with CLD, especially those with chronic cholestatic disease. Pruritus has a prevalence of up to 70% in patients with PBC. Severe pruritus can have debilitating effects and can lead to a significant reduction in a patient's quality of life. Although the pathogenesis of CLD-aP remains poorly understood, it is likely multifactorial including evidence for an imbalance in the endogenous opioid system driven by higher mu receptor activation (pruritic) versus kappa receptor activation (antipruritic). Consequently, the use of selective kappa-opioid receptor agonists has been suggested for the treatment of pruritus in patients with CLD.

In June 2019, we announced the initiation of a Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in patients with hepatic impairment due to PBC. The Phase 2 multicenter, randomized, double-blind, placebo-controlled 16-week trial is designed to evaluate the safety and efficacy of 1 mg tablet of Oral KORSUVA (CR845/difelikefalin) taken twice daily or BID versus placebo in approximately 60 patients with PBC and moderate-to-severe pruritus. The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour worst itching NRS score at week 16 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of week 16 as assessed by the Skindex-10 and 5-D itch scales, as well as the assessment of proportion of patients achieving an improvement from baseline of ≥3 points with respect to the weekly mean of the daily 24-hour worst itching NRS score at week 16. We continue to screen patients in this ongoing Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) and aim to have top-line data in the first half of 2021, due in part to delays related to the ongoing COVID-19 pandemic.

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

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

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

In January 2020, we expanded this Phase 2 trial to include approximately 320 adult AD patients with moderate-to-severe pruritus and incorporated an interim conditional power assessment into the design, to be conducted after approximately 50% of the targeted patient number complete the designated 12-week treatment period. In June 2020, we announced that based on the Independent Data Monitoring Committee's, or IDMC's, recommendation, the trial will be increased by approximately 28%, from the previous enrollment target of 320 patients to 410 patients, to maintain the prespecified statistical power of 80% or greater on the trial's primary endpoint of change from baseline in the weekly mean of the daily 24-hour worst itching NRS score and key secondary endpoint of proportion of patients achieving a $\geq$ 4 point improvement in itch NRS score at week 12. The IDMC's recommendation was based on the results of the prespecified interim conditional power assessment conducted after approximately 50% of the originally targeted patient number completed the designated 12-week treatment period.

Based on current sample size and ongoing enrollment rates, we expect to complete full trial enrollment in the fourth quarter of 2020 and we aim to report the top-line results from this trial in the first half of 2021, subject to any delays related to the ongoing COVID-19 pandemic.

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.

In June 2018, we reported positive top-line date from the adaptive Phase 2/3 study of CR845/difelikefalin in patients undergoing abdominal surgery. CR845 injection achieved statistical significance for the primary endpoint of pain relief as measured by Area Under the Curve, or AUC, 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.

We have completed an advisory meeting with the FDA regarding the potential regulatory path forward for PONV and we are currently evaluating potential next steps.

Human Abuse Liability Trial of CR845/Difelikefalin Injection

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

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 (1.0 mcg/kg and 5.0 mcg/kg) versus placebo on three measures of respiratory drive in 15 healthy volunteers. The primary safety endpoints were: a >10 mmHg sustained (≥30 seconds duration)

increase in end-tidal CO_2, or $ETCO_2$, above baseline or to >50 mmHg, and a sustained reduction in oxygen saturation, or SpO_2, to <92%.

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

Collaboration and License Agreements

Vifor Fresenius Medical Care Renal Pharma Ltd.

In May 2018, we entered into a license agreement, or the VFMCRP Agreement, with VFMCRP, a joint venture between Vifor Pharma Group and Fresenius Medical Care, under which we granted VFMCRP a license to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA (CR845/difelikefalin) injection for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients worldwide (excluding the United States, Japan and South Korea). We retain full development and commercialization rights for KORSUVA injection for the treatment of CKD-aP in dialysis patients in the U.S. except in the dialysis clinics of Fresenius Medical Care North America, or FMCNA, where we and VFMCRP will promote KORSUVA injection under a profit-sharing arrangement.

We are eligible to receive from VFMCRP 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, of KORSUVA (CR845/difelikefalin) injection in the licensed territories. In the United States, we and VFMCRP will promote KORSUVA (CR845/difelikefalin) injection in the dialysis clinics of FMCNA under a profit-sharing arrangement (subject to the terms and conditions of the VFMCRP Agreement) based on net FMCNA clinic sales recorded by us.

Maruishi Pharmaceutical Co., Ltd.

In April 2013, we entered into a license agreement with Maruishi, or the Maruishi Agreement, under which we granted Maruishi an exclusive license to develop, manufacture and commercialize drug products containing CR845/difelikefalin in Japan in the acute pain and uremic pruritus fields. Maruishi has a right of first negotiation for any other indications for which we develop CR845/difelikefalin and, under certain conditions, Maruishi may substitute another pruritus indication for the uremic pruritus indication originally included in its license from us. If we abandon development of CR845/difelikefalin and begin development of another kappa opioid receptor agonist that is covered by the claims of the patents we licensed to Maruishi, such other agonist will automatically be included in the license to Maruishi. Maruishi is required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in Japan. We are required to use commercially reasonable efforts, at our expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in the United States.

Under the terms of the Maruishi Agreement, we are eligible to receive up to an aggregate of $10.5 million in clinical development and regulatory milestones, of which $2.5 million (before contractual foreign currency exchange adjustments) has been received as of June 30, 2020. We are also eligible to receive a one-time sales milestone of one billion Yen when a certain sales level is attained. We also receive a mid-double-digit percentage of all non-royalty payments received by Maruishi from its sublicensees, if any. We are also eligible to receive tiered royalties based on net sales, if any, with minimum royalty rates in the low double digits and maximum royalty rates in the low twenties. Maruishi’s obligation to pay us royalties continues, on a product-by-product basis, until the expiration of the last-to-expire licensed patent covering such product or the later expiration of any market exclusivity period. The Maruishi Agreement continues until terminated.

Chong Kun Dang Pharmaceutical Corporation

In April 2012, we entered into a license agreement with CKDP, or the CKDP Agreement, under which we granted CKDP an exclusive license to develop, manufacture and commercialize drug products containing CR845/difelikefalin in South Korea. CKDP is required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in South Korea. We are required to use commercially reasonable efforts, at our expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in the United States.

Under the terms of the CKDP Agreement, we are eligible to receive up to an aggregate of $3.8 million in development and regulatory milestones (before South Korean withholding taxes). In May 2020, we met the milestone criteria, as set forth in the CKDP Agreement, for completion of a Phase 3 trial for uremic pruritus in the United States. As a result, in June 2020, we received a milestone payment of $0.6 million (net of South Korean withholding tax) from CKDP. As of June 30, 2020, we have received $2.3 million (before South Korean withholding tax) of development and regulatory milestones. We are also eligible to receive a mid-double-digit percentage of all non-royalty payments received by CKDP from its sublicensees, if any, and tiered royalties ranging from the high single digits to the high teens based on net sales, if any. CKDP's obligation to pay us royalties continues, on a product-by-product basis, until the expiration of the last-to-expire licensed patent covering such product or the later expiration of any market exclusivity period. The CKDP Agreement continues until CKDP no longer has any obligation to pay us royalties on any product.

Manufacturing and License Agreements

Enteris Biopharma, Inc.

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

As consideration for the licensed rights under the Enteris License Agreement, we paid an upfront fee equal to $8.0 million, consisting of $4.0 million in cash and $4.0 million in shares of our common stock.

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

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

Patheon UK Limited

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

The MSA has an initial term ending December 31, 2023, and will automatically renew after the initial term for successive terms of two years each if there is a Product Agreement in effect, unless either party gives notice of its intention to terminate the MSA at least 18 months prior to the end of the then current term.

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

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 $6.6 million in clinical development or regulatory milestone payments 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 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 2020 will increase over those for 2019. 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, information technology 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 2020 will increase as compared to 2019 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, net

Other income, net 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. In the event we record a credit loss expense on our available-for-sale debt securities, those expenses would be offset against other income.

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, 2020 and 2019

Revenue

	Three Months Ended June 30,			Six Months Ended June 30,		
	2020	2019	% change	2020	2019	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
License and milestone fees revenue	$ 5,099	$ 5,208	-2%	$ 13,120	$ 9,450	39%
Clinical compound revenue	535	—	100%	607	140	334%
Total revenue	$ 5,634	$ 5,208	8%	$ 13,727	$ 9,590	43%

License and milestone fees revenue

License and milestone fees revenue of $5.1 million and $5.2 million for the three months ended June 30, 2020 and 2019, respectively, were related to license fees of $4.5 and $5.2 million, respectively, earned by us during the respective periods in connection with the VFMCRP Agreement, as well as $0.6 million (net of South Korean withholding taxes) earned by us during the three months ended June 30, 2020 for achieving a development milestone under the CKDP Agreement (see Note 10 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

License and milestone fees revenue of $13.1 million and $9.5 million for the six months ended June 30, 2020 and 2019, respectively, were related to license fees of $12.5 million and $9.5 million, respectively, earned by us during the respective periods in connection with the VFMCRP Agreement, as well as $0.6 million (net of South Korean withholding taxes) earned by us during the six months ended June 30, 2020 for achieving a development milestone under the CKDP Agreement (see Note 10 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

Clinical compound revenue

Clinical compound revenue of $535 thousand for the three months ended June 30, 2020 was related to the sales of clinical compound to VFMCRP for $88 thousand and to Maruishi for $447 thousand. Clinical compound revenue of $607 thousand for the six months ended June 30, 2020 was related to the sales of clinical compound to VFMCRP for $88 thousand and to Maruishi for $519 thousand. Clinical compound revenue of $140 thousand for the six months ended June 30, 2019 was related to the sale of clinical compound to Maruishi. There were no sales of clinical compound during the three months ended June 30, 2019.

Research and Development Expense

	Three Months Ended June 30,			Six Months Ended June 30,		
	2020	2019	% change	2020	2019	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 17,063	$ 17,542	-3%	$ 42,802	$ 35,283	21%
Consultant services in support of clinical trials	1,398	1,122	25%	2,673	2,380	12%
Stock-based compensation	2,803	1,929	45%	4,426	3,011	47%
Depreciation and amortization	27	27	0%	55	55	0%
Other R&D operating expenses	4,817	3,736	29%	9,688	7,235	34%
Total R&D expense	$ 26,108	$ 24,356	7%	$ 59,644	$ 47,964	24%

For the three months ended June 30, 2020 compared to the three months ended June 30, 2019, the net decrease in direct clinical trial costs and related consultant costs primarily resulted from decreases totaling $7.8 million, mainly from

activities related to the KALM-1 Phase 3 efficacy trial and the 52-week open-label extension study of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients and costs associated with a supportive Phase 1 study. Those costs were partially offset by an increase of $7.2 million, mainly from the Phase 2 efficacy trial for pruritus associated with AD, the KALM-2 Phase 3 efficacy trial and up to 12 week Phase 3 safety trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis and costs associated with a supportive Phase 1 study. There was also an increase of $0.5 million in drug manufacturing costs. The increase in stock-based compensation expense was primarily the result of additional stock option and restricted stock unit grants to new and existing employees. The increase in other R&D operating expenses primarily resulted from an increase in payroll and related costs and cost of clinical compound sales, partially offset by a decrease in conferences and travel and related costs for the three months ended June 30, 2020.

For the six months ended June 30, 2020 compared to the six months ended June 30, 2019, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $20.7 million, mainly from activities related to the KALM-2 Phase 3 efficacy trial and up to 12 week Phase 3 safety trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the Phase 2 efficacy trial for pruritus associated with AD and costs associated with supportive Phase 1 studies. There was also an increase of $1.2 million in drug manufacturing costs. Those costs were partially offset by a decrease of $14.0 million, mainly from the KALM-1 Phase 3 efficacy trial and the 52-week open-label extension study of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients, costs associated with a supportive Phase 1 study and other license fees. The increase in stock-based compensation expense was primarily the result of additional stock option and restricted stock unit grants to new and existing employees. The increase in other R&D operating expenses primarily resulted from an increase in payroll and related costs and cost of clinical compound sales for the six months ended June 30, 2020.

The following table summarizes our R&D expenses by programs for the three and six months ended June 30, 2020 and 2019:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2020	2019	% change	2020	2019	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
I.V. CR845 - Pruritus	$ 12,160	$ 13,298	-9%	$ 31,151	$ 27,188	15%
I.V. CR845 - Pain	25	160	-85%	56	359	-84%
Oral CR845 - Pruritus	6,225	5,195	20%	14,195	10,094	41%
Oral CR845 - Pain	6	12	-52%	15	22	-34%
Internal research and development expenses	7,692	5,691	35%	14,227	10,301	38%
Total research and development expenses	$ 26,108	$ 24,356	7%	$ 59,644	$ 47,964	24%

General and Administrative Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2020	2019	% change	2020	2019	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 1,306	$ 903	45%	$ 2,437	$ 1,832	33%
Stock-based compensation	1,815	2,085	-13%	3,039	3,238	-6%
Depreciation and amortization	21	22	-9%	41	44	-7%
Other G&A operating expenses	2,268	1,984	14%	4,451	3,788	18%
Total G&A expense	$ 5,410	$ 4,994	8%	$ 9,968	$ 8,902	12%

For the three months ended June 30, 2020 compared to the three months ended June 30, 2019, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs and legal fees. The decrease in stock-based compensation expense was primarily the result of the resignation of our former Chief Financial Officer in December 2019 and the issuance of common stock relating to the consulting agreement that ended in 2019, partially offset by additional stock option grants to employees and members of our Board of Directors. The increase in other G&A operating expenses was primarily the result of increases in insurance costs.

For the six months ended June 30, 2020 compared to the six months ended June 30, 2019, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs and accounting and legal fees. The decrease in stock-based compensation expense was primarily the result of the resignation of our former Chief Financial Officer in December 2019 and the issuance of common stock relating to the consulting agreement that ended in 2019, partially offset by additional stock option grants to employees and members of our Board of Directors. The increase in other G&A operating expenses was primarily the result of increases in insurance and payroll and related costs.

Other Income, Net

	Three Months Ended June 30,			Six Months Ended June 30,		
	2020	2019	% change	2020	2019	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other income, net	$ 634	$ 947	-33%	$ 1,591	$ 2,036	-22%

During the three months ended June 30, 2020 compared to the three months ended June 30, 2019, the decrease in other income, net was primarily due to a decrease in net accretion income and a decrease in interest income resulting from a lower yield on our portfolio of investments in the 2020 period.

During the six months ended June 30, 2020 compared to the six months ended June 30, 2019, the decrease in other income, net was primarily due to a decrease in net accretion income partially offset by an increase in interest income resulting from a higher average balance of our portfolio of investments in the 2020 period.

Benefit from Income Taxes

For the three months ended June 30, 2020 and 2019, pre-tax losses were $25.3 million and $23.2 million, respectively, and we recognized a benefit from income taxes of $182 thousand and $235 thousand, respectively. For the six months ended June 30, 2020 and 2019, pre-tax losses were $54.3 million and $45.2 million, respectively, and we recognized a benefit from income taxes of $304 thousand and $320 thousand, respectively.

The benefit from income taxes relates to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, as discussed above. We recognized a full valuation allowance against deferred tax assets at June 30, 2020 and December 31, 2019.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception and through June 30, 2020, we have raised an aggregate of approximately $624.5 million to fund our operations, including (1) net proceeds of $446.3 million from the sale of shares of our common stock in five public offerings, including our initial public offering; (2) proceeds of $73.3 million from the sale of shares of our convertible preferred stock and from debt financings prior to our initial public offering; (3) payments of approximately $90.3 million under our license agreements, primarily with VFMCRP, Maruishi, CKDP and an earlier product candidate for which development efforts ceased in 2007; and (4) net proceeds of $14.6 million from the purchase of our common

stock in relation to the license agreement with VFMCRP (see Note 10 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

In order to fund our future operations, including our planned clinical trials, we filed the Shelf Registration Statement (File No. 333-230333), which provides for aggregate offerings of up to $300.0 million of common stock, preferred stock, debt securities, warrants or any combination thereof and was declared effective on April 4, 2019. The securities registered under the Shelf Registration Statement include unsold securities that had been registered under our previous Registration Statement on Form S-3 (File No. 333-216657) that was declared effective on March 24, 2017. To date, we have offered and sold an aggregate of approximately $145.5 million of securities under this Shelf Registration Statement. We believe that our Shelf Registration Statement provides us with the flexibility to raise additional capital to finance our operations as needed. We may offer additional securities under our Shelf Registration Statement from time to time in response to market conditions or other circumstances if we believe such a plan of financing is in the best interests of our stockholders.

As of June 30, 2020, we had $153.0 million in unrestricted cash and cash equivalents and available-for-sale marketable securities. We believe our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient to fund our currently anticipated operating expenses and capital expenditures into the second half of 2021, without giving effect to any potential milestone payments we may receive under our licensing and collaboration agreements with VFMCRP, Maruishi and CKDP. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs.

Under the VFMCRP Agreement, we are eligible to receive regulatory and commercial milestone payments in the aggregate of up to $470.0 million, consisting of up to $30.0 million in regulatory milestones and up to $440.0 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. As of June 30, 2020, we have not received any milestone payments under the VFMCRP Agreement.

Under the Maruishi Agreement, we are also potentially eligible to earn up to an aggregate of $6.0 million in clinical development milestones and $4.5 million in regulatory milestones, before any foreign exchange adjustment, as well as tiered royalties, with percentages ranging from the low double digits to the low twenties, based on net sales of products containing CR845/difelikefalin in Japan, if any, and share in any sub-license fees. As of June 30, 2020, we have received milestone payments of $2.5 million before contractual foreign currency exchange adjustments under the Maruishi Agreement.

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. In May 2020, the criteria for revenue recognition for a milestone event set forth in the CKDP Agreement was achieved, and we recorded $0.6 million (net of South Korean withholding tax) as license and milestone fees revenue relating to the milestone payment received from CKDP. As of June 30, 2020, $2.3 million (before South Korean withholding tax) of development and regulatory milestones have been received.

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 $25.1 million and $23.0 million for the three months ended June 30, 2020 and 2019, respectively, and $54.0 million and $44.9 million for the six months ended June 30, 2020 and 2019, respectively. As of June 30, 2020, we had an accumulated deficit of $454.7 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. Further, the timing of any of the above may be impacted by the ongoing COVID-19 pandemic, introducing additional uncertainty.

Because our product candidates are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the actual 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, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. In particular, because we do not have sufficient financial resources to meet all of our development objectives, especially the completion of our planned development of I.V. and Oral CR845/difelikefalin for the treatment of pruritus, we will need to raise additional capital. If we are not able to do so, we could be required to postpone, scale back or eliminate some, or all, of these objectives. To the extent that we raise additional capital through the future sale of equity or convertible debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on timing expectations and projected costs for our current clinical development plans, which include completing our Phase 3 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients suffering from moderate-to-severe CKD-aP to enable the submission of a new drug application, conducting supportive Phase 1 trials and Phase 2 trials of Oral KORSUVA (CR845/difelikefalin) in patients with pruritus associated with CKD, CLD and AD, we expect that our existing cash and cash equivalents and available-for-sale marketable securities as of June 30, 2020 will be sufficient for us to fund our currently anticipated operating expenses and capital expenditures into the second half of 2021, without giving effect to any potential milestone payments we may receive under our collaboration agreements with VFMCRP, Maruishi and CKDP. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs. Because the process of testing product candidates in clinical trials is costly and the timing of progress in these trials is uncertain, it is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we presently expect.

Cash Flows

The following is a summary of the net cash flows provided by (used in) our operating, investing and financing activities for the six months ended June 30, 2020 and 2019:

	Six Months Ended June 30,	
	2020	2019
	Dollar amounts in thousands	
Net cash used in operating activities	$ (65,955)	$ (52,422)
Net cash provided by investing activities	104,341	51,627
Net cash provided by financing activities	276	4,208
Net increase in cash, cash equivalents and restricted cash	$ 38,662	$ 3,413

Net cash used in operating activities

Net cash used in operating activities for the six months ended June 30, 2020 consisted primarily of a net loss of $54.0 million, a $7.3 million cash outflow from net changes in operating assets and liabilities and a $4.7 million cash outflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of a cash outflow of $5.7 million from a decrease in accounts payable and accrued expenses and a cash outflow of $1.3 million from an increase in prepaid expenses, primarily related to an increase in prepaid clinical costs. Net non-cash charges primarily consisted of a decrease of $12.5 million in deferred revenue associated with our VFMCRP Agreement, partially offset by stock-based compensation expense of $7.5 million.

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

Net cash provided by investing activities

Net cash provided by investing activities was $104.3 million for the six months ended June 30, 2020, which primarily included cash inflows of $114.7 million from maturities and redemptions of available-for-sale marketable securities and proceeds of $10.7 million from sales of available-for-sale marketable securities, partially offset by cash outflows of $21.0 million for the purchases of available-for-sale marketable securities.

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

Net cash provided by financing activities

Net cash provided by financing activities for the six months ended June 30, 2020 and 2019 consisted of proceeds of $276 thousand and $4.2 million, respectively, received from the exercise of stock options.

Significant Contractual Obligations and Commitments

Contractual obligations and commitments as of June 30, 2020 consisted of an operating lease obligation in connection with the lease agreement for our operating facility in Stamford, Connecticut we entered into in December

2015 and amended in June 2020, the Enteris License Agreement we entered into in August 2019, and the MSA we entered into with Patheon in July 2019. However, we have no material non-cancelable purchase commitments with these contract manufacturers or service providers, as we have generally contracted on a cancelable purchase order basis. Furthermore, milestone payments potentially owed by us in connection with the Enteris License Agreement relate to milestone events that may or may not be achieved.

See Note 15 of Notes to Condensed Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q.

Recent Accounting Pronouncements

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

Off-Balance Sheet Arrangements

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

Discussion of Critical Accounting Policies

The preparation of financial statements in conformity with GAAP requires us to use judgment in making certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities and the reported amounts of revenues and expenses in our condensed financial statements and accompanying notes. Critical accounting policies are those that are most important to the portrayal of our financial condition and results of operations and require difficult, subjective and complex judgments by management in order to make estimates about the effect of matters that are inherently uncertain. During the three and six months ended June 30, 2020, 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, 2019.

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

Interest Rate Risk

As of June 30, 2020, we invested a majority of our cash reserves in a variety of available-for-sale marketable securities, including investment-grade debt instruments, principally corporate bonds, commercial paper, municipal bonds and direct obligations of the U.S. government and U.S. government-sponsored entities, and in cash equivalents. See Note 3 of Notes to Condensed Financial Statements, *Available-for-Sale Marketable Securities*, in this Quarterly Report on Form 10-Q for details about our available-for-sale marketable securities.

As of June 30, 2020, we had invested $96.1 million of our cash reserves in such marketable securities. Those marketable securities included $96.1 million of investment grade debt instruments with a yield of approximately 1.70% and maturities through December 2021. As of December 31, 2019, we had invested $199.9 million of our cash reserves in such marketable securities. Those marketable securities included $199.9 million of investment grade debt instruments with a yield of approximately 2.08% and maturities through December 2021.

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 to meet operating needs. Our investments are subject to interest rate risk and will decrease in value if market interest rates increase. However, due to the conservative nature of our investments and relatively short duration, interest rate risk is mitigated.

Duration is a sensitivity measure that can be used to approximate the change in the fair value of a security that will result from a change in interest rates. Applying the duration model, a hypothetical 1% increase in interest rates as of June 30, 2020 and December 31, 2019, 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 Principal Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of June 30, 2020. Based on such evaluation, our Chief Executive Officer and Principal Financial Officer have concluded that, as of June 30, 2020, 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, 2020, we implemented ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326), Measurement of Credit Losses on Financial Instruments*, or ASU 2016-13. Although ASU 2016-13 did not have a material impact on our results of operations, financial position or cash flows upon adoption, we did revise our internal controls and procedures to review qualitative and quantitative factors to determine whether the unrealized loss for each available-for-sale debt security at any balance sheet date is due to a credit loss during the six months ended June 30, 2020.

There was no other change in our internal control over financial reporting that occurred during the quarter ended June 30, 2020 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 Principal 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*****.**

In addition to other information contained in this Quarterly Report on Form 10-Q, the following risks should be considered in evaluating our business and future prospects and an investment in our common stock. The risks and uncertainties described below are not the only ones we face. If any of the following risks and uncertainties develops into actual events, our business, financial condition, results of operations and cash flows could be materially adversely affected. In that case, the price of our common stock could decline and you may lose all or part of your investment.

Risks Related to Our Financial Condition and Capital Requirements

We have incurred significant losses since our inception, anticipate that we will incur continued losses for the foreseeable future, and may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company. For the last several years, we have focused our efforts primarily on developing I.V. and Oral CR845/difelikefalin with the goal of achieving regulatory approval. Since inception, we have incurred significant operating and net losses. Our net losses were $25.1 million and $23.0 million for the three months ended June 30, 2020 and 2019, respectively, and $54.0 million and $44.9 million for the six months ended June 30, 2020 and 2019, respectively. As of June 30, 2020, we had an accumulated deficit of $454.7 million. We expect to continue to incur significant expenses and operating and net losses over the next several years, as we continue to develop and seek marketing approval for I.V. and Oral CR845/difelikefalin. Our net losses may fluctuate significantly from year to year, depending on the timing of our clinical trials, the receipt of additional milestone payments, if any, under our agreements with VFMCRP, Maruishi and CKDP, the receipt of payments under any future agreements we may enter into, and our expenditures on other R&D activities as well as any payments owed under the License Agreement with Enteris and any future similar agreements.

In addition, we expect to incur significant sales, marketing and manufacturing expenses related to the commercialization of I.V. and Oral CR845/difelikefalin, if they are approved by the FDA. As a result, we expect to continue to incur significant losses for the foreseeable future. We anticipate that our expenses will increase significantly as we:

- continue the development of KORSUVA (CR845/difelikefalin) injection for CKD-aP;
- continue the development of Oral KORSUVA (CR845/difelikefalin) for CKD-aP and CLD-aP;
- expand our Oral KORSUVA (CR845/difelikefalin) program into certain dermatologic conditions, including AD;
- explore further development of CR845/difelikefalin injection in the post-operative setting;
- seek regulatory approvals for KORSUVA (CR845/difelikefalin) injection and any other product candidate that successfully completes 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.

To become and remain profitable, we must succeed in developing and eventually commercializing one or more products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing clinical trials of KORSUVA (CR845/difelikefalin) injection and Oral KORSUVA (CR845/difelikefalin), discovering additional product candidates and completing preclinical testing and clinical trials for those product candidates, potentially entering into collaboration and license agreements, obtaining regulatory approval for product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We may never succeed in these activities and, even if we do, may never achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA or foreign regulatory authorities, to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our R&D efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

Our operating history makes it difficult to evaluate our business and prospects.

We commenced operations in 2004, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital and advancing our product candidates, including KORSUVA (CR845/difelikefalin) injection and Oral KORSUVA (CR845/difelikefalin), through clinical development. We have not yet demonstrated an ability to obtain regulatory approval for, or successfully commercialize, a product candidate. If our product candidates are approved by the FDA, we will need to expand our capabilities to support commercial activities. We may not be successful in adding such capabilities. Consequently, any predictions about our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

We will need additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Conducting clinical trials, pursuing regulatory approvals, establishing outsourced manufacturing relationships and successfully manufacturing and commercializing our product candidates is expensive. We will need to raise additional capital to:

- progress our KORSUVA (CR845/difelikefalin) injection CKD-aP program through Phase 3 pivotal trials and NDA filing;
- continue the further development of Oral KORSUVA (CR845/difelikefalin) for CKD-aP and CLD-aP;

- expand our Oral KORSUVA (CR845/difelikefalin) program into certain dermatologic conditions, including AD;
- explore further development of CR845/difelikefalin injection in the post-operative setting;
- fund our operations and continue our efforts to hire additional personnel and build a commercial infrastructure to prepare for the commercialization of KORSUVA (CR845/difelikefalin) injection, if approved by the FDA;
- qualify and outsource the commercial-scale manufacturing of our products, including KORSUVA (CR845/difelikefalin) injection under cGMP; and
- in-license other product candidates.

We believe that with our available cash and cash equivalents and marketable securities balances as of June 30, 2020, we will have sufficient funds to meet our projected operating requirements into the second half of 2021, without giving effect to any potential milestone payments we may receive under our collaboration agreements. We have based this estimate on assumptions that may prove to be wrong and we could spend our available financial resources faster than we currently expect. Further, because we do not have sufficient financial resources to meet all of our development objectives, especially our efforts to build a commercial infrastructure to prepare for the commercialization of KORSUVA (CR845/difelikefalin) injection, if approved, and the completion of our development of Oral KORSUVA (CR845/difelikefalin) for the treatment of CKD-aP and CLD-aP, 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. Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and costs related to our Phase 3 development of KORSUVA (CR845/difelikefalin) injection and Phase 2 development of Oral KORSUVA (CR845/difelikefalin) for CKD-aP, CLD-aP and other indications;
- the rate of progress and costs of our efforts to prepare for the submission of an NDA for KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in hemodialysis patients or for any product candidates that we may in-license or acquire in the future, and the potential that we may need to conduct additional clinical trials to support applications for regulatory approval;
- the costs of establishing a commercial organization to sell, market and distribute KORSUVA (CR845/difelikefalin) injection, if approved;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates, including any such costs we may be required to expend if our licensors are unwilling or unable to do so;
- the cost and timing of manufacturing sufficient supplies of KORSUVA (CR845/difelikefalin) injection in preparation for commercialization, if approved;
- the effect of competing technological and market developments;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish; and
- the success of the commercialization of KORSUVA (CR845/difelikefalin) injection, if approved, and any future product candidates.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. Until we can generate a sufficient amount of product revenue, if ever, we expect to finance future cash needs through public or private equity offerings, debt financings, milestone and royalty payments from corporate collaboration and licensing arrangements, as well as through interest income earned on cash and investment balances. We cannot be certain that additional funding will be available on acceptable terms, or at all, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If adequate funds are not available, we may be required to delay, reduce the scope of, or eliminate, one or more of our development programs or our commercialization efforts.

Risks Related to Our Business and the Development of Our Product Candidates

We are substantially dependent on the success of our lead product candidate, KORSUVA (CR845/difelikefalin) injection being developed for the treatment of CKD-aP in hemodialysis patients, and cannot guarantee that this product candidate will successfully complete Phase 3 clinical trials, receive regulatory approval or be successfully commercialized.

We currently have no products approved for commercial distribution. We have invested a significant portion of our efforts and financial resources in the development of KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in patients undergoing hemodialysis. Our business depends entirely on the successful development and commercialization of our product candidates, and in particular, KORSUVA (CR845/difelikefalin) injection, which may never occur. Our ability to generate product revenues in the near term is dependent on our ability to complete the development of, obtain regulatory approval for, and then successfully commercialize KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in patients undergoing hemodialysis. We currently generate no revenues from sales of any products, and we may never be able to develop or commercialize a marketable product.

Based on the results from our efficacy and safety trials for KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP, we expect to submit an NDA to the FDA for KORSUVA (CR845/difelikefalin) injection in the second half of 2020, and expect our partner, VFMCRP, to submit an MAA to the EMA shortly thereafter; however, we cannot assure you that the results of our trials will successfully support our regulatory applications for approval.

KORSUVA (CR845/difelikefalin) injection will require regulatory approval, establishment of a commercial organization, significant marketing efforts and further investment before we generate any revenues from product sales. We are not permitted to market or promote any of our product candidates, including KORSUVA (CR845/difelikefalin) injection, before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. If we do not receive FDA approval for, and successfully commercialize KORSUVA (CR845/difelikefalin) injection, we will not be able to generate revenue in the United States in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing CR845/difelikefalin injection will have a substantial adverse impact on our business and financial condition.

We have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any future product candidates will be successful in clinical trials or receive regulatory approval. Even though KORSUVA (CR845/difelikefalin) injection recently completed the efficacy phase of two Phase 3 clinical trials for the treatment of dialysis patients with CKD-aP, it is, nonetheless, susceptible to the risks of failure inherent at any stage of product development, including the appearance of unexpected adverse events. Further, KORSUVA (CR845/difelikefalin) injection may not receive regulatory approval even if it is successful in clinical trials. If approved for marketing by applicable regulatory authorities, our ability to generate revenues from KORSUVA (CR845/difelikefalin) injection will depend on our ability to:

- create market demand for KORSUVA (CR845/difelikefalin) injection through our own marketing and sales activities in the United States, and any other arrangements to promote this product candidate we may otherwise establish;

- hire, train and deploy a sales force to commercialize KORSUVA (CR845/difelikefalin) injection in the United States;
- manufacture KORSUVA (CR845/difelikefalin) injection in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter;
- establish and maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- maintain existing partnerships and/or create new partnerships with, or offer licenses to, third parties to promote and sell KORSUVA (CR845/difelikefalin) injection in foreign markets where we receive marketing approval;
- maintain patent and trade secret protection and regulatory exclusivity for KORSUVA (CR845/difelikefalin) injection;
- launch commercial sales of KORSUVA (CR845/difelikefalin) injection, whether alone or in collaboration with others;
- achieve market acceptance of KORSUVA (CR845/difelikefalin) injection by patients, the medical community and third-party payers;
- achieve coverage and adequate reimbursement from third-party payers for KORSUVA (CR845/difelikefalin) injection;
- effectively compete with other competing therapies; and
- maintain a continued acceptable safety profile of KORSUVA (CR845/difelikefalin) injection following launch.

As we continue to develop our other current or future product candidates, including Oral KORSUVA (CR845/difelikefalin), we expect to face similar risks to our ability to develop, obtain regulatory approval for and successfully commercialize such product candidates as we face with KORSUVA (CR845/difelikefalin) injection.

Our business, operations and clinical development and regulatory timelines and plans have been, and could continue to be, adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic.

Our business, operations and clinical development timelines and plans have been, and could continue to be, adversely affected by health epidemics in regions where we have concentrations of third-party manufacturers, clinical trial sites or other business operations, and could cause significant disruption in the operations of third-party manufacturers or CROs upon whom we rely. In December 2019, a novel strain of coronavirus, SARS-CoV-2, causing the Coronavirus Disease 2019 (COVID-19), was reported and since then, COVID-19 has spread worldwide.

The President of the United States has declared the COVID-19 pandemic a national emergency, and many state, local and foreign governments have put in place, and continue to enforce in full or in part, quarantines, executive orders, shelter-in-place orders and similar government orders and restrictions in order to control the spread of the disease. Such orders or restrictions, and the perception that such orders or restrictions could occur, have resulted in business closures, work stoppages, slowdowns and delays, work-from-home policies, travel restrictions and cancellation of events, among other effects that have negatively impacted the global economy and could disrupt our business and operations. We have implemented a work-from-home policy for all employees, and we may take further actions that alter our operations as may be required by federal, state or local authorities, or which we determine are in the best interests of our employees. Moreover, our clinical development and regulatory timelines and plans could be affected by the ongoing COVID-19 pandemic. Site initiation and patient enrollment has been, and could in the future be, affected and some patients may not be able to comply with clinical trial protocols and the ability to conduct follow up visits with treated patients may be limited if quarantines impede patient movement or interrupt healthcare services. For example, we experienced a delay in initiation of certain trial sites for our ongoing Phase 2 clinical trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in patients with hepatic impairment due to PBC, and in patient enrollment for our Phase 2 clinical trial of Oral KORSUVA (CR845/difelikefalin) for moderate-to-severe pruritus in patients with AD. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 could be adversely impacted. Furthermore, our third-party manufacturers may be shut-down or have difficulty meeting their contractual obligations. In addition, COVID-19 may cause our third-party manufacturers of KORSUVA (CR845/difelikefalin) injection to operate at reduced capacity. While we currently do not expect any significant delays in our clinical development or commercial timelines, the ultimate impact of the evolving COVID-19 pandemic remains difficult to predict.

Further, the spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by and the duration of COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global COVID-19 pandemic continues to rapidly evolve, and we will continue to monitor the COVID-19 situation closely. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of the potential impacts on our business, our clinical trials, healthcare systems or the global economy as a whole.

CR845/difelikefalin acts as a selective kappa opioid receptor agonist, which is a drug class that has not previously yielded a successful commercial product for pruritus or pain indications.

The development of product candidates based on peripheral kappa opioid receptor agonists is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates that work through this mechanism are relatively recent. The scientific evidence to support the feasibility of developing differentiated product candidates based on these discoveries is both preliminary and limited. We believe that we are among a relatively small group of companies that are pursuing the development of product candidates based on peripherally acting kappa opioid receptor agonists. In addition, we believe that companies that previously explored the development of kappa opioid receptor agonists abandoned these efforts because those prior generation kappa agonists, which were centrally active, resulted in psychiatric side effects. Although CR845/difelikefalin is a peripherally acting kappa opioid receptor agonist and these side effects have not been observed in any of our clinical trials to date, it is possible that we could

observe similar side effects, or other unacceptable adverse events. As a result, our approach to developing product candidates based on peripheral kappa opioid receptor agonists may not be successful and may never lead to marketable products.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both its regulatory approval and commercialization. As such, we are currently primarily focused on the development of KORSUVA (CR845/difelikefalin) injection for CKD-aP in hemodialysis patients and Oral KORSUVA (CR845/difelikefalin) for CKD-aP in pre-dialysis patients, CLD-aP and certain dermatological conditions, including AD. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future R&D programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Our future growth may depend on our ability to identify and develop products and if we do not successfully identify and develop product candidates or integrate them into our operations, we may have limited growth opportunities.

A component of our business strategy is to continue to develop a pipeline of product candidates by developing products that we believe are a strategic fit with our focus on pain and pruritus therapeutics. However, these business activities may entail numerous operational and financial risks, including:

- difficulty or inability to secure financing to fund development activities for such development;
- disruption of our business and diversion of our management’s time and attention;
- higher than expected development costs;
- exposure to unknown liabilities;
- difficulty in managing multiple product development programs; and
- inability to successfully develop new products or clinical failure.

We have limited resources to identify and execute the development of products. Moreover, we may devote resources to potential development that are never completed, or we may fail to realize the anticipated benefits of such efforts. If we do not successfully develop and commercialize product candidates, we may not be able to obtain product revenues in future periods.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates as expected, and our ability to generate revenue will be materially impaired.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of

clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates, including KORSUVA (CR845/difelikefalin) injection and Oral KORSUVA (CR845/difelikefalin), or any product candidates we may seek to develop in the future, will ever obtain regulatory approval.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA, and similar regulatory authorities outside the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing that product candidate. We have no experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs and consultants to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy for that indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful. For example, the fact that we reported positive results from the double blinded phase of our KALM-1 trial of KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in patients undergoing hemodialysis does not mean that our ongoing Phase 3 efficacy and safety trials for KORSUVA (CR845/difelikefalin) injection will be completed successfully. We may also experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to suspend clinical trials, as in the case of the IND clinical hold placed on our adaptive Phase 3 trial of I.V. CR845/difelikefalin for postoperative pain in February 2016, which was subsequently removed in April 2016, or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;

- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- changes in marketing approval policies during the development period;
- changes in or the enactment of additional statutes or regulations;
- changes in regulatory review for each submitted product application;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

In addition, unfavorable changes in our industry or the global economy, including as a result of the ongoing COVID-19 pandemic, could contribute to some of the events listed above and further impact our ability to progress our clinical trials, submit for marketing approval or commercialize our product candidates, if approved, as planned. Further, if and to the extent, global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could affect our ability to obtain marketing approval for any of our product candidates, including KORSUVA (CR845/difelikefalin), for which we remain on track to submit our NDA to the FDA in the fourth quarter of 2020 and our MAA to the EMA shortly thereafter.

Moreover, if we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

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

Furthermore, regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies, including with respect to third-party technology used in any of our product candidates such as the excipient we intend to use for Oral KORSUVA (CR845/difelikefalin). In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Finally, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of these scenarios could compromise the commercial prospects for our product candidates to assure safe use of the product candidates, either as a condition of product candidate approval or on the basis of new safety information.

If we experience delays in obtaining approval, if we fail to obtain approval of a product candidate or if the label for a product candidate does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, the commercial prospects for such product candidate may be harmed and our ability to generate revenues will be materially impaired.

We have been granted breakthrough therapy designation for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe pruritus associated with CKD in hemodialysis patients, however, it may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that KORSUVA (CR845/difelikefalin) injection will receive marketing approval.

In June 2017, the FDA granted breakthrough therapy designation for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe uremic pruritus in CKD patients undergoing hemodialysis. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for accelerated approval if the relevant criteria are met.

The receipt of a breakthrough therapy designation for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe uremic pruritus in CKD patients undergoing hemodialysis may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that it no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

The FDA may determine that I.V. CR845/difelikefalin, or any of our other current or future product candidates, has undesirable side effects that could limit dosage in development, delay or prevent their regulatory approval or commercialization.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to limit dosage in development or interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. For example, in February 2016, the FDA placed our adaptive trial of I.V. CR845/difelikefalin for postoperative pain on IND clinical hold pending a safety review. The clinical hold was based on a stopping rule related to elevated serum sodium levels of greater than 150 mmol/L. After the safety review was completed, the FDA removed this clinical hold in April 2016 and the clinical trial was resumed in June 2016. If other concerns are raised regarding the safety of a new drug as a result of undesirable side effects identified during clinical testing, the FDA may order us to cease further development, decline to approve the drug or issue a letter requesting additional data or information prior to making a final decision regarding whether or not to approve the drug. The number of such requests for additional data or information issued by the FDA in recent years has increased and resulted in substantial delays in the approval of several new drugs. Undesirable side effects caused by I.V. CR845/difelikefalin or any of our other current or future product candidates could also result in denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications or the inclusion of unfavorable information in our product labeling, and in turn prevent us from commercializing and generating revenues from the sale of I.V. CR845/difelikefalin or any other product candidate.

To date, the side effects observed in the completed I.V. CR845/difelikefalin clinical trials include dizziness, transient facial tingling, a state of near-sleep, or somnolence, and hypernatremia, an electrolyte disturbance that is defined by an elevated sodium level in the blood, which we believe is secondary, at least in part, to another side effect, aquaresis, that is defined as electrolyte-free urination. As described above, the observation of mild to moderate hypernatremia in our adaptive trial for postoperative pain triggered a stopping rule in the trial protocol and led the FDA to institute an IND clinical hold related to the trial, pending a safety review. Prolonged aquaresis can result in a negative fluid balance if the excreted water is not replaced by oral or intravenous fluids, and although we recommend steps to control fluid balance, we cannot be certain that such instructions will be followed by healthcare providers and/or patients, and failure to follow such instructions may be accompanied by adverse events associated with negative fluid balance, including disability and death. We believe that one such adverse event, which has been observed, postural tachycardia, an elevation of heart rate upon standing up, is a physiological reflex that can be triggered as a result of decreased intravascular volume caused by a negative fluid balance. We have observed transient prolactin elevations, which are brief increases in the concentration of the hormone prolactin in the bloodstream, in response to I.V. CR845/difelikefalin, which we have measured as a nonselective opioid biomarker since both kappa and mu opioids elicit this effect. We cannot be certain that such elevations in prolactin will be transient, safe, and well tolerated in all patients. In addition, previously developed kappa opioid agonists, the pharmacological class of drugs that CR845/difelikefalin belongs to, have been associated with poorly tolerated psychiatric side effects, such as a feeling of emotional and mental discomfort, or dysphoria, and hallucinations, at high doses, particularly for prior generations of kappa opioid agonists with substantially unrestricted or only partially restricted entry to the CNS. Although we have not observed psychiatric side effects in any CR845/difelikefalin clinical trials to date, we cannot be certain that these side effects or others will not be observed in the future, or that the FDA will not require additional trials or impose more severe labeling restrictions due to these side effects or other concerns. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients, if not already required pursuant to a REMS;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, results of operations and prospects.

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

We may not be able to initiate or continue conducting clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the eligibility criteria for, and design of, the trial in question;
- the perceived risks and benefits of the product candidate under study;
- competition in recruiting and enrolling patients in clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- delays or difficulties due to the ongoing COVID-19 pandemic.

For example, we experienced a delay in patient enrollment for our Phase 2 clinical trial of Oral KORSUVA (CR845/difelikefalin) for moderate-to-severe pruritus in patients with AD due to closure of certain clinical sites, and could in the future experience delays in either of our ongoing Phase 2 clinical trials as patient enrollment in both of these trials is not yet complete.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. We may encounter difficulties and/or delays in completing our planned enrollments. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, or the inability to complete development of our product candidates, which would cause the value of our company to decline, limit our ability to obtain additional financing, and materially impair our ability to generate revenues.

CR845/difelikefalin is a kappa opioid receptor agonist and, if approved, will exist in the marketplace with mu opioid products that are subject to restrictive marketing and distribution regulations, which if applied to our product candidates would restrict their use and harm our ability to generate profits.

Many currently approved mu opioid receptor agonists require REMS as part of their approval by the FDA. REMS programs may require medication guides for patients, special communication plans to healthcare professionals or elements to assure safe use, such as restricted distribution methods, patient registries and/or other risk minimization tools. While CR845/difelikefalin has been well tolerated in clinical trials to date and has not shown any evidence of the euphoria that has led to misuse, abuse and addiction of mu opioids, including the results of our Human Abuse Liability, or HAL, trial, which we successfully completed in the fourth quarter of 2014, the FDA may still determine that CR845/difelikefalin-based products require a REMS program, including for its use in non-pain indications such as

KORSUVA (CR845/difelikefalin) injection for CKD-aP in hemodialysis patients or Oral KORSUVA (CR845/difelikefalin) for CKD-aP in pre-dialysis patients and CLD-aP. We cannot predict whether REMS will be required as part of the FDA's approval of our product candidates and, if required, what those requirements might be. Any limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of our product candidates, if approved. If a REMS program is required, depending on the extent of the REMS requirements, the program might significantly increase our costs to commercialize these product candidates. Furthermore, risks of our product candidates that are not adequately addressed through proposed REMS for such product candidates may also prevent or delay their approval for commercialization.

In addition, currently approved mu opioids with which CR845/difelikefalin -based products may compete are controlled substances, which are subject to state, federal and foreign laws and regulations regarding their manufacture, use, sale, importation, exportation and distribution. Controlled substances are regulated under the federal Controlled Substances Act of 1970 and regulations of the DEA. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances.

The results from our HAL trial suggest that CR845/difelikefalin may have the potential to be a Schedule V or non-scheduled peripheral opioid. However, while CR845/difelikefalin-based products have not demonstrated any evidence of the euphoria that has led to misuse, abuse, and addiction of mu opioids, and while CR845/difelikefalin-based products are not being treated as a controlled substance in clinical trials, it is possible that the DEA could determine that CR845/difelikefalin-based products should be regulated as controlled substances. Even if the DEA does not regulate CR845/difelikefalin-based products, including KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in hemodialysis patients and Oral KORSUVA (CR845/difelikefalin) for other pruritic conditions such as CKD-aP in pre-dialysis patients and CLD-aP, as controlled substances, public perception surrounding opioids as a class may lead to public opposition to approvability of CR845/difelikefalin and limit its commercial potential. The 'opioid crisis' currently discussed among federal, state and local policymakers fails to distinguish between mu opioids and other opioids.

Various states also independently regulate controlled substances. Though state-controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs as well. While some states automatically schedule a drug when the DEA does so, in other states there must be rulemaking or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could impair the commercial attractiveness of such product. We or our collaborators may also be requested to obtain separate state registrations in order to be able to obtain, handle and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

If any of our product candidates are classified as controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors would be required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. Also, if any of our product candidates were classified as controlled substances, there is a risk that DEA regulations could limit the supply of the compounds used in clinical trials and, in the future, the ability to produce and distribute our products in the volume needed to meet commercial demand.

Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates including controlled substances. The DEA, and some states, conduct periodic inspections of registered establishments that handle controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary

registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of the restrictive nature of these regulations, if it were determined that our product candidates are subject to these restrictions, the commercialization of our product candidates could be limited.

We will need to obtain FDA approval of any proposed product names, and any failure or delay associated with such approval may adversely affect our business.

We have received conditional approval from the FDA for the use of KORSUVA as the proprietary name for our product candidate I.V. CR845/difelikefalin for the treatment of itch or pruritus. However, this approval is conditional upon a further and final review by the FDA at the time of NDA approval. Additionally, any name we intend to use for our other current or future product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the USPTO. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. The FDA may also object to a product name if it believes the name inappropriately implies medical claims or contributes to an overstatement of efficacy. If the FDA objects to any of our proposed product names, we may be required to adopt alternative names for our product candidates. If we adopt alternative names, we would lose any goodwill or brand recognition developed for the KORSUVA mark as well as the benefit of our existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In order to market and sell our products in the European Union, or EU, and many other jurisdictions, we or our collaborators or partners must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, the failure to obtain approval in one jurisdiction may compromise our or our collaborators' or partners' ability to obtain approval elsewhere. We or our collaborators or partners may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Regulatory approval is limited by the FDA to those specific indications and conditions for which clinical safety and efficacy have been demonstrated, and we may be subject to fines, penalties or injunctions if we are determined to be promoting the use of our products for unapproved or "off-label" uses, resulting in damage to our reputation and business.

When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific indications for which a product is approved. If we are not able to obtain FDA approval for any desired future indications for our products and product candidates, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians may choose to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, we are prohibited from marketing and promoting the products for indications that are not specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians

in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by pharmaceutical companies on off-label use. If the FDA determines that our promotional activities constitute promotion of an off-label use, it could request that we modify our promotional materials or subject us to regulatory or enforcement actions by other agencies, including issuance of warning letters or untitled letters, suspension or withdraw an approved product from the market, mandatory or voluntary recalls, civil fines, disgorgement of money, operating restrictions, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement, injunctions or criminal prosecution, any of which could significantly harm our business.

Even if one of our CR845/difelikefalin-based product candidates receives regulatory approval, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, packaging, distribution, adverse event reporting, storage, recordkeeping, export, import, advertising and promotional activities for such product, will be subject to extensive and ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, continued compliance with cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping and cGCPs for any clinical trials that we conduct post-approval. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including any requirement to implement a REMS. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on manufacturing such products;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;

- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained.

Risks Related to the Commercialization of Our Product Candidates

We face significant competition from other pharmaceutical and biotechnology companies, academic institutions, government agencies and other research organizations. Our operating results will suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of pain and pruritus. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

There are a large number of companies developing or marketing therapies for the treatment and management of pruritus, including many major pharmaceutical and biotechnology companies. Among the companies that currently market or are developing therapies that, if approved, our product candidates may potentially compete with include: Pfizer, Trevi, Vanda, Tioga, Leo Pharma, Chugai and others. Additionally, the market for the prevention and treatment of PONV is highly fragmented. There are a number of different agents alone or in combination (particularly in patients with a high risk for PONV) with different mechanism of actions to try to manage PONV. If approved, I.V. CR845/difelikefalin would likely be competing within the overall PONV market, although we expect that it would primarily be utilized as an add-on therapy in patients with a higher risk of PONV. Although most of the PONV products are generically available, there is still a significant segment of high-risk patients where their PONV is not adequately managed, which can increase the hospital length of stay and add significant cost to managing a post-operative patient.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products. Generic products are currently on the market for some of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

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

If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they are approved, we may be unable to generate product revenues.

We currently do not have a commercial infrastructure for the marketing, sale and distribution of pharmaceutical products. If approved, in order to commercialize our products, we must build our marketing, sales and distribution capabilities or make arrangements with third parties to perform these services. We may not be successful in doing so. If KORSUVA (CR845/difelikefalin) injection is approved by the FDA, we plan to build a commercial infrastructure, including our own specialty sales force, to launch KORSUVA (CR845/difelikefalin) injection in the hemodialysis setting in the United States. We may seek to further penetrate the U.S. market in the future by expanding our sales force or through collaborations with other pharmaceutical or biotechnology companies or third-party manufacturing and sales organizations. If approved for marketing outside the United States, our existing or new partners will commercialize KORSUVA (CR845/difelikefalin) injection outside the United States with their own, or their collaborators', sales force.

We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in the building and managing of a commercial infrastructure. The establishment and development of our own sales force and related compliance plans to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our partners or collaborators, will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, manage and retain marketing and sales personnel. In the event that we are unable to develop a marketing and sales infrastructure, we may not be able to commercialize KORSUVA (CR845/difelikefalin) injection or any of our other current or future product candidates, which would limit our ability to generate product revenues. Factors that may inhibit our or our partners' or collaborators' efforts to commercialize KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates include:

- inability to recruit, train, manage and retain adequate numbers of effective sales and marketing personnel;
- inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates;
- inability to effectively oversee a geographically dispersed sales and marketing team;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Although our current plan is to hire most of our sales and marketing personnel only if KORSUVA (CR845/difelikefalin) injection is approved by the FDA, we will incur expenses prior to product launch in recruiting this sales force and developing a marketing and sales infrastructure. If the commercial launch of KORSUVA (CR845/difelikefalin) injection is delayed as a result of FDA requirements or other reasons, we would incur these expenses prior to being able to realize any revenue from sales of KORSUVA (CR845/difelikefalin) injection. Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing KORSUVA (CR845/difelikefalin) injection or any of our other current or future product candidates.

In the event that we are unable to collaborate with a third-party marketing and sales organization to commercialize any approved product candidates outside the United States, our ability to generate product revenues may be limited. To the extent that we rely on third parties to commercialize any products for which we obtain regulatory approval, we may receive less revenues than if we commercialized these products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts.

To the extent that any of our product candidates, if approved, does not achieve broad market acceptance, the revenues that we generate from its sales will be limited.

We have never commercialized a product candidate for any indication. Even if KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any of our other current or future product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may not gain acceptance among physicians, hospitals, dialysis providers, patients and third-party payers. If any product candidates for which we obtain regulatory approval do not gain an adequate level of market acceptance, we may not generate significant product revenues or become profitable. Market acceptance of KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) and any future product candidate by physicians, hospitals, dialysis providers, patients and third-party payers will depend on a number of factors, some of which are beyond our control. The degree of market acceptance of any of our product candidates will depend on a number of factors, including:

- the prevalence and severity of adverse events associated with such product candidate;
- limitations or warnings contained in the product's FDA-approved labeling, including potential limitations or warnings for such product candidate, that may be more restrictive than other pain management or pruritus products;
- changes in the standard of care for the targeted indications for such product candidate, which could reduce the marketing impact of any claims that we could make following FDA approval, if obtained;
- the relative convenience and ease of administration of such product candidate;
- cost of treatment versus economic and clinical benefit in relation to alternative treatments or therapies;
- the availability of coverage and adequate reimbursement by third-party payers, such as insurance companies and other healthcare payers, and by government healthcare programs, including Medicare and Medicaid;
- the extent and strength of our marketing and distribution of such product candidate;
- the safety, efficacy and other potential advantages over, and availability of, alternative treatments already used to treat acute pain, chronic pain and/or pruritus;
- distribution and use restrictions imposed by the FDA with respect to such product candidate or to which we agree as part of a mandatory risk evaluation and mitigation strategy or voluntary risk management plan;
- the timing of market introduction of such product candidate, as well as competitive products;
- our ability to offer such product candidate for sale at competitive prices;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; and
- the clinical indications for such product candidate if approved.

Our ability to effectively promote and sell KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) and any future product candidates, if approved, will also depend on pricing and cost effectiveness, including our ability to produce a product at a competitive price and achieve acceptance of the product onto dialysis organization or hospital formularies, and our ability to obtain sufficient third-party coverage or reimbursement. Generally, before we can attempt to sell CR845/difelikefalin injection in a hospital or dialysis provider, CR845/difelikefalin injection must be approved for addition to that institution's list of drugs approved for use in that institution, or formulary list. In evaluating drugs for inclusion on the formulary list, hospitals and dialysis providers evaluate a variety of factors, including cost. The frequency with which hospitals and dialysis providers add and remove drugs from their formulary lists varies from organization to organization, and institutions often require additional information prior to adding new drugs to their formulary, which may result in substantial delays in our receiving formulary approval for CR845/difelikefalin injection. Since most hospitals are members of group purchasing organizations, which leverage the purchasing power of a group of entities to obtain discounts based on the collective buying power of the group, our ability to attract customers in the hospital marketplace will also depend on our ability to effectively promote our product candidates to group purchasing organizations. We will also need to demonstrate acceptable evidence of safety and efficacy, as well as relative convenience and ease of administration. Market acceptance could be limited depending on the prevalence and severity of any expected or unexpected adverse side effects associated with our product candidates.

Our efforts to educate the medical community and third-party payers on the benefits of our product candidates may require significant resources and may never be successful. Even if the medical community accepts that one of our product candidates is safe and effective for its approved indications, physicians and patients may not immediately be receptive to such product candidate and may be slow to adopt it as an accepted treatment of pain or pruritus. It is unlikely that any labeling approved by the FDA will contain claims that one of our product candidates is safer or more effective than competitive products or will permit us to promote such product candidate as being superior to competing products. Further, the availability of inexpensive generic forms of products for acute and chronic pain as well as pruritus may also limit acceptance of our product candidates among physicians, patients and third-party payers. If KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any future product candidate, is approved but does not achieve an adequate level of acceptance among physicians, patients and third-party payers, we may not generate meaningful revenues from KORSUVA (CR845/difelikefalin) injection, Oral CR845/difelikefalin or such other product candidate, and we may not become profitable.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for KORSUVA (CR845/difelikefalin) injection or other product candidates that we may develop and may have to limit their commercialization.

The use of KORSUVA (CR845/difelikefalin) injection or Oral KORSUVA (CR845/difelikefalin) and any future product candidate in clinical trials and the sale of any products for which we obtain regulatory approval expose us to the risk of product liability claims. We face inherent risk of product liability related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Product liability claims might be brought against us by consumers, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- loss of revenue from decreased demand for our products and/or product candidates;
- impairment of our business reputation or financial stability;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;

- diversion of management attention;
- withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs;
- the inability to commercialize our product candidates;
- significant negative media attention;
- initiation of investigations by regulators; and
- product recalls, withdrawals or labeling, marketing or promotional restrictions.

We have obtained limited product liability insurance coverage for our products and our clinical trials with a $10.0 million annual aggregate coverage limit in the United States and various other coverage limits outside of the United States. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain FDA approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing, or at all. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

We rely on third-party CROs to conduct our preclinical and clinical trials for all of our product candidates, and do not plan to independently conduct clinical trials of any other potential product candidates. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our preclinical studies and clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that would delay our product development activities and adversely affect our business.

Our reliance on these third parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical trials are conducted in accordance with GLP, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require

us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Our CROs may also have relationships with other entities, some of which may be our competitors. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going clinical, non-clinical and preclinical programs. In addition, the operations of our CROs may be constrained or disrupted by the ongoing COVID-19 pandemic. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

If the manufacturers upon whom we rely fail to produce our product candidates in the volumes that we require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the development and commercialization of, or be unable to meet demand for, our products and may lose potential revenues.

We do not manufacture any of our product candidates, and we do not currently plan to develop any capacity to do so. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. It is our intention that by the time of any regulatory approvals for commercialization, we will have negotiated long-term commitments with at least one primary supplier for each manufacturing and distribution function, and in July 2019, we entered into a non-exclusive commercial manufacturing agreement with Patheon for KORSUVA (CR845/difelikefalin) injection. Any problems or delays we experience in preparing for commercial-scale manufacturing of a product candidate may result in a delay in FDA approval of the product candidate or may impair our ability to manufacture commercial quantities, which would adversely affect our business. For example, our manufacturers will need to produce specific batches of our product candidates to demonstrate acceptable stability under various conditions and for commercially viable lengths of time. We and our contract manufacturers will need to demonstrate to the FDA and other regulatory authorities this acceptable stability data for our product candidates, as well as validate methods and manufacturing processes, in order to receive regulatory approval to commercialize KORSUVA (CR845/difelikefalin) injection or any other product candidates. Furthermore, if our commercial manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, we would likely be unable to meet demand for our products and we would lose potential revenues.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign

regulations. Our manufacturers may not perform as agreed. If our manufacturers were to encounter any of these difficulties, our ability to provide product candidates to patients in our clinical trials would be jeopardized.

Further, we may rely on proprietary technology developed by our contract manufacturers for purposes of manufacturing certain of our product candidates and our failure to negotiate or maintain the long-term use of any such proprietary technology or the inability for our contract manufacturers to produce our product candidates or components of our product candidates in the volumes that we require on a timely basis, may lead to delays or interruptions in the regulatory approval or commercialization process, as well as increased costs. For example, in August 2019, we entered into the Enteris License Agreement and intend to use Enteris's Peptelligence® technology to develop, manufacture and commercialize Oral KORSUVA (CR845/difelikefalin). If we experience any interruptions in the manufacture, delivery or scale-up of the Enteris formulation technology, we may experience delays in the development and commercialization of Oral KORSUVA (CR845/difelikefalin). Further, if we are unable to maintain our relationship with Enteris, we may be forced to reformulate Oral KORSUVA (CR845/difelikefalin) which could result in significantly delaying commercializing Oral KORSUVA (CR845/difelikefalin) and require us to incur additional costs in connection with such reformulation and potentially needed to seek additional approvals from the FDA. The operations of our third-party manufacturers have been and may in the future be constrained or disrupted and their operating capacity may be reduced by the ongoing COVID-19 pandemic, which could negatively impact our clinical development and commercialization timelines.

In addition, all manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. We have little control over our manufacturers' compliance with these regulations and standards. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension, delay or denial of product approval, product seizure or recall, or withdrawal of product approval. If the safety of any quantities supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

We may rely on third parties to perform many essential services for any products that we commercialize, including services related to warehousing and inventory control, distribution, customer service, accounts receivable management, cash collection and adverse event reporting. If these third parties fail to perform as expected or to comply with legal and regulatory requirements, our ability to commercialize I.V. CR845/difelikefalin or any other product candidate, will be significantly impacted and we may be subject to regulatory sanctions.

We may retain third-party service providers to perform a variety of functions related to the sale and distribution of KORSUVA (CR845/difelikefalin) injection and our other current or future product candidates, key aspects of which will be out of our direct control. These service providers may provide key services related to warehousing and inventory control, distribution, customer service, accounts receivable management and cash collection, and, as a result, most of our inventory may be stored at a single warehouse maintained by one such service provider. If we retain this provider, we would substantially rely on it as well as other third-party providers that perform services for us, including entrusting our inventories of products to their care and handling. If these third-party service providers fail to comply with applicable laws and regulations, fail to meet expected deadlines, or otherwise do not carry out their contractual duties to us, or encounter physical or natural damage at their facilities, our ability to deliver product to meet commercial demand would be significantly impaired. In addition, we may engage third parties to perform various other services for us relating to adverse event reporting, safety database management, fulfillment of requests for medical information regarding our product candidates and related services. If the quality or accuracy of the data maintained by these service providers is

insufficient, or these third parties otherwise fail to comply with regulatory requirements related to adverse event reporting, we could be subject to regulatory sanctions.

We are dependent on our collaboration agreements for certain revenues, and if our commercial partners do not perform their obligations under such agreements, we could lose revenues.

In May 2018, we entered into an agreement with VFMCRP under which we granted VFMCRP a license to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA (CR845/difelikefalin) injection for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients worldwide (excluding the United States, Japan and South Korea). In April 2013, we entered into an agreement with Maruishi under which we granted Maruishi an exclusive license to develop, manufacture and commercialize products containing CR845/difelikefalin in Japan. Also, in April 2012, we entered into an agreement with CKDP under which we granted CKDP an exclusive license to develop, manufacture and commercialize products containing CR845/difelikefalin in South Korea. Under the VFMCRP Agreement, we are responsible, at our own cost, to undertake clinical and non-clinical development. We are also responsible to provide all content and subject matter expertise required for registration with the EMA in the EU that will be needed by VFMCRP for such registration, including participation in regulatory meetings, as needed. If third-party costs incurred by us with respect to our clinical development for the EMA registration exceed $20,000, such excess costs will be shared equally by us and VFMCRP. VFMCRP will contribute, at its own cost, its clinical development expertise as reasonably useful for such development activities, such as preparing the clinical results that we present to it in a format acceptable to the EMA to obtain marketing approval in the EU. Maruishi and CKDP are required to use commercially reasonable efforts, at their expense, to develop, obtain regulatory approval for and commercialize CR845/difelikefalin in Japan and South Korea, respectively. Our receipt of milestone payments and royalties under these agreements is dependent on the continued efforts by VFMCRP, Maruishi and CKDP, respectively, and their failure to adequately develop or commercialize the licensed products, or any default or inability to meet their payment obligations under their respective agreements, could harm our revenues and business.

Any collaboration arrangements that we are a party to or may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

Our business model is to commercialize our product candidates in the United States and generally to seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our product candidates in the rest of the world. We currently have license agreements with VFMCRP (I.V. CR845/difelikefalin for CKD-aP in dialysis patients) as well as Maruishi and CKDP (CR845/difelikefalin – both I.V. and Oral). In addition to our existing agreements, we may enter into additional collaboration arrangements in the future on a selective basis. Our existing collaborations and future collaboration arrangements may not be successful. The success of our existing and future collaboration arrangements will depend heavily on the efforts and activities of our collaborators.

Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaboration arrangements. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. For example, the VFMCRP, Maruishi and CKDP Agreements may be terminated by our collaborator for our breach or insolvency, VFMCRP may terminate its agreement (in its entirety or with respect to any countries within the Territory upon written notice to us) upon the earlier of (1) 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. Maruishi may terminate its agreement with us at will, and CKDP may terminate its agreement with us in certain circumstances relating to patent invalidity or unenforceability or generic entry by a third party, as further described in the section titled “Business — Commercial Partnerships” above. Any such termination or expiration would adversely affect

us financially and could harm our business reputation. Our current collaborations and any future collaborations we might enter into may pose a number of risks, including the following:

- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could fail to make timely regulatory submissions for a product candidate;
- collaborators may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations, including our collaboration with Maruishi, may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our current collaborations or any other collaborations we might enter into in the future do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed

and we may need additional resources to develop our product candidates and our product platform. All of the risks relating to our product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators in their respective jurisdictions.

Additionally, if any current or future collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation in the business and financial communities could be adversely affected.

For KORSUVA (CR845/difelikefalin) injection and any other current or future product candidates, we may in the future determine to collaborate with additional pharmaceutical and biotechnology companies for their development and potential commercialization. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform and our business may be materially and adversely affected.

We are dependent on third parties to decide to utilize KORSUVA (CR845/difelikefalin) injection and to make it readily available at the point of care throughout their dialysis centers or hospitals.

In addition to extensive internal efforts, the successful commercialization of KORSUVA (CR845/difelikefalin) injection will require many third parties, over whom we have no control, to decide to utilize KORSUVA (CR845/difelikefalin) injection and to make it readily available at the point of care throughout their hospitals. These third parties include physicians, dialysis providers, pharmacists and hospital pharmacy and therapeutics committees, which are commonly referred to as P&T committees. Generally, even if CR845/difelikefalin injection is approved by the FDA, before we can attempt to sell CR845/difelikefalin injection in a hospital or dialysis center, CR845/difelikefalin injection must be approved for addition to that hospital or dialysis center's list of approved drugs, or formulary list, by the institution's P&T committee. An institutional P&T committee typically governs all matters pertaining to the use of medications within the institution, including review of medication formulary data and recommendations for the appropriate use of drugs within the institution to the medical staff. The frequency of P&T committee meetings at various institutions varies considerably, and P&T committees often require additional information to aid in their decision-making process, so we may experience substantial delays in obtaining formulary approvals. Additionally, institutions may be concerned that the cost of acquiring CR845/difelikefalin injection for use in their institutions will adversely impact their overall pharmacy budgets, which could cause institution staff to resist efforts to add CR845/difelikefalin injection to the formulary, or to implement restrictions on the usage of the drug in order to control costs, either initially or later, when the increasing use of CR845/difelikefalin injection within their institution begins to significantly impact their budgets. We cannot guarantee that we will be successful in getting the approvals we need from enough P&T committees and overcoming any financial objections raised by institution staff quickly enough to maintain and grow institutional sales of CR845/difelikefalin injection.

Risks Related to Legal and Compliance Matters

If we fail to comply with federal and state healthcare laws, including fraud and abuse, transparency and health information laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, transparency and patients' rights may be applicable to our business. The healthcare laws and regulations that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which regulates, among other things, our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchase, recommendation, lease, order or furnishing of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws, including without limitation the federal civil False Claims Act, and civil monetary penalties law, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment or approval from a federal health care program (including Medicare and Medicaid);

- HIPAA, which created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program, regardless of the payer (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick, scheme or device a material fact or making any materially false statements in connection with the delivery of, or payment for, health care benefits, items or services relating to healthcare matters;

- federal transparency laws, including the federal Physician Payments Sunshine Act, that requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS, or Centers for Medicare & Medicaid Services, information related to payments and other transfers of value provided to physicians, as defined by such law, and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to the pricing of certain drugs, as well as payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and local laws that require the registration of pharmaceutical sales representatives, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under these laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Pharmaceutical and other healthcare companies continue to be prosecuted under the federal false claims laws for numerous activities, including those related to research, sales, marketing and promotional programs. In

addition, recent health care reform legislation has strengthened these laws. For example, the Health Care Reform Law among other things, amends the intent requirement of the federal Anti-Kickback Statute and certain other criminal healthcare fraud statutes. As a result, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to commit a violation. Moreover, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, exclusion from participation in U.S. federal or state health care programs, contractual damages, reputational harm, imprisonment, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state transparency and fraud and abuse laws may prove costly. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to significant criminal, civil or administrative sanctions, including but not limited to, exclusions from participation in government healthcare programs, which could also materially affect our business.

Changes in and failures to comply with applicable U.S. and foreign privacy and data protection laws, regulations and standards may subject us to liabilities and adversely affect our business, operations and financial performance.

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention, and security of personal data, such as information that we collect about participants and healthcare providers in connection with clinical trials in the U.S. and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

In the U.S., HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, including health plans, healthcare clearinghouses, certain healthcare providers, and their business associates that perform services for them that involve the creation, use, maintenance or disclosure of, individually identifiable health information. In the event we are subject to HIPAA and fail to properly maintain the privacy and security of certain individually identifiable health information, or we are responsible for an inadvertent disclosure or security breach of such individually identifiable health information, we could be subject to enforcement measures, including civil and criminal penalties and fines for violations of state and federal privacy or security standards, such as HIPAA and HITECH, and their respective implementing regulations. Additionally, certain states have adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. On June 28, 2018, California enacted the California Consumer Privacy Act, or CCPA, which takes effect on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the

beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. Many countries in these regions have established or are in the process of establishing privacy and data security legal frameworks with which we or our partners, collaborators, customers, or service providers must comply. For example, the EU has adopted the General Data Protection Regulation, or GDPR, which went into effect in May 2018 and introduced strict requirements for processing personal data. The GDPR is likely to increase compliance burden on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and leverage information about them or how we obtain consent from them. The processing of sensitive personal data, such as physical health condition, may impose heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators and supervisory bodies involved in the review and approval of clinical trials. In addition, the GDPR provides for breach reporting requirements, more robust regulatory enforcement and fines of up to 20 million euros or up to 4% of the annual global revenue. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

U.S. and foreign data protection laws, regulations and standards are subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. Any liability from failure to comply with the requirements of these laws, to the extent such requirements are deemed to apply to our operations, could adversely affect our financial condition. The costs of complying with privacy and security related legal and regulatory requirements are burdensome and could have a material adverse effect on our results of operations.

If the government or other third-party payers fail to provide coverage and adequate reimbursement and payment rates for KORSUVA (CR845/difelikefalin) injection or any of our other current or future product candidates, if any, or if providers choose to use therapies that are less expensive, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, sales of our future products will depend in part upon the availability of coverage and reimbursement from third-party payers. Such third-party payers include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. KORSUVA (CR845/difelikefalin) injection for the treatment of pruritus in hemodialysis patients may be designated as a component of the government's bundled reimbursement for end stage renal disease treatment.

On October 31, 2019, CMS issued a final rule that revises payment policies and rates under the End-Stage Renal Disease Prospective Payment System, or ESRD PPS, for renal dialysis services furnished to beneficiaries on or after January 1, 2020. The final rule also updates the Transitional Drug Add-On Payment Adjustment, or TDAPA. In the final rule, CMS revised ESRD PPS eligibility to focus on innovative drugs and excluded certain drugs from being eligible for the TDAPA. CMS will pay the revised TDAPA adjustment, which is called the Transitional Add-on Payment Adjustment for New and Innovative Equipment and Supplies , or TPNIES, for equipment and supplies that: (1) have been designated by CMS as a renal dialysis service, (2) are new, meaning granted marketing authorization by FDA on or after January 1, 2020, (3) are commercially available by January 1 of the particular calendar year, meaning the year in which the payment adjustment would take effect, (4) have a Healthcare Common Procedure Coding System, or HCPCS, application submitted in accordance with the official Level II HCPCS coding procedures by September 1 of the particular calendar year, (5) are innovative, meaning they meet the substantial clinical improvement criteria specified in the Inpatient Prospective Payment System regulations and related guidance, and (6) are not capital-related assets. Based on this ruling, we expect KORSUVA (CR845/difelikefalin) injection, if approved for CKD-aP in hemodialysis patients, will qualify for TDAPA payments for two years post approval. However, there is no assurance that KORSUVA (CR845/difelikefalin) injection will qualify for TDAPA payments or, even if it does, that it will be able to maintain its price established in the TDAPA period in the post-TDAPA timeframe.

Additionally, many U.S. hospitals receive a fixed reimbursement amount per procedure for certain surgeries and other treatment therapies they perform, or a pre-determined rate for all hospital inpatient care provided as payment in full. Because, in these instances, the amount of reimbursement that such providers receive may not be based on the actual expenses the provider incurs, providers may choose to use therapies which are less expensive when compared to our product candidates. Accordingly, KORSUVA (CR845/difelikefalin) injection or any of our other current or future product candidates, if approved, will face competition from other therapies and drugs for these limited provider financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals, other target customers and their third-party payers. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Third-party coverage and adequate reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third-party coverage and reimbursement for our products or product candidates for which we receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a negative effect on our business, results of operations, financial condition and prospects.

We are subject to recent legislation, regulatory proposals and healthcare payer initiatives that may increase our costs of compliance and adversely affect our ability to market our products, obtain collaborators and raise capital.

In March 2010, President Obama signed the Health Care Reform Law, which includes provisions that have changed, and likely will continue to change, health care financing and the delivery of health care in the United States. Among the provisions of the Health Care Reform Law of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers’ Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing both the volume of sales and manufacturers’ Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- new transparency requirements under the federal Physician Payments Sunshine Act;
- a new requirement to annually report certain drug samples that manufacturers and distributors provide to licensed practitioners, or to pharmacies of hospitals or other healthcare entities;
- a licensure framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare & Medicaid Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending; and
- expansion of healthcare fraud and abuse laws, including the federal civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance.

There remain judicial and Congressional challenges to certain aspects of the Health Care Reform Law, as well as efforts by the Trump administration to repeal or replace certain aspects of the Health Care Reform Law. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the Health Care Reform Law or otherwise circumvent some of the requirements for health insurance mandated by the Health Care Reform Law. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Health Care Reform Law. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the Health Care Reform Law have been signed into law. The Tax Cuts and Jobs Act, or TCJA, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Health Care Reform Law on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the Health Care Reform Law’s mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the Health Care Reform Law, effective January 1, 2019, to close the coverage gap in most Medicare drug plans. In December 2018, CMS published a new final rule permitting further collections and payments to and from certain Health Care Reform Law qualified health plans and health insurance issuers under the Health Care Reform Law risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the Health Care Reform Law is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the TCJA. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the Health Care Reform Law are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the Health Care Reform Law will impact the Health Care Reform Law and our business.

In addition, other legislative changes have been proposed and adopted since the Health Care Reform Law was enacted. These changes include, among other things, aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went effective on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2015, and subsequent legislative amendments, including the BBA, will remain in effect until 2029, unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

We expect that the Health Care Reform Law, as well as other federal and state healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price

that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payers. In addition, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2020 contains additional drug price control measures that could be enacted during the budget process or in other future legislation, such as measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. Moreover, the Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing.

Legislation and regulations that, among other things, reduce drug prices or require the implementation of costly compliance measures could result in decreased net revenues from our pharmaceutical products and decrease potential returns from our development efforts, and we cannot predict what legislation will be enacted in the future.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. There can be no assurance that our products will be considered cost-effective by third-party payers, that an adequate level of reimbursement will be available or that the third-party payers' reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Our employees, independent contractors, consultants, and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants and commercial partners. Misconduct by such individuals could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, report financial information or data accurately or disclose unauthorized activities to us. Third party misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our business involves the use of hazardous materials and we must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our manufacturing activities involve the controlled storage, use and disposal of hazardous materials, including the components of our products, product candidates and other hazardous compounds. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling, release and disposal of, and exposure to, these hazardous materials. Violation of these laws and regulations could lead to substantial fines and penalties. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state or federal authorities may curtail our use of these materials and interrupt our business operations. In addition, we could become subject to potentially material liabilities relating to the investigation and cleanup of any contamination, whether currently unknown or caused by future releases.

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

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Intellectual Property

It is difficult and costly to protect our proprietary rights and as a result we may not be able to ensure their protection and all patents will eventually expire.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for CR845/difelikefalin and for any other product candidates that we may develop, license or acquire and the methods we use to manufacture them, as well as successfully defending these patents and trade secrets against third-party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute to issuance all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our R&D output before it is too late to obtain patent protection. Moreover, should we enter into additional collaborations we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance and enforcement of our patents. Therefore, these patents and applications may not be successfully prosecuted to issuance and enforced in a manner consistent with the best interests of our business. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. The degree of future protection for our proprietary rights is uncertain, because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Moreover, the patent application process is also subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting CR845/difelikefalin and any other product candidates that we may develop, license or acquire by obtaining and defending patents. For example:

- we may not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- we may not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our product candidates or technologies;
- it is possible that none of the pending patent applications will result in issued patents;
- the issued patents covering our product candidates may not provide a basis for commercially viable active products, may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable;
- patents of others may have an adverse effect on our business;
- noncompliance with governmental patent agencies requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction, potentially allowing competitors to enter the market earlier than would otherwise have been the case;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential product candidates; or
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of available patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent Office has developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the

Leahy-Smith Act, including and in particular, the first to file provisions, became effective on March 16, 2013. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our currently pending and future patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Patent applications in the United States are generally maintained in confidence for at least 18 months after their earliest effective filing date and in certain circumstances not until granted when no foreign counterpart patent applications are filed. Furthermore, published patent applications may issue at a later date with new and/or amended claims substantially different from those published earlier. Consequently, we cannot be certain we were the first to invent or the first to file patent applications on CR845/difelikefalin or any other product candidates that we may develop, license or acquire.

Until recent changes to the U.S. Patent Laws, patents and patent applications relating to substantially similar claimed inventions were potentially subject to interference proceedings to determine the first applicant to invent the claimed subject matter. For an interference to be declared against Cara's patents and patent applications, any such interference would be under the 1952 law which was eliminated by the America Invents Act, or AIA, enacted in 2011 and fully effective in 2013. Such an interference would therefore have to relate to a patent or application with an effective filing date before March 16, 2013. No interference with such a patent or application has been declared to date. Therefore, it seems extremely unlikely that we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office to determine priority of invention in the United States against one or more parties claiming the same or similar invention. However, in the unlikely event that such interference was to be declared, the costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our U.S. patent position. The results of these types of proceedings could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such results could have a material adverse effect on our results of operations.

In addition, the patentability of claims in pending patent applications covering a CR845/difelikefalin-based product can be challenged by third parties during prosecution in the U.S. Patent and Trademark Office under the new AIA law of 2013, for example by third party observations and derivation proceedings, and the validity of claims in issued patents can be challenged by third parties in various post-grant proceedings such as Post-Grant Review, Inter-partes Reexamination, and Inter-partes Review proceedings.

Furthermore, we may not have identified all United States and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market. In addition, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans, and in these countries patent protection may not be available at all to protect our product candidates. Even if patents issue, we cannot guarantee that the claims of those patents will be valid and enforceable or provide us with any significant protection against competitive products, or otherwise be commercially valuable to us.

We also rely on trade secrets to protect our technology, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our licensors, employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we fail to obtain or maintain patent protection or trade secret protection for CR845/difelikefalin or any other product candidate that we may develop, license or acquire, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and achieve profitability.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

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

If we or any current or future collaboration partner are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market and sell KORSUVA (CR845/difelikefalin) injection or any of our other current of future product candidates depends upon our ability to avoid infringing the proprietary rights of third parties, and our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the general field of pain management and cover the use of numerous compounds and formulations in our targeted markets. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and our licensors may not be successful in defending intellectual property claims by third parties, which could have a material adverse effect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates may infringe. There could also be existing patents of which we are not aware that KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates may inadvertently infringe.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third-party claims that we infringe on their products or technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, can be expensive and time consuming to litigate and can divert management’s attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor’s patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our processes so they do not infringe, which may not be possible or could require substantial funds and time.

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

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and may ultimately be unsuccessful.

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology, or enter into development partnerships that would help us bring our product candidates to market.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development or commercialization of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms or at all, which could materially harm our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual

property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

The validity and enforceability of the patents and applications that cover our CR845/difelikefalin product candidates can be challenged by competitors.

If KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any future product candidate is approved by the FDA, one or more third parties may challenge the patents covering these product candidates, which could result in the invalidation of, or render unenforceable, some or all of the relevant patent claims. For example, if a third party files an Abbreviated New Drug Application, or ANDA, for a generic drug product containing CR845/difelikefalin, and relies in whole or in part on studies conducted by or for us, the third party will be required to certify to the FDA that either: (1) there is no patent information listed in the FDA's Orange Book with respect to our NDA for KORSUVA (CR845/difelikefalin) injection; (2) the patents listed in the Orange Book have expired; (3) the listed patents have not expired, but will expire on a particular date and approval is sought after patent expiration; or (4) the listed patents are invalid or will not be infringed by the manufacture, use or sale of the third-party's generic drug product. A certification that the new product will not infringe the Orange Book-listed patents for CR845/difelikefalin, or that such patents are invalid, is called a paragraph IV certification. If the third party submits a paragraph IV certification to the FDA, a notice of the paragraph IV certification must also be sent to us once the third-party's ANDA is accepted for filing by the FDA. We may then initiate a lawsuit to defend the patents identified in the notice. The filing of a patent infringement lawsuit within 45 days of receipt of the notice automatically prevents the FDA from approving the third-party's ANDA until the earliest of 30 months or the date on which the patent expires, the lawsuit is settled, or the court reaches a decision in the infringement lawsuit in favor of the third party. If we do not file a patent infringement lawsuit within the required 45-day period, the third-party's ANDA will not be subject to the 30-month stay. Litigation or other proceedings to enforce or defend intellectual property rights are often very complex in nature, may be very expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could adversely impact our ability to prevent third parties from competing with our products.

Risks Related to Employee Matters and Managing Growth

Our internal information technology systems, or those of our CROs, contract manufacturers or other contractors or consultants, may fail or suffer security breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability, which could adversely affect our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to intellectual property, proprietary business information and personal information). It is critical that we do so in

a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party contractors who have access to our confidential information.

Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third-party CROs, contract manufacturers and other contractors and consultants are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners and/or other third parties, or from cyber-attacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to data leakage. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and reputational damage and the further development and commercialization of our product candidates could be delayed.

While we have not experienced any such system failure, accident or security breach to date, we cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems or other cyber incidents that could adversely affect our business. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development and commercialization of CR845/difelikefalin injection, if approved, could be delayed. In addition, the loss of clinical trial data could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation and/or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information and personal information), which could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could adversely affect our business.

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

As of August 6, 2020, we had 72 employees. We will need to substantially expand our managerial, commercial, financial, manufacturing and other personnel resources in order to manage our operations and prepare for the commercialization of CR845/difelikefalin injection, if approved. Our management and personnel systems and facilities currently in place may not be adequate to support this future growth. In addition, we may not be able to recruit and retain qualified personnel in the future, particularly for sales and marketing positions, due to competition for personnel among pharmaceutical businesses, and the failure to do so could have a significant negative impact on our future product revenues and business results. Our need to effectively manage our operations, growth and various projects requires that we:

- continue the hiring and training of an effective commercial organization in anticipation of the potential approval of KORSUVA (CR845/difelikefalin) injection, and establish appropriate systems, policies and infrastructure to support that organization;

- ensure that our consultants and other service providers successfully carry out their contractual obligations, provide high quality results, and meet expected deadlines;

- continue to carry out our own contractual obligations to our licensors and other third parties; and

- continue to improve our operational, financial and management controls, reporting systems and procedures.

We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our development and commercialization goals.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and commercial, scientific and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the skills and leadership of our management team, including Derek Chalmers, our President and Chief Executive Officer. Our senior management may terminate their employment with us at any time. If we lose one or more members of our senior management team, our ability to successfully implement our business strategy could be seriously harmed. Replacing these employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate additional key personnel. We do not maintain “key person” insurance for any of our executives or other employees.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act of 2002 and the rules and regulations of The Nasdaq Global Market. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are now required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting and we are also required to have our independent registered public accounting firm issue an opinion on the effectiveness of our internal control over financial reporting on an annual basis.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. Further, we may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Moreover, our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Moreover, we are aware that the remote working arrangements implemented in connection with the COVID-19 pandemic potentially present new areas of risk, and we are carefully monitoring any impact to our internal controls and procedures.

If we are unable to assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion on the effectiveness of our internal control over financial reporting, investors could lose confidence in the reliability of our financial statements, the market price of our stock could decline and we could be subject to sanctions or investigations by The Nasdaq Global Market, the SEC or other regulatory authorities.

We no longer qualify as an emerging growth company and are required to comply with certain provisions of the Sarbanes-Oxley Act and we may no longer take advantage of reduced disclosure requirements.

As of December 31, 2019, we were considered a large accelerated filer and, as a consequence, have lost our status as an emerging growth company. We are no longer permitted to take advantage of certain exemptions from various disclosure and reporting requirements that are applicable to emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in periodic reports and proxy statements, and exemptions from the requirements of holding a non-binding advisory vote on executive compensation. As a result, we expect to incur additional legal, accounting and other expenses and devote significant management attention as we implement additional corporate governance practices and seek to comply with these additional disclosure and reporting requirements. Compliance with these requirements for the first time may be more difficult and consume more resources than we anticipate.

Risks Related to Ownership of Our Common Stock

The market price of our common stock has been, and is likely to continue to be, highly volatile, and you may not be able to resell your shares at or above the price you paid for them.

Since our initial public offering in January 2014, our stock price has been volatile and it is likely that the trading price of our common stock will continue to be volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- delays in the commencement, enrollment and ultimate completion of our clinical trials, including our ongoing Phase 3 clinical trials for KORSUVA (CR845/difelikefalin) injection for CKD-aP and our ongoing and planned trials for KORSUVA injection and Oral KORSUVA in other indications;
- any delay or refusal on the part of the FDA in approving an NDA for KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates;
- the commercial success of KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any future product candidates, if approved by the FDA;
- results of clinical trials of KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any future product candidate or those of our competitors;
- actual or anticipated variations in quarterly or annual operating results;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community, including securities analysts;
- introduction of competitive products or technologies;
- changes or developments in laws or regulations applicable to our product candidates;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- general trends in our industry or economic and market conditions and overall fluctuations in U.S. equity markets, including as a result of the ongoing COVID-19 pandemic;

- developments concerning our sources of manufacturing supply, warehousing and inventory control;
- disputes or other developments relating to patents or other proprietary rights;
- additions or departures of key scientific or management personnel;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- capital commitments;
- investors' general perception of our company and our business;
- announcements and expectations of additional financing efforts, including the issuance of debt, equity or convertible securities;
- sales of our common stock, including sales by our directors and officers or significant stockholders;
- changes in the market valuations of companies similar to us;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, or divestitures;
- changes in the structure of healthcare payment systems; and
- the other factors described in this "Risk Factors" section.

In addition, the stock market in general, and the market for small pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors, such as those related to the ongoing COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance.

Further, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If equity research analysts cease to publish research or reports about us or if they publish unfavorable research or reports about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock is likely to be influenced by the research and reports that equity research analysts publish about us and our business. As a relatively newly public company, to date we have only limited equity research analyst coverage. Additionally, we do not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- the successful progress of our clinical trials for KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) and other potential future product candidates;

- whether the FDA requires us to complete additional, unanticipated studies, tests or other activities prior to approving KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates, which would likely further delay any such approval;

- if KORSUVA (CR845/difelikefalin) injection or any of our other current or future product candidates is approved, our ability to establish the necessary commercial infrastructure to launch this product candidate without substantial delays, including hiring sales and marketing personnel and contracting with third parties for warehousing, distribution, cash collection and related commercial activities;

- our ability to identify, enter into and maintain third party manufacturing arrangements capable of manufacturing KORSUVA (CR845/difelikefalin) injection or our other current or future product candidates in commercial quantities;

- our execution of other collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;

- variations in the level of expenses related to our future development programs;

- any product liability or intellectual property infringement lawsuit in which we may become involved;

- regulatory developments affecting KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin), any of our future product candidates, or the product candidates of our competitors; and

- if KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) or any of our future product candidates receives regulatory approval, the level of underlying demand for such product candidate and wholesaler buying patterns.

If our quarterly or annual operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. Any debt financing that we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. 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 product development or future

commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

The use of our net operating loss carryforwards and research tax credits may be limited.

Our net operating loss, or NOL, carryforwards and R&D tax credits may expire and not be used. As of December 31, 2019, we had federal and state NOL carryforwards of approximately $349.5 million and $189.2 million, respectively, and we also had federal and state R&D tax credit carryforwards of approximately $15.3 million and $1.4 million, respectively. Our NOL carryforwards will begin expiring in 2026 for federal purposes (to the extent such federal NOLs are generated in taxable years ending on or before December 31, 2017) and 2027 for state purposes if we have not used them prior to that time, and our federal R&D tax credits will begin expiring in 2025 unless previously used. Under the TCJA, the use of NOLs generated in taxable years ending after December 31, 2017 are subject to a limitation of 80% of taxable income, and such NOLs can be carried forward indefinitely (but carryback is generally prohibited). It is uncertain if and to what extent various states will conform to the TCJA. To the extent that we have not exchanged our Connecticut R&D tax credits for a tax refund, those tax credits carryforward indefinitely. Additionally, our ability to use any NOL and R&D tax credit carryforwards to offset taxable income or tax, respectively, in the future will be limited under Internal Revenue Code Sections 382 and 383, respectively, if we have a cumulative change in ownership of our stock of more than 50% within a three-year period. The completion of our initial public offering in 2014 and our follow-on public offerings in 2015, 2017, 2018 and 2019, together with private placements and other transactions that have occurred, may have triggered such ownership changes. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo ownership changes in the future. We have never completed an analysis as to whether such a change of ownership has occurred, but in such an event, we will be limited regarding the amount of NOL carryforwards and R&D tax credits that could be utilized annually in the future to offset taxable income or tax, respectively. Any such annual limitation may significantly reduce the utilization of the NOL carryforwards and R&D tax credits before they expire. In addition, certain states have in the past suspended use of NOL carryforwards for certain taxable years, and other states are considering similar measures. As a result, we may incur higher state income tax expense in the future. Depending on our future tax position, limitations on our ability to use NOL carryforwards in states in which we are subject to income tax could have an adverse impact on our results of operations and financial condition.

New or future changes to tax laws could materially adversely affect our company.

On December 22, 2017, President Trump signed into law the TCJA, which significantly amends the Internal Revenue Code of 1986. The TCJA, among other things, reduces the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limits the tax deduction for interest expense to 30% of taxable income, eliminates certain NOL carrybacks, imposes a one-time tax on offshore earnings at reduced rates regardless of whether they are repatriated, allows immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifies or repeals many business deductions and credits. We continue to examine the impact these changes may have on our business. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the TCJA is uncertain and our business and financial condition could be adversely affected. The impact of the TCJA on holders of our common stock is also uncertain and could be adverse.

Because we do not intend to pay dividends on our common stock, your returns will be limited to any increase in the value of our stock.

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not anticipate declaring or paying any cash dividends on our common stock for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock, if any. Investors seeking cash dividends should not purchase our common stock.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws, as amended, that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our Board of Directors has the authority to issue up to 5,000,000 shares of preferred stock and to fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- our Board of Directors are divided into three classes, with only one class of directors elected each year;
- our stockholders are entitled to remove directors only for cause upon a 66 2/3% vote;
- our stockholders are not permitted to take actions by written consent;
- our stockholders are not permitted to call a special meeting of stockholders; and
- our stockholders must give us advance notice of their intent to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

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

None.

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

None.

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

Not applicable.

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

None.

Item 6. ***Exhibits.***

Exhibit No.	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit No.	Date Filed
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-36279	3.1	February 7, 2014
3.2	Amended and Restated Bylaws.	8-K	001-36279	3.2	February 7, 2014
10.1+	Amended and Restated Non-Employee Director Compensation Policy.	10-Q	001-36279	10.1	May 11, 2020
10.2†	Amendment to Lease Agreement between the Registrant and Four Stamford Plaza Owner L.L.C. Stamford Lease, dated June 23, 2020.				
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 Principal 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 Principal 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.CAL†	Inline XBRL Taxonomy Extension Calculation Linkbase.				
101.INS†	Inline XBRL Instance Document.				
101.LAB†	Inline XBRL Taxonomy Extension Label Linkbase.				
101.PRE†	Inline XBRL Taxonomy Extension Presentation Linkbase.				
101.SCH†	Inline XBRL Taxonomy Extension Schema Linkbase.				
101.DEF†	Inline XBRL Taxonomy Extension Definition Linkbase Document.				
104†	Cover page interactive data file (formatted as Inline XBRL and contained in Exhibit 101).				

+ Indicates management contract or compensatory plan.

† Filed herewith.

* This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

SIGNATURES

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

CARA THERAPEUTICS, INC.

Date: August 10, 2020

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

Date: August 10, 2020

By /s/ RICHARD MAKARA
Richard Makara
VP, Head of Accounting & Controller
(Principal Financial and Accounting Officer)

Exhibit 10.2

FIRST AMENDMENT TO LEASE

This **FIRST AMENDMENT TO LEASE** (this "**Amendment**") is made and entered into as of June 23, 2020 between **FOUR STAMFORD PLAZA OWNER LLC**, a Delaware limited liability company ("**Landlord**") and **CARA THERAPEUTICS, INC.**, a Delaware corporation ("**Tenant**").

RECITALS:

A. Landlord and Tenant are parties to that certain Office Lease Agreement dated as of December 21, 2015 (the "**Lease**"). Pursuant to the Lease, Landlord has leased to Tenant certain premises containing approximately **24,029** rentable square feet known as Suite 900 (the "**Existing Premises**") and located on the 9th floor of the building commonly known as Four Stamford Plaza located at 107 Elm Street, Stamford, Connecticut 06902 (the "**Building**"). The Building contains 263,194 rentable square feet. Tenant's current Pro Rata Share is **9.1298%**. Tenant is currently entitled to use seventy-two (72) unreserved parking spaces based on the ratio of three (3) unreserved parking spaces per 1,000 rentable square feet of the Existing Premises in the Building's garage at no additional charge to Tenant.

B. The Lease by its terms is set to expire on November 30, 2023 (the "**Current Expiration Date**").

C. Landlord and Tenant desire to (i) extend the Term of the Lease by one (1) month, (ii) expand the Existing Premises by adding to the Existing Premises an additional **11,685** rentable square feet of space known as Suite 1001 located on the 10th floor of the Building (the "**Expansion Premises**"), as shown on Exhibit A attached hereto, and (iii) modify the Lease on the terms and conditions set forth herein. The Existing Premises and the Expansion Premises are hereinafter, collectively, sometimes referred to as the "**Entire Premises**".

D. Landlord is currently holding a Letter of Credit in the amount of $408,493.00 as a Security Deposit under the Lease.

E. All capitalized terms used herein shall have the meanings set forth in the Lease unless otherwise specified herein.

NOW THEREFORE, in consideration of the above recitals which by this reference are incorporated herein, the mutual covenants and conditions contained herein and other valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree as follows:

1. Lease of Expansion Premises. Effective on the Expansion Premises Commencement Date (as defined below), the "**Premises**" as such term is used in the Lease, shall include the Existing Premises and the Expansion Premises (totaling an aggregate of **35,714** rentable square feet). From and after the Expansion Premises Commencement Date and through and including the Extended Expiration Date (as defined below), the Expansion Premises shall be considered part of the Premises and all references to the Premises shall be and be deemed to include the Expansion Premises. The Expansion Premises shall be subject to all of the terms and conditions of the Lease except as expressly set forth herein and except that Tenant shall not be entitled to receive any allowances, Base Rent abatements or other financial concessions with respect to the Expansion Premises (even if such allowances, abatements or concessions were granted in connection with the Existing Premises) unless such concessions are expressly provided for in this Amendment with respect to the Expansion Premises or are expressly set forth in the Lease for a failure of Landlord to perform an obligation thereunder or in connection with a casualty or condemnation.

2. Expansion Premises Commencement Date.

2.01 The "**Expansion Premises Commencement Date**" shall be the date on which Landlord's Expansion Premises Work (as defined in Exhibit C attached to this Amendment) is Substantially Complete (as defined below) in the Expansion Premises. Notwithstanding the foregoing, if on the date on which Landlord's Expansion Premises Work is Substantially Complete, any applicable governmental authority having jurisdiction over the Building, including the City of Stamford, the State of Connecticut and/or the federal government of the United States, has any outstanding order(s) which explicitly prohibit all (as opposed to some) of Tenant's employees from occupying and/or working out of the Expansion Premises at the same time (as opposed to an order which requires that employees attend their workplace on part-time and/or staggered and/or alternating shifts, timetables and/or

days) (a "**Stay At Home Order**"), then the Expansion Premises Commencement Date shall be delayed until such Stay At Home Order is revised, rescinded, reversed or no longer applicable to Tenant (the "**Expansion Premises Commencement Date Delay Condition**"); provided that, Tenant may, in its sole discretion, waive the Expansion Premises Commencement Date Delay Condition by written notice to Landlord at any time, whereby the Expansion Premises Commencement Date shall occur on the date that is the later to occur of (i) the date on which Landlord's Expansion Premises Work is Substantially Complete, or (ii) five (5) days following the date of Tenant's notice to Landlord. For the avoidance of doubt, in the event that a Stay At Home Order is in place on the date that Landlord's Work is Substantially Complete, so long as such Stay At Home Order permits at least one of Tenant's employees to work out of the Expansion Premises, then the Expansion Premises Commencement Date shall not be delayed.

2.02 Landlord's Expansion Premises Work in the Expansion Premises shall be deemed to be "**Substantially Complete**" on the date that (i) all Landlord's Expansion Premises Work has been performed, other than any minor details of construction, mechanical adjustment or any other similar matter, the non-completion of which does not materially interfere with Tenant's use of the Expansion Premises, (ii) a certificate of occupancy for the Expansion Premises, if required by applicable Law in connection with the lawful use and occupancy thereof, has been obtained, (iii) the Expansion Premises is in vacant, broom clean condition and free of Hazardous Materials, with all Building systems serving the Expansion Premises in good working order and with the Expansion Premises in compliance with all applicable Laws, and (iv) possession of the Expansion Premises is delivered to Tenant in accordance with the terms and conditions of this Amendment. Landlord shall notify Tenant of the date that Landlord's Expansion Premises Work is Substantially Complete, provided that if Landlord's Expansion Premises Work will be Substantially Complete more than two (2) weeks prior to October 1, 2020 (the "**Target Substantial Completion Date**"), Landlord shall notify Tenant of the anticipated Expansion Premises Commencement Date at least ten (10) days prior to the Expansion Premises Commencement Date. If Landlord is delayed in the performance of Landlord's Expansion Premises Work as a proximate result of any acts of Tenant or its contractors or vendors, including, without limitation, Tenant's failure to deliver the demolition plans and specifications for demolition of the Expansion Premises to Landlord for approval on or before the Demolition Plans Submission Date (as defined in Exhibit C), Tenant's failure to deliver the architectural and engineering plans and specifications for build out of the Expansion Premises to Landlord for approval on or before the Plans Submission Date (as defined in Exhibit C), changes requested by Tenant to approved Plans (as defined in Exhibit C), Tenant's failure to timely comply with any of its obligations under the Lease, as amended hereby, or Tenant's specification of any materials or equipment with long lead times after having first been informed by Landlord that such materials or equipment will cause a delay and Tenant chooses not to substitute with materials or equipment that do not have long lead times (any such delay, a "**Tenant Delay**"), Landlord's Expansion Premises Work shall be deemed to be Substantially Complete on the date that Landlord's Expansion Premises Work would have been Substantially Complete absent the Tenant Delay. Promptly upon the determination of the actual Expansion Premises Commencement Date pursuant to this Amendment, the Expansion Premises Commencement Date shall be set forth in a commencement letter to be prepared by Landlord in the form attached hereto as Exhibit B. Landlord shall be responsible for latent defects in Landlord's Expansion Premises Work of which Tenant notifies Landlord within one (1) year following the Expansion Premises Commencement Date.

2.03 In the event that for any reason Landlord's Expansion Premises Work is not Substantially Complete on or before October 31, 2020 (the "**Penalty Date**"), which date shall be extended by reason of Tenant Delay or Force Majeure (including any delays caused by the COVID-19 pandemic, which shall be considered a Force Majeure event), then the Base Rent and Additional Rent in respect of the Expansion Premises shall abate for one (1) day for each day after the Penalty Date (as the same may have been so extended) that the Landlord's Expansion Premises Work is not Substantially Complete. If Tenant shall be entitled to an abatement of Base Rent and Additional Rent in respect of the Expansion Premises as set forth herein, then commencing on the Expansion Premises Commencement Date, Tenant shall be entitled to a credit against the first Rent payment(s) becoming due following the Expansion Premises Commencement Date in an amount equal to the amount of such abatement which so accrued under this Section 2.03.

3. Term. The Term of the Lease is hereby extended for a period of one (1) month, commencing on December 1, 2023 and expiring on December 31, 2023 (the "**Extended Expiration Date**"); provided, however, notwithstanding the foregoing, in the event that the Expansion Premises Commencement Date is delayed as a result of the issuance of a Stay At Home Order, then the Extended Expiration Date shall be extended one day for each day that

the Expansion Premises Commencement Date is so delayed. If, as a result of such extension, the Extended Expiration Date does not fall on the last day of a calendar month, the Extended Expiration Date shall be adjusted to the last day of the calendar month in which the Extended Expiration Date occurs. The Term of the Lease with respect to the Expansion Premises shall commence on the Expansion Premises Commencement Date and shall expire coterminously with the Existing Premises on the Extended Expiration Date, as extended, if applicable.

4. Base Rent.

4.01 Base Rent for Existing Premises. Section 1.03 of the Lease is hereby amended by deleting the number "90" in the last row of the first column of the Base Rent table and substituting "Extended Expiration Date" therefor. Tenant shall continue to pay Base Rent and Additional Rent for the Existing Premises through the Extended Expiration Date in accordance with the terms of the Lease.

4.02 Base Rent for Expansion Premises. In addition to the Base Rent for the Existing Premises, commencing on the Expansion Premises Commencement Date through the Extended Expiration Date, Tenant shall pay to Landlord Base Rent for the Expansion Premises in accordance with the following schedule:

Full Calendar Months of the Term	Annual Rate Per RSF	Rentable Square Feet	Annual Base Rent	Monthly Base Rent
Expansion Premises Commencement Date - 12	$56.00	11,685	$654,360.00	$54,530.00
13 - 24	$57.00	11,685	$666,045.00	$55,503.75
25 - 36	$58.00	11,685	$677,730.00	$56,477.50
37 – Extended Expiration Date	$59.00	11,685	$689,415.00	$57,451.25

All such Base Rent and Additional Rent shall be payable by Tenant in accordance with the terms of the Lease.

4.03 At Landlord's option and upon prior written notice to Tenant, all billing by Landlord may be delivered to Tenant through a secure online portal (the "**Tenant Portal**"). Landlord shall provide Tenant with set-up instructions for use of the Tenant Portal (along with the ability to utilize at least two (2) logins to Tenant's account) and Landlord shall not charge a fee to Tenant for use of the Tenant Portal. Upon receipt of the set-up instructions for the Tenant Portal, Tenant shall be solely responsible for retrieving all invoices from the Tenant Portal and Landlord shall not be obligated to deliver invoices to Tenant through any other means. Notwithstanding anything to the contrary contained herein, all notices (other than invoices for Rent) shall continue to be delivered in accordance with Section 24 of the Lease.

5. Tenant's Pro Rata Share. Tenant's Pro Rata Share for the Existing Premises is 9.1298% and as of the Expansion Premises Commencement Date, Tenant's Pro Rata Share for the Expansion Premises is 4.4397% for a total of 13.5695%.

6. Expense Excess and Tax Excess. Tenant shall continue to pay Tenant's Pro Rata Share of Expense Excess and Tax Excess for the Existing Premises in accordance with the terms of the Lease through the Extended Expiration Date. Commencing on the Expansion Premises Commencement Date, Tenant shall pay Tenant's Pro Rata Share of Expense Excess and Tax Excess for the Expansion Premises in accordance with the terms of the Lease through the Extended Expiration Date, except that the "Base Year" for Expenses and the "Base Year" for Taxes, respectively, for the Expansion Premises only will be Base Year for Expenses of calendar year 2020 and a Base Year for Taxes of calendar year 2020. The parties agree that the Base Year for Expenses and the Base Year for Taxes for the Existing Premises is and shall remain calendar year 2016.

7. Electricity.

7.01 Tenant shall continue to pay Landlord for Tenant's consumption of electricity in the Existing Premises in accordance with the terms of the Lease through the Extended Expiration Date.

7.02 Commencing on the Expansion Premises Commencement Date through the Extended Expiration Date, Tenant shall pay to Landlord an "**Expansion Premises Electric Charge**" for the Expansion Premises of $33,185.40 per annum ($2.84 per RSF), payable in twelve (12) equal monthly payments of $2,765.45.

8. Improvements to Expansion Premises. Prior to the Expansion Premises Commencement Date, Landlord shall complete the Landlord's Expansion Premises Work in the Expansion Premises using building standard and other materials as shown on and in accordance with the Work Letter and Plans attached hereto as Exhibits C, C-1 and C-2, which Tenant hereby approves. Subject to Landlord's obligation to perform the Landlord's Expansion Premises Work, the Expansion Premises is accepted by Tenant in "as is" condition and configuration without any representations or warranties by Landlord, except as otherwise provided herein. By taking possession of the Expansion Premises, subject to the other terms and conditions of this Amendment, Tenant agrees that the Expansion Premises are in good order and satisfactory condition and that Landlord has fully and satisfactorily performed and completed all work required to be performed by Landlord prior to Tenant's occupancy, except for any Punchlist Items as provided in Exhibit C attached hereto.

9. Architectural Services Allowance. Provided Tenant is not in Default, Landlord shall provide Tenant with an allowance in the aggregate amount of $51,414.00 (Fifty-One Thousand Four Hundred Fourteen and 00/100 Dollars) (the "**Architectural Services Allowance**") to reimburse Tenant for actual expenses incurred by Tenant as follows: (i) up to $0.15 per RSF of the Expansion Premises ($1,752.75) for Tenant's architect to create a test-fit of the Expansion Premises, (ii) up to $2.50 per RSF of the Expansion Premises ($29,212.50) for Tenant's architect to create construction documents, and (iii) up to $1.75 per RSF of the Expansion Premises ($20,448.75) for Tenant's MEP engineer selected from Landlord's approved list of MEP Engineers (a "**Landlord Approved MEP Engineer**") to create mechanical, electrical and plumbing drawings. The Architectural Services Allowance shall be paid to Tenant in periodic disbursements within thirty (30) days following Landlord's receipt of Tenant's written request for disbursement, together with copies of invoices or other supporting data evidencing such costs and expenses as Landlord may reasonably require. In no event shall Landlord be required to disburse the Architectural Services Allowance more than one time per month.

10. Condition of Existing Premises. Tenant is in possession of the Existing Premises and confirms its acceptance of the same "as is" without any agreements, representations, understandings or obligations on the part of Landlord to perform any alterations, preparatory repairs or improvements thereto. Notwithstanding the foregoing, on or before July 31, 2020, Landlord, at Landlord's expense, shall install mutually agreed-upon sound reduction/sound attenuation material to the offices and conference room ceilings in the Existing Premises (collectively, the "**Sound Reduction Work**"). The Sound Reduction Work may be performed during Business Service Hours until July 1, 2020, and thereafter any Sound Reduction Work shall be performed outside of Building Service Hours. Landlord and Tenant agree to cooperate with each other in order to enable the Sound Reduction Work to be performed in a timely manner and with as little inconvenience to the operation of Tenant's business as is reasonably possible. Notwithstanding anything herein to the contrary, any delay in the completion of the Sound Reduction Work or inconvenience suffered by Tenant during the performance of the Sound Reduction Work shall not subject Landlord to any liability for any loss or damage resulting therefrom or entitle Tenant to any credit, abatement or adjustment of Rent or other sums payable under the Lease, as amended hereby.

11. Renewal Option. Section 2 of Exhibit F to the Lease is hereby amended to provide that the Renewal Option shall apply to the Entire Premises.

12. Right of First Offer. Section 3 of Exhibit F to the Lease is hereby amended to also include any portion of the 11th floor of the Building in the definition of "**First Offer Space**". Landlord hereby represents that there are no superior rights or other options to the First Offer Space (other than current tenant(s) in occupancy) that exist on the date of this Amendment.

13. Parking. As of the Expansion Premises Commencement Date, Section 1.14 of the Lease is hereby deleted in its entirety and the following substituted therefor: "One hundred seven (107) unreserved parking spaces in the Building's Garage, based on the ratio of three (3) unreserved parking spaces per 1,000 rentable square feet of the Entire Premises, at no additional charge to Tenant. Tenant may, at its sole option, lease reserved parking spaces in the Building Garage at the rate of $150.00 per month per reserved parking space. Any such reserved spaces shall be in a location mutually agreed upon by Landlord and Tenant."

14. Notice Addresses. Section 1.10 of the Lease is hereby deleted in its entirety and replaced with the following:

""Notice Address(es)":

Landlord:	Tenant:
Four Stamford Plaza Owner LLC c/o RFR Realty LLC 263 Tresser Boulevard, 4th Floor Stamford, Connecticut 06901 Attn: Property Manager	Cara Therapeutics, Inc. Four Stamford Plaza 107 Elm Street, Suite 900 Stamford, Connecticut 06902 Attn: Chief Financial Officer
With a copy to:	With a copy to:
RFR Realty LLC 390 Park Avenue New York, New York 10022 Attn: President	Wiggin and Dana LLP One Century Tower 265 Church Street New Haven, CT 06510-7001 Attention: Elliot G. Kaiman, Esq.
with a copy of any default notices to:	
Day Pitney LLP One Stamford Plaza 263 Tresser Boulevard, 7th Floor Stamford, Connecticut 06901 Attn: Real Estate Department	

A copy of any notice to Landlord shall also be sent to any Mortgagee (as hereinafter defined) who may have requested the same, provided the name and address of such Mortgagee shall have been provided to Tenant in writing."

15. Miscellaneous.

15.01 Entire Agreement. This Amendment sets forth the entire agreement between the parties with respect to the matters set forth herein. There have been no additional oral or written representations or agreements. Under no circumstances shall Tenant be entitled to any Rent abatement, improvement allowance, leasehold improvements, or other work to the Premises, or any similar economic incentives that may have been provided Tenant in connection with entering into the Lease, unless expressly set forth in this Amendment or the Lease (it being understood that this shall not apply to any abatements expressly set forth in the Lease for a failure of Landlord to perform an obligation thereunder or in connection with a casualty or condemnation). Landlord and Tenant each agrees that it shall comply with Section 26.11 of the Lease with respect to the disclosure of any matters set forth in this Amendment or the dissemination or distribution of any information concerning the terms, details or conditions of this Amendment.

15.02 Representations. Tenant hereby represents and warrants to Landlord that as of the date hereof: (i) all of Tenant's estate, right, title and interest in and to the Lease is free and clear of assignments, sublettings, liens and encumbrances; (ii) the Lease is in full force and effect; (iii) Tenant is presently in possession of the Existing Premises; (iv) the Lease has not been modified, supplemented or amended in any way, except as may be indicated in the recitals set forth above or by this Amendment; and (v) to Tenant's knowledge (without investigation) as of the date hereof, Tenant is not aware of any actionable defenses, claims or set-offs under the Lease against rents or charges due or to become due thereunder. Landlord hereby represents and warrants to Tenant that as of the date hereof: (i) the Lease is in full force and effect; (ii) the Lease has not been modified, supplemented or amended in any way, except as may be indicated in the recitals set forth above or by this Amendment; and (iii) to Landlord's knowledge (without investigation) as of the date hereof, Landlord is not aware of any defaults by Tenant under the Lease.

15.03 Effect of Amendment; Ratification. Except as herein modified or amended, the provisions, conditions and terms of the Lease shall be incorporated hereby by this reference and shall remain unchanged and in full force and effect. The Lease as hereby amended is hereby ratified and confirmed by the parties hereto.

15.04 Inconsistency. In the case of any inconsistency between the provisions of the Lease and this Amendment, the provisions of this Amendment shall govern and control.

15.05 Solicitation of Offer. Submission of this Amendment by Landlord is not an offer to enter into this Amendment but rather is a solicitation for such an offer by Tenant.

Neither Landlord nor Tenant shall be bound by this Amendment until this Amendment has been fully executed and delivered by both Landlord and Tenant.

15.06 Broker. Tenant hereby represents to Landlord that Tenant has dealt with no broker in connection with this Amendment other than Choyce Peterson, Inc. (the "**Broker**"). Landlord hereby represents to Tenant that Landlord has dealt with no broker in connection with this Amendment other than the Broker. Tenant agrees to indemnify and hold Landlord and the Landlord Related Parties harmless from all claims of any brokers claiming to have represented Tenant in connection with this Amendment except for the Broker. Landlord agrees to pay the Broker a commission pursuant to a separate agreement. Landlord agrees to indemnify and hold Tenant and the Tenant Related Parties harmless from all claims of any brokers claiming to have represented Landlord in connection with this Amendment.

15.07 Authority. Each signatory of this Amendment represents hereby that he or she has the authority to execute and deliver the same on behalf of the party hereto for which such signatory is acting.

15.08 Governing Law. This Amendment shall be deemed to have been made in Fairfield County, Connecticut, and shall be governed by and construed in accordance with the laws of the State of Connecticut, without regard to conflicts of laws principles.

15.09 SNDA. Landlord shall use commercially reasonable efforts to obtain a subordination, non-disturbance and attornment agreement ("**SNDA**") from Landlord's current Mortgagee on a commercially reasonable form of agreement.

15.10 Counterparts; Electronic Signatures. This Amendment may be executed in counterparts, including both counterparts that are executed on paper and counterparts that are in the form of electronic records and are executed electronically. All executed counterparts shall constitute one agreement, and each counterpart shall be deemed an original. The parties hereby acknowledge and agree that electronic records and electronic signatures, as well as facsimile signatures, may be used in connection with the execution of this Amendment and electronic signatures, facsimile signatures or signatures transmitted by electronic mail in so-called pdf format shall be legal and binding and shall have the same full force and effect as if a paper original of this Amendment had been delivered and had been signed using a handwritten signature. Landlord and Tenant (i) agree that an electronic signature, whether digital or encrypted, of a party to this Amendment is intended to authenticate this writing and to have the same force and effect as a manual signature, (ii) intend to be bound by the signatures (whether original, faxed or electronic) on any document sent or delivered by facsimile or, electronic mail, or other electronic means, (iii) are aware that the other party will rely on such signatures, and (iv) hereby waive any defenses to the enforcement of the terms of this Amendment based on the foregoing forms of signature.

[Signatures follow on next page.]

IN WITNESS WHEREOF, the parties hereto have executed this Amendment as of the date first above written.

LANDLORD:

FOUR STAMFORD PLAZA OWNER LLC,
a Delaware limited liability company

By: /s/ Thomas L. Lavin
Name: Thomas L. Lavin
Title: Vice President

TENANT:

CARA THERAPEUTICS, INC., a Delaware corporation

By: /s/ Derek Chalmers
Name: Derek Chalmers
Title: CEO

Cara Legal
Approved as to form

/s/ST

EXHIBIT 31.1

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

I, Derek Chalmers, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 10, 2020

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

EXHIBIT 31.2

Certification of Principal 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, Richard Makara, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 10, 2020

By: /s/ Richard Makara
RICHARD MAKARA
VP, HEAD OF ACCOUNTING & CONTROLLER
(*PRINCIPAL FINANCIAL OFFICER*)

EXHIBIT 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended June 30, 2020, 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 Richard Makara, as VP, Head of Accounting & Controller 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 knowledge, based upon a review of the Report:

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

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

/s/ DEREK CHALMERS
Name: Derek Chalmers, Ph.D., D.Sc.
Title: Chief Executive Officer
Date: August 10, 2020

/s/ RICHARD MAKARA
Name: Richard Makara
Title: VP, Head of Accounting & Controller
(*Principal Financial Officer*)
Date: August 10, 2020