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

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2021

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 the definitions of "large accelerated filer", "accelerated filer", "smaller reporting company", and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer	☒	Accelerated Filer	☐
Non-Accelerated Filer	☐	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 5, 2021 was: 50,089,936.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2021

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, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 22,335	$ 31,683
Marketable securities	132,841	149,242
Income tax receivable	697	1,507
Other receivables	305	557
Prepaid expenses	8,295	12,076
Total current assets	164,473	195,065
Operating lease right-of-use assets	3,641	4,279
Marketable securities, non-current	52,216	70,565
Property and equipment, net	716	840
Restricted cash	408	408
Total assets	$ 221,454	$ 271,157
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 13,493	$ 16,881
Operating lease liabilities, current	1,677	1,602
Total current liabilities	15,170	18,483
Operating lease liabilities, non-current	2,818	3,673
Commitments and contingencies (Note 15)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at June 30, 2021 and December 31, 2020, zero shares issued and outstanding at June 30, 2021 and December 31, 2020	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at June 30, 2021 and December 31, 2020, 50,088,161 shares and 49,872,213 shares issued and outstanding at June 30, 2021 and December 31, 2020, respectively	50	50
Additional paid-in capital	649,784	641,195
Accumulated deficit	(446,363)	(392,317)
Accumulated other comprehensive (loss) income	(5)	73
Total stockholders' equity	203,466	249,001
Total liabilities and stockholders' equity	$ 221,454	$ 271,157

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, 2021	June 30, 2020	June 30, 2021	June 30, 2020
Revenue:				
License and milestone fees	$ —	$ 5,099	$ 1,192	$ 13,120
Collaborative revenue	—	—	706	—
Clinical compound revenue	—	535	37	607
Total revenue	—	5,634	1,935	13,727
Operating expenses:				
Research and development	25,225	26,108	44,356	59,644
General and administrative	5,651	5,410	12,016	9,968
Total operating expenses	30,876	31,518	56,372	69,612
Operating loss	(30,876)	(25,884)	(54,437)	(55,885)
Other income, net	131	634	391	1,591
Loss before benefit from income taxes	(30,745)	(25,250)	(54,046)	(54,294)
Benefit from income taxes	—	182	—	304
Net Loss	$ (30,745)	$ (25,068)	$ (54,046)	$ (53,990)
Net Loss per share:				
Basic and Diluted	$ (0.61)	$ (0.54)	$ (1.08)	$ (1.15)
Weighted average shares:				
Basic and Diluted	50,059,984	46,799,703	49,989,379	46,762,327
Other comprehensive income (loss), net of tax of $0:				
Change in unrealized gains (losses) on available-for-sale marketable securities	(17)	703	(78)	465
Total comprehensive loss	$ (30,762)	$ (24,365)	$ (54,124)	$ (53,525)

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, 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

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2020	49,872,213	$ 50	$ 641,195	$ (392,317)	$ 73	$ 249,001
Stock-based compensation expense	—	—	2,744	—	—	2,744
Shares issued upon exercise of stock options	45,035	—	688	—	—	688
Shares issued upon vesting of restricted stock units	109,419	—	1,388	—	—	1,388
Net loss	—	—	—	(23,301)	—	(23,301)
Other comprehensive loss	—	—	—	—	(61)	(61)
Balance at March 31, 2021	50,026,667	$ 50	$ 646,015	$ (415,618)	$ 12	$ 230,459
Stock-based compensation expense	—	—	3,376	—	—	3,376
Shares issued upon exercise of stock options	25,494	—	293	—	—	293
Shares issued upon vesting of restricted stock units	36,000	—	100	—	—	100
Net loss	—	—	—	(30,745)	—	(30,745)
Other comprehensive loss	—	—	—	—	(17)	(17)
Balance at June 30, 2021	50,088,161	$ 50	$ 649,784	$ (446,363)	$ (5)	$ 203,466

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Six Months Ended	
	June 30, 2021	**June 30, 2020**
Operating activities		
Net loss	$ (54,046)	$ (53,990)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	7,608	7,465
Depreciation and amortization	124	96
Amortization expense component of lease expense	638	325
Amortization/(accretion) of available-for-sale marketable securities, net	384	(34)
Realized gain on sale of available-for-sale marketable securities	(39)	(60)
Realized gain on sale of property and equipment	(70)	—
Deferred revenue	—	(12,494)
Changes in operating assets and liabilities:		
Income tax receivable	810	(304)
Other receivables	252	485
Prepaid expenses	3,781	(1,261)
Accounts payable and accrued expenses	(3,388)	(5,713)
Operating lease liabilities	(780)	(470)
Net cash used in operating activities	(44,726)	(65,955)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	80,470	97,645
Proceeds from redemptions of available-for-sale marketable securities, at par	8,600	17,035
Proceeds from sale of available-for-sale marketable securities	9,029	10,677
Purchases of available-for-sale marketable securities	(63,772)	(21,016)
Proceeds from sale of property and equipment	70	—
Net cash provided by investing activities	34,397	104,341
Financing activities		
Proceeds from the exercise of stock options	981	276
Net cash provided by financing activities	981	276
Net (decrease) increase in cash, cash equivalents and restricted cash	(9,348)	38,662
Cash, cash equivalents and restricted cash at beginning of period	32,091	18,713
Cash, cash equivalents and restricted cash at end of period	$ 22,743	$ 57,375

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, 2021, 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 earned approximately $203,800 under its license agreements for CR845/difelikefalin, primarily with Vifor (International) Ltd., or Vifor, 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 October 2020, the Company received net proceeds of $38,449 from the issuance and sale of 2,939,552 shares of the Company's common stock to Vifor in connection with the Company's license agreement with Vifor. Furthermore, 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 in connection with the Company's license agreement with VFMCRP (see Note 10, *Collaboration and Licensing Agreements*).

As of June 30, 2021, the Company had unrestricted cash and cash equivalents and marketable securities of $207,392 and an accumulated deficit of $446,363. 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 $30,745 and $25,068 for the three months ended June 30, 2021 and 2020, respectively, and $54,046 and $53,990 for the six months ended June 30, 2021 and 2020, respectively, and had net cash used in operating activities of $44,726 and $65,955 for the six months ended June 30, 2021 and 2020, 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, 2020 were derived from audited financial statements, but do not include all disclosures required by GAAP. These unaudited interim

CARA THERAPEUTICS, INC.

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

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, 2020.

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. The more significant estimates include the fair value of marketable securities that are classified as level 2 of the fair value hierarchy, 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, 2020, except for the recent adoption of new accounting pronouncements as disclosed below.

Accounting Pronouncements Recently Adopted

In December 2019, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 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. 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

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
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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. The Company adopted ASU 2019-12 on January 1, 2021 and it did not have a material effect on its results of operations, financial position, and cash flows due to the full valuation allowance recorded.

3. Available-for-Sale Marketable Securities

As of June 30, 2021 and December 31, 2020, 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, 2021 and December 31, 2020:

As of June 30, 2021

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 10,106	$ 3	$ —	$ 10,109
U.S. government agency obligations	14,572	5	(10)	14,567
Corporate bonds	44,850	15	(31)	44,834
Commercial paper	99,705	13	(1)	99,717
Municipal bonds	15,829	17	(16)	15,830
Total available-for-sale marketable securities	$ 185,062	$ 53	$ (58)	$ 185,057

As of December 31, 2020

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 20,710	$ 41	$ (1)	$ 20,750
U.S. government agency obligations	22,125	4	(1)	22,128
Corporate bonds	49,080	61	(23)	49,118
Commercial paper	116,139	5	(17)	116,127
Municipal bonds	11,680	12	(8)	11,684
Total available-for-sale marketable securities	$ 219,734	$ 123	$ (50)	$ 219,807

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, 2021 and December 31, 2020:

CARA THERAPEUTICS, INC.

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

As of June 30, 2021

	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. government agency obligations	$ 6,990	$ (10)	$ —	$ —	$ 6,990	$ (10)
Corporate bonds	30,166	(31)	—	—	30,166	(31)
Commercial paper	9,492	(1)	—	—	9,492	(1)
Municipal bonds	6,404	(16)	—	—	6,404	(16)
Total	$ 53,052	$ (58)	$ —	$ —	$ 53,052	$ (58)

As of December 31, 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
U.S. Treasury securities	$ 12,682	$ (1)	$ —	$ —	$ 12,682	$ (1)
U.S. government agency obligations	2,500	(1)	—	—	2,500	(1)
Corporate bonds	23,553	(23)	—	—	23,553	(23)
Commercial paper	68,897	(17)	—	—	68,897	(17)
Municipal bonds	6,259	(8)	—	—	6,259	(8)
Total	$ 113,891	$ (50)	$ —	$ —	$ 113,891	$ (50)

As of June 30, 2021 and December 31, 2020, 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 is as follows:

As of June 30, 2021 and December 31, 2020, the Company held a total of 24 out of 59 positions and 30 out of 59 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.

U.S. government agency obligations. The unrealized losses on the Company's investments in direct obligations of U.S. government agencies were due to changes in interest rates and non-credit related factors. The contractual terms of these investments do not permit the issuer to repay principal at a price less than the amortized cost bases of the investments, which is equivalent to the par value on the maturity date. The Company expects to recover the entire amortized cost bases of these securities on the maturity date. The Company does not intend to sell these investments, and it is not more likely than not that the Company will be required to sell these investments before recovery of their amortized cost bases. The Company held 2 out of 4 positions for its U.S. government agency obligations that were in unrealized loss positions as of June 30, 2021.

Corporate bonds, commercial paper, and municipal bonds. The unrealized losses on the Company's investments in corporate bonds, commercial paper and municipal bonds were due to changes in interest rates and non-credit related factors. The credit ratings of these investments in the Company's portfolio have not been downgraded below investment

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
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grade status. The contractual terms of these investments do not permit the issuer to repay principal at a price less than the amortized cost bases of the investments, which is equivalent to the par value on the maturity date. The Company expects to recover the entire amortized cost bases of these securities on the maturity date. The Company does not intend to sell these investments, and it is not more likely than not that the Company will be required to sell these investments, before recovery of their amortized cost bases. The Company held 13 out of 18 positions for its corporate bonds, 3 out of 23 positions for its commercial paper, and 6 out of 11 positions for its municipal bonds, that were in unrealized loss positions as of June 30, 2021.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of June 30, 2021, the Company's marketable debt securities mature at various dates through May 2024. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows.

	As of June 30, 2021		As of December 31, 2020	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 132,817	$ 132,841	$ 149,164	$ 149,242
One year to three years	52,245	52,216	70,570	70,565
Total	$ 185,062	$ 185,057	$ 219,734	$ 219,807

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, net 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.

During the three and six months ended June 30, 2021, the Company sold certain shares of its available-for-sale debt securities with a total fair value of $1,000 and $9,029, respectively, which resulted in no realized gains or losses for the three months ended June 30, 2021, and $39 of realized gains for the six months ended June 30, 2021, respectively. 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, which resulted in realized gains of $60 during the three and six months ended June 30, 2020.

As of June 30, 2021 and December 31, 2020, accrued interest receivables on our available-for-sale debt securities were $305 and $311, respectively.

CARA THERAPEUTICS, INC.

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

4. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss), net of tax, from unrealized gains (losses) on available-for-sale marketable securities, the Company's only component of accumulated other comprehensive income (loss), for the six months ended June 30, 2021 and June 30, 2020.

	Total Accumulated Other Comprehensive Income (Loss)
Balance, December 31, 2020	$ 73
Other comprehensive loss before reclassifications	(39)
Amount reclassified from accumulated other comprehensive income	(39)
Net current period other comprehensive loss	(78)
Balance, June 30, 2021	$ (5)
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

Amounts reclassified out of accumulated other comprehensive income (loss) into net loss are determined by specific identification. The reclassifications out of accumulated other comprehensive income (loss) and into net loss were as follows:

Component of Accumulated Other Comprehensive Income (Loss)	Three Months Ended June 30,		Six Months Ended June 30,		Affected Line Item in the Condensed Statements of Comprehensive Income (Loss)
	2021	2020	2021	2020	
Unrealized gains (losses) on available-for-sale marketable securities:					
Realized gains on sales of securities	$ —	$ 60	$ 39	$ 60	Other income, net
Income tax effect	—	—	—	—	Benefit from income taxes
Realized gains on sales of securities, net of tax	$ —	$ 60	$ 39	$ 60	

5. Fair Value Measurements

As of June 30, 2021 and December 31, 2020, 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 at their fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services, as described below.

The valuation techniques used by the Company 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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
(amounts in thousands, except share and per share data)
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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, 2021 or December 31, 2020.

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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, 2021 and December 31, 2020.

Fair value measurement as of June 30, 2021:

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	$ 22,335	$ 22,335	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	10,109	—	10,109	—
U.S. government agency obligations	14,567	—	14,567	—
Corporate bonds	44,834	—	44,834	—
Commercial paper	99,717	—	99,717	—
Municipal bonds	15,830	—	15,830	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 207,800	$ 22,743	$ 185,057	$ —

Fair value measurement as of December 31, 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	$ 31,683	$ 31,683	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	20,750	—	20,750	—
U.S. government agency obligations	22,128	—	22,128	—
Corporate bonds	49,118	—	49,118	—
Commercial paper	116,127	—	116,127	—
Municipal bonds	11,684	—	11,684	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 251,898	$ 32,091	$ 219,807	$ —

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, 2021 and 2020, respectively. There were no transfers of financial assets into or out of Level 3 classification during the three and six months ended June 30, 2021 and 2020, 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, 2021, the restricted cash balance for the Stamford Lease was invested in a commercial money market account.

As of June 30, 2021 and December 31, 2020, 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, 2021	December 31, 2020
Cash and cash equivalents	$ 22,335	$ 31,683
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 22,743	$ 32,091

7. Prepaid expenses

As of June 30, 2021, prepaid expenses were $8,295, consisting of $6,287 of prepaid R&D clinical costs, $1,392 of prepaid insurance and $616 of other prepaid costs. As of December 31, 2020, prepaid expenses were $12,076, consisting of $11,286 of prepaid R&D clinical costs, $223 of prepaid insurance, and $567 of other prepaid costs.

8. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	June 30, 2021	December 31, 2020
Accounts payable	$ 3,386	$ 4,893
Accrued research projects	6,193	6,194
Accrued compensation and benefits	3,147	4,955
Accrued professional fees and other	767	839
Total	$ 13,493	$ 16,881

9. Stockholders' Equity

In June 2021, as a result of the completion of the one-year vesting period, an aggregate of 36,000 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 February and March 2021, as a result of the achievement of certain performance targets, an aggregate of 76,750 performance-based 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 February 2021, as a result of the completion of the first year of the three-year vesting period, an aggregate of 32,669 time-based 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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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*).

10. Collaboration and Licensing Agreements

Vifor (International) Ltd.

In October 2020, the Company entered into a license agreement with Vifor, or the Vifor Agreement, under which the Company granted Vifor an exclusive license solely in the United States to use, distribute, offer for sale, promote, sell and otherwise commercialize CR845/difelikefalin injection for all therapeutic uses relating to the inhibition, prevention or treatment of itch associated with pruritus in hemodialysis and peritoneal dialysis patients in the United States. Under the Vifor Agreement, the Company retains all rights with respect to the clinical development of, and activities to gain regulatory approvals of, CR845/difelikefalin injection in the United States.

The Vifor Agreement provides full commercialization rights in dialysis clinics to Vifor in the United States under a profit-sharing arrangement. Pursuant to the profit-sharing arrangement, the Company will generally be entitled to 60% of the net profits (as defined in the Vifor Agreement) from sales of CR845/difelikefalin injection in the United States (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by the VFMCRP Agreement) and Vifor is entitled to 40% of such net profits, subject to potential temporary adjustment in future years based on certain conditions. Under the Vifor Agreement, in consideration of Vifor's conduct of the marketing, promotion, selling and distribution of CR845/difelikefalin injection in the United States, the Company will pay a marketing and distribution fee to Vifor based on the level of annual net sales. This fee will be deducted from product sales in calculating the net profits that are subject to the profit-sharing arrangement under the Vifor Agreement.

Under the terms of the Vifor Agreement, the Company received from Vifor an upfront payment of $100,000 and an additional payment of $50,000 for the purchase of an aggregate of 2,939,552 shares of the Company's common stock at a price of $17.0094 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.

Upon U.S. regulatory approval of CR845/difelikefalin, the Company will also be eligible to receive an additional $50,000 common stock investment at a 20% premium to the 30-day trailing average price of the Company's common stock as of such date. In addition, pursuant to the Vifor Agreement, the Company is eligible to receive payments of up to $240,000 upon the achievement of certain sales-based milestones.

The Company retains the rights to make and have made CR845/difelikefalin injection, or the Licensed Product, on a non-exclusive basis, in the United States for commercial sale of the Licensed Product for use in all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients, or the Field, anywhere in the world and for supply of Licensed Product to Vifor under the terms of a supply agreement, or the Vifor Supply Agreement. The supply price will be the Company's cost of goods sold, as calculated under GAAP, plus an agreed upon margin. The Vifor Supply Agreement will co-terminate with the Vifor Agreement. Regarding the supply agreement, the Vifor Agreement only includes a requirement for the Company to negotiate in good faith with Vifor.

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After the execution of the Vifor Agreement, a separate agreement to supply them with the Licensed Product would be entered into, although the Company has no obligation to execute a supply agreement.

The Vifor Supply Agreement will be accounted for as a customer option that is not a material right because the selling price of the Licensed Product under the Vifor 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 Vifor is not a performance obligation under the Vifor Agreement but rather the Vifor Supply Agreement is a separate agreement from the Vifor Agreement. The only performance obligation under the Vifor Supply Agreement is the delivery of the Licensed Product to Vifor for commercialization. Revenue from the sale of the Licensed Product to Vifor will be recognized in the Company's Condensed Statements of Comprehensive Loss as sales of the Licensed Product occur. As of June 30, 2021, no supply agreement has been entered into between the Company and Vifor.

Vifor Fresenius Medical Care Renal Pharma Ltd.

In May 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 the Licensed Product for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in 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.

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 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

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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. There were no sales of clinical compound to VFMCRP during the three and six months ended June 30, 2021. 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.

Maruishi Pharmaceutical Co., Ltd.

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

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

There were no sales of clinical compound to Maruishi during the three months ended June 30, 2021. 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 prior period. During the six months ended June 30, 2021 and 2020, the Company recognized clinical compound revenue of $37 and $519, respectively, from the sale of clinical compound to Maruishi, and as a result, the Company incurred R&D expense of $33 and $467, respectively, during these periods.

Chong Kun Dang Pharmaceutical Corporation

In April 2012, the Company entered into a license agreement, or the CKDP Agreement, with 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.

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11. Revenue Recognition

The Company currently recognizes revenue in accordance with FASB Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*, as amended, or ASC 606, for the Vifor, 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 and CKDP agreements, from clinical development milestone payments. The Company has also recognized revenue from a sub-license payment earned under the Maruishi Agreement. Under the Maruishi and CKDP agreements, the Company may earn additional future milestone payments upon the achievement of defined clinical events, and under the Vifor, VFMCRP, Maruishi and CKDP agreements, upon the achievement of defined regulatory events, and under the Vifor, VFMCRP and Maruishi agreements, from sales milestones. The Company may also recognize revenue in the future from royalties on net sales under the VFMCRP, Maruishi and CKDP agreements. In addition, the Company has recognized revenue upon the delivery of clinical compound to VFMCRP and Maruishi in accordance with separate supply agreements.

Contract balances

As of June 30, 2021 and December 31, 2020, there were no material balances of receivables, and no other assets or deferred revenue related to the Vifor, VFMCRP, Maruishi and CKDP agreements.

Performance obligations

Under the Vifor Agreement, the Company's only performance obligation is granting a license to allow Vifor to commercialize CR845/difelikefalin in the United States, which occurred at inception of the contract in October 2020 (see Note 10, *Collaboration and Licensing Agreements*).

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, were not distinct, and were accounted for as a single performance obligation during the period that the R&D services were 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 (see Note 10, *Collaboration and Licensing Agreements*).

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.

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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 (see Note 10, *Collaboration and Licensing Agreements*).

Upon execution of the Vifor, VFMCRP, Maruishi and CKDP agreements, 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 Vifor Agreement, the entire transaction price of $111,551 was allocated to the one performance obligation, as described above, and was recognized as license and milestone fees revenue for the year ended December 31, 2020 as the license was granted to Vifor in October 2020. As of June 30, 2021, there were no remaining performance obligations under the Vifor Agreement. The Company is eligible to receive milestone payments in the future.

At inception of the VFMCRP Agreement, the entire transaction price of $55,444 was allocated to the one combined performance obligation, as described above. As of June 30, 2021, there were no remaining performance obligations, and the entire transaction price has been recognized as license and milestone fees revenue through December 31, 2020 since R&D services have been completed during 2020. The Company is eligible to receive milestone payments and sales royalties in the future.

As of June 30, 2021, there were no remaining performance obligations under either the Maruishi or CKDP agreements, although the Company is eligible to receive milestone payments and sales royalties in the future.

Significant judgments

In applying ASC 606, as amended, to its four 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.

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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 Vifor and CKDP agreements is the granting of the license.

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

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

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

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

Under the Vifor Agreement, the one performance obligation was satisfied when the license was granted to Vifor in October 2020, and as a result, $111,551 (including the upfront payment of $100,000 and the premium on the common stock purchased by Vifor of $11,551) was recognized as license and milestone fees revenue during the year ended December 31, 2020. The remaining potential consideration was considered to be variable consideration and was constrained at inception of the contract, which includes regulatory and sales milestones (see Note 10, *Collaboration and Licensing Agreements*).

Under the VFMCRP Agreement, the single combined performance obligation was satisfied as the R&D services were 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, was recognized as revenue as the R&D services were 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*).

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All performance obligations under the Maruishi and CKDP agreements 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. The remaining potential consideration was considered to be variable consideration and was constrained at inception of the contract, including clinical, regulatory and sales milestones, and sales royalties (see Note 10, *Collaboration and Licensing Agreements*).

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

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

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

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

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

Since the Vifor, VFMCRP and CKDP agreements 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 Vifor, Maruishi and CKDP were accounted for as distinct performance obligations. As discussed below, both licenses

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relate to functional IP for which revenue is recognized at a point in time – in the case of these three 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 Vifor, 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 Vifor, Maruishi or CKDP. Therefore, the Company's ongoing development efforts do not significantly affect the IP's utility to which Vifor, Maruishi or CKDP have rights. Furthermore, if the Company abandons its development efforts, Vifor, Maruishi or CKDP may still continue to develop CR845/difelikefalin in their respective countries.

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

Similarly, under the VFMCRP Agreement, revenue related to the single distinct performance obligation, which includes both granting of the license and performance of the R&D services, was recognized as the R&D services were performed, based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation. As of June 30, 2021, there is no remaining amount of the transaction price to be recognized as license and milestone fees revenue as all R&D services were completed in 2020.

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 Vifor, VFMCRP, Maruishi and CKDP agreements contain potential payments related to achievement of defined milestone events and royalties (excluding Vifor) 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).

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In January 2021, the criteria for revenue recognition for a milestone event set forth in the Maruishi Agreement was achieved, and the Company recorded $1,192 as license and milestone fees revenue and $706 as collaboration revenue based on the relative standalone selling prices described above at contract inception for the six months ended June 30, 2021. In May 2021, the Company received the $1,898 payment (after contractual foreign currency exchange adjustments) from Maruishi for the milestone event achieved.

There were no milestone events related to the Maruishi Agreement that were probable of occurrence or achieved during the three months ended June 30, 2021, or during the three and six months ended June 30, 2020.

Sublicense payments

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

Sales-based Royalty Payments

The VFMCRP, Maruishi and CKDP agreements 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, 2021 and 2020, 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.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Basic:				
Weighted average common shares outstanding	50,059,984	46,799,703	49,989,379	46,762,327
Diluted:				
Weighted average common shares outstanding - Basic	50,059,984	46,799,703	49,989,379	46,762,327
Common stock equivalents*	—	—	—	—
Denominator for diluted net loss per share	50,059,984	46,799,703	49,989,379	46,762,327

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

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Net loss - basic and diluted	$ (30,745)	$ (25,068)	$ (54,046)	$ (53,990)
Weighted-average common shares outstanding:				
Basic and diluted	50,059,984	46,799,703	49,989,379	46,762,327
Net loss per share, Basic and Diluted:	$ (0.61)	$ (0.54)	$ (1.08)	$ (1.15)

As of June 30, 2021, 5,995,223 stock options and 409,031 restricted stock units 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 as a result of the net loss for the period.

In addition, the Company entered into the Vifor Agreement in October 2020. The Company will be eligible to receive an additional $50,000 common stock investment upon U.S. regulatory approval of CR845/difelikefalin at a 20% premium to the 30-day trailing average price of the Company's common stock as of such date, which could potentially dilute basic earnings per share in the future (see Note 10, *Collaboration and Licensing Agreements*).

As of June 30, 2020, 4,964,766 stock options and 272,000 restricted stock units 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 as a result of the net loss for the period.

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13. Stock-Based Compensation

2019 Inducement Plan

In October 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 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 made automatically at Annual Meetings of Stockholders vest fully on the earlier of the first anniversary of the date of grant and the next Annual Meeting of Stockholders. 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, 2021, the aggregate number of shares of common stock that may be issued pursuant to Stock Awards under the 2014 Plan automatically increased from 7,488,513 to 8,984,679. 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 43,200 restricted stock units were granted to non-employee directors on June 3, 2021, the date of the Company's 2021 Annual Meeting of Stockholders, under the 2014 Plan with a grant date fair value of $13.06 per share. The restricted stock units will vest on the earlier of (i) June 3, 2022 and (ii) immediately prior to the Company's next Annual Meeting of Stockholders

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following the grant date, subject to the recipient's continued service through such date. As a result, the Company recognizes compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For each of the three and six months ended June 30, 2021, stock compensation expense of $42 was recognized in general and administrative, or G&A, expense. As of June 30, 2021, none of the 43,200 restricted stock units were vested or settled in shares of the Company's common stock.

On March 30, 2021, the Compensation Committee of the Company's Board of Directors approved and granted a total of 176,000 restricted stock units to executive officers under the 2014 Plan with a grant date fair value of $20.59 per share. Vesting of the restricted stock units is contingent on the achievement of certain performance targets related to clinical and regulatory milestones, subject to the recipient's continuous service through each performance target. Recognition of compensation expense associated with these awards begins when, and to the extent, the performance criteria is probable of achievement and the employee has met the service conditions. For the three and six months ended June 30, 2021, no stock compensation expense relating to these restricted stock units was recognized, as the performance criteria are not probable of achievement. As of June 30, 2021, none of the restricted stock units were vested or settled in shares of the Company's common stock.

Additionally on March 30, 2021, the Compensation Committee of the Company's Board of Directors also approved and granted a total of 100,000 time-based restricted stock units to certain executive officers under the 2014 Plan with a grant date fair value of $20.59 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 and six months ended June 30, 2021, the Company recognized $171 of stock compensation expense, with $55 recorded in R&D expense and $116 in G&A expense. As of June 30, 2021, none of the 100,000 restricted stock units were vested or settled in shares of the Company's common stock.

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 fully vested on June 3, 2021. As a result, the Company has 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, 2021, stock compensation expense of $100 and $239, respectively, was recognized in G&A expense. For each of the three and six months ended June 3, 2020, $40 of stock compensation expense was recognized in G&A expense. All of the 36,000 restricted stock units vested and were settled in shares of the Company's common stock as of June 30, 2021.

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 clinical and regulatory milestones, subject to the recipient's continuous service through each performance target. Recognition of compensation expense associated with these awards begins when, and to the extent, the performance criteria is probable of achievement and the employee has met the service conditions. In February and March 2021, performance targets relating to 36,750 and 40,000 restricted stock units, respectively, had been achieved and thus restricted stock units vested and the awards were settled in shares of common stock. For the six months ended June 30, 2021, the Company recognized $1,256 of stock compensation expense relating to the vesting of these restricted stock units, with $524 recorded in R&D expense and $732 in G&A expense. For the three months ended June 30, 2021, and the three and six months ended June 30, 2020, no stock compensation expense relating to these restricted stock units were recognized. As of June 30, 2021, 113,500 of the 138,000 restricted stock units vested and were settled in shares of the Company's common stock.

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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. In February 2021, 32,669 of these restricted stock units vested and were settled in shares of the Company's common stock in satisfaction of the first year of vesting. For the three months ended June 30, 2021, the Company recognized $133 of stock compensation expense, with $43 recorded in R&D expense and $90 in G&A expense. For the six months ended June 30, 2021, the Company recognized $265 of stock compensation expense, with $86 recorded in R&D expense and $179 recorded in G&A expense. For the three months ended June 30, 2020, the Company recognized $142 of stock compensation expense, with $47 recorded in R&D expense and $95 in G&A expense. For the six months ended June 30, 2020, the Company recognized $186 of stock compensation expense, with $61 recorded in R&D expense and $125 recorded in G&A expense. As of June 30, 2021, 32,669 of the 98,000 restricted stock units vested and were settled in shares of the Company's common stock.

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 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 were recorded in G&A expense. As of June 30, 2020, all of the 24,000 restricted stock units vested and were settled in shares of the Company's common stock.

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 clinical milestones, subject to the recipient's continuous service through the vesting events. Recognition of compensation expense associated with these awards begins when, and to the extent, the performance criteria is probable of achievement and the employee has met the service conditions. 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. During each of 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, with $1,087 recorded in R&D expense and $456 recorded in G&A expense. As of June 30, 2020, all of the 215,000 restricted stock units either vested and were settled in shares of the Company's common stock or were forfeited.

A summary of restricted stock unit activity related to employees and non-employee members of the Company's Board of Directors as of and for the six months ended June 30, 2021 is presented below:

	Number of Units	Weighted Average Grant Date Fair Value
Outstanding, December 31, 2020	235,250	$ 16.25
Awarded	319,200	19.57
Vested and released	(145,419)	16.18
Outstanding, June 30, 2021	409,031	$ 18.87
Restricted stock units exercisable (vested and deferred), June 30, 2021	—	

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Stock Options

Under the 2014 Plan, the Company granted 116,050 and 147,000 stock options during the three months ended June 30, 2021 and 2020, respectively, and 789,250 and 820,350 stock options during the six months ended June 30, 2021 and 2020, respectively. No stock options were granted under the 2019 Inducement Plan during the three and six months ended June 30, 2021 and 2020. The fair values of stock options granted during the three and six months ended June 30, 2021 and 2020 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,	
	2021	2020	2021	2020
Risk-free interest rate	1.07% - 1.23%	0.42% - 0.54%	0.66% - 1.23%	0.42% - 1.57%
Expected volatility	71.78% - 83.48%	73.73% - 74.80%	71.62% - 83.48%	73.72% - 74.80%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee and Board options (in years)	6.25	6.25	6.25	6.25

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, 2021 and 2020 was $10.88 and $10.23, respectively, and during the six months ended June 30, 2021 and 2020 was $12.25 and $10.53, respectively. No options were granted to non-employee consultants during the three and six months ended June 30, 2021 and 2020.

During the three and six months ended June 30, 2021 and 2020, the Company recognized compensation expense relating to stock options as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Research and development	$ 1,805	$ 1,670	$ 3,395	$ 3,279
General and administrative	1,225	1,142	2,239	2,212
Total stock option expense	$ 3,030	$ 2,812	$ 5,634	$ 5,491

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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 $98 in R&D expense and $206 in G&A expense for the three months ended June 30, 2021, and $665 in R&D expense and $1,027 in G&A expense for the six months ended June 30, 2021; (ii) 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 3, 2020; (iii) compensation expense relating to the Board of Directors' restricted stock units for $142 and $281 in G&A expense for the three and six months ended June 30, 2021, respectively; and (iv) 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.

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, 2021 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2020	5,469,393	$ 15.02
Granted	789,250	18.94
Exercised	(70,529)	13.92
Forfeited	(192,891)	16.99
Outstanding, June 30, 2021	5,995,223	$ 15.49
Options exercisable, June 30, 2021	3,636,786	

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, 2021 and 2020.

14. Income Taxes

For the three months ended June 30, 2021 and 2020, pre-tax losses were $30,745 and $25,250, respectively, and for the six months ended June 30, 2021 and 2020, pre-tax losses were $54,046 and $54,294, respectively. The Company recognized a full tax valuation allowance against its deferred tax assets as of June 30, 2021 and December 31, 2020. 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 $304 for the three and six months ended June 30, 2020, 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. Because the Company's revenue in 2020 exceeded $70,000, it is not eligible to exchange its 2021 R&D tax credit for cash, therefore there was no benefit from income taxes for the three and six months ended June 30, 2021.

As of June 30, 2021 and December 31, 2020, 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.

On March 27, 2020, former President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act of 2020, or the CARES Act (H.R. 748), which was further expanded with the signing of the Consolidation

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Appropriations Act of 2021 (H.R. 133) on December 27, 2020. The CARES Act (and December expansion) includes a variety of economic and tax relief measures intended to stimulate the economy, including loans for small businesses, payroll tax credits/deferrals, and corporate income tax relief. Due to the Company's history of tax loss carryforwards and full valuation allowance, the CARES Act did not have a significant effect to the income tax provision, as the corporate income tax relief was directed towards cash taxpayers.

15. Commitments and Contingencies

License Agreement with Enteris Biopharma, Inc.

In August 2019, the Company entered into a non-exclusive license agreement, or 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.

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. In June 2021, the Company paid a $10,000 milestone payment to Enteris based on a successful End of Phase 2 Meeting with the FDA in April 2021, which was recorded in R&D expense for the three and six months ended June 30, 2021. During the three and six months ended June 30, 2020, no milestone payments or royalties were paid to Enteris by the Company in relation to the Enteris License Agreement.

Manufacturing Agreement

In July 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.

In July 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

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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.

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 FASB 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 right-of-use, or 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.

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 began when renovation of the additional space was completed and the Company took possession of the additional space in October 2020, or the Amendment Commencement Date, and ends on December 31, 2023. The Lease Amendment is also renewable for one five-year term. 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 began paying rent for the Lease Amendment on the Amendment Commencement Date.

In October 2020, the Company recorded an operating lease liability of $1,934 for the Lease Amendment as the sum of the present value of the future minimum lease payments over the term for the new lease. The Company also recorded a corresponding ROU asset of $1,934, as no lease incentives were identified in the Lease Amendment.

Under ASC 842, lease expenses on the Stamford Lease and Lease Amendment are recognized on a straight-line basis over the lease term. As a result, $406 and $236 of operating lease cost, or lease expense, was recognized for the three months ended June 30, 2021 and 2020, respectively, consisting of $284 relating to R&D lease expense and $122 relating to G&A lease expense for the Stamford Lease and Lease Amendment in the 2021 period, and $165 relating to R&D lease expense and $71 relating to G&A lease expense for the Stamford Lease in the 2020 period. For the six months ended June 30, 2021 and 2020, $812 and $470, respectively, of operating lease cost, or lease expense, was recognized, consisting of $568 relating to R&D lease expense and $244 relating to G&A lease expense for the Stamford Lease and Lease Amendment in the 2021 period, and $329 relating to R&D lease expense and $141 relating to G&A lease expense for the Stamford Lease in the 2020 period.

CARA THERAPEUTICS, INC.

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

Other information related to the Stamford Lease and Lease Amendment was as follows:

	Three Months Ended		Six Months Ended	
	June 30, 2021	June 30, 2020	June 30, 2021	June 30, 2020
Cash paid for amounts included in the measurement of lease liabilities:				
Operating cash outflows relating to operating leases	$ 478	$ 309	$ 954	$ 615
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ —	$ —	$ —
Remaining lease term - operating leases (years)	2.5	3.5	2.5	3.5
Discount rate - operating leases	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, 2021, were as follows:

Year Ending December 31,	
2021 (Excluding the six months ended June 30, 2021)	$ 967
2022	1,957
2023	1,992
Total future minimum lease payments, undiscounted	4,916
Less imputed interest	(421)
Total	$ 4,495

Operating lease liabilities reported as of June 30, 2021:	
Operating lease liabilities - current	$ 1,677
Operating lease liabilities - non-current	2,818
Total	$ 4,495

16. Subsequent Event

On July 26, 2021, the Company entered into an API Commercial Supply Agreement with Polypeptide Laboratories S.A., or PPL, that defines each party's responsibilities with respect to PPL's manufacture and supply of the active pharmaceutical agreement CR845/difelikefalin, or API, for the CR845/difelikefalin injection product candidate. Under the API Commercial Supply Agreement, PPL shall manufacture API at its facility for sale and supply to the Company, in the amounts as set forth in purchase orders to be provided by the Company. The Company will be required to purchase its requirements of API for each year of the term of the agreement, based on internal forecasts.

The API Commercial Supply Agreement will continue until the fifth anniversary of the approval by the FDA of the new drug application for CR845/difelikefalin injection, unless the API Commercial Supply Agreement is earlier terminated, and will automatically be extended for successive five year periods unless either party gives notice to the other party of its intention to terminate.

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 "aim," "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 Oral KORSUVA (CR845/difelikefalin) in CKD-aP, chronic liver disease associated pruritus, or CLD-aP, pruritus associated with atopic dermatitis, or AD, and pruritus associated with notalgia paresthetica, or NP;
- 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, AD, and NP 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 Biopharma, Inc.'s, or 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, Vifor (International) Ltd., or Vifor, 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 the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2020 for a discussion of material 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, 2020.

Overview

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, and Vifor to commercialize KORSUVA (CR845/difelikefalin) injection in dialysis patients with CKD-aP in the U.S. under profit share agreements. We have partnered with VFMCRP to commercialize KORSUVA worldwide, excluding Japan (Maruishi/sub-licensee Kissei), and South Korea (CKDP).

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 agreements with VFMCRP and Vifor for U.S. and certain ex-U.S. territories 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. In December 2020, we submitted a New Drug Application, or NDA, to the FDA for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe pruritus in hemodialysis patients. In February 2021, the FDA accepted the NDA for filing, and in March 2021, the FDA granted Priority Review for the NDA with a Prescription Drug User Fee Act, or PDUFA, target action date of August 23, 2021. KORSUVA's 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, subsequent waves and variants 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 COVID-19 pandemic has affected the initiation of certain trial sites and patient enrollment for certain of our clinical trials, including our ongoing Phase 2 clinical trials of Oral KORSUVA (CR845/difelikefalin) for NP and for the treatment of pruritus in patients with hepatic impairment due to primary biliary cholangitis, or PBC, and the pandemic may continue to affect these and other planned future trials. 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.

API Commercial Supply Agreement

On July 26, 2021, we entered into an API Commercial Supply Agreement with Polypeptide Laboratories S.A., or PPL, that defines each party's responsibilities with respect to PPL's manufacture and supply of the active pharmaceutical agreement CR845/difelikefalin, or API, for the CR845/difelikefalin injection product candidate. Under the API Commercial Supply Agreement, PPL shall manufacture API at its facility for sale and supply to us, in the amounts as set forth in purchase orders to be provided by us. We will be required to purchase our requirements of API for each year of the term of the agreement, based on internal forecasts.

The API Commercial Supply Agreement will continue until the fifth anniversary of the approval by the FDA of the new drug application for KORSUVA (CR845/difelikefalin) injection, unless the API Commercial Supply Agreement is earlier terminated, and will automatically be extended for successive five year periods unless either party gives notice to the other party of its intention to terminate.

FDA Acceptance and Priority Review of NDA Filing

In February 2021, the FDA accepted our NDA submitted in December 2020 for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe pruritus in hemodialysis patients. In March 2021, the FDA granted Priority Review for the NDA. The PDUFA target action date for KORSUVA (CR845/difelikefalin) injection is August 23, 2021. The FDA stated that currently it is not planning to hold an advisory committee meeting to discuss the application.

Marketing Authorization Application Submission

Our partner, VFMCRP, submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, in March 2021, which was accepted for review by the EMA. If approved, KORSUVA (CR845/difelikefalin) injection would receive marketing authorization in all member states of the European Union, or EU, as well as in Iceland, Liechtenstein, and Norway. The EMA's decision on the EU MAA is expected in the second quarter of 2022.

Overview of Our Product Candidates

Our product candidate, CR845/difelikefalin, is a new chemical entity, which is designed to selectively stimulate kappa, rather than mu, and delta opioid receptors. 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 systematic conditions such as CKD and CLD, dermatological conditions such as AD, and neurological conditions such as NP, 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	• NDA accepted by FDA in February 2021 and Priority Review granted in March 2021; PDUFA target action date - August 23, 2021 • EMA MAA accepted in March 2021 • Phase 3 safety/efficacy trials completed	VFMCRP/Vifor (United States); Maruishi (Japan); CKDP (South Korea); VFMCRP (Worldwide, other than United States, Japan and South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus Atopic Dermatitis (AD)	• Phase 2 trial completed; top-line data reported	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus NDD-CKD	• 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 - Primary Biliary Cholangitis (PBC)	• Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Notalgia Paresthetica (NP)	• KOMFORT Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
Post-Op Setting	CR845/difelikefalin Injection	Acute Post-Operative Pain/PONV	• Adaptive Phase 2/3 trial completed; top-line data 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 submitted

an NDA to the FDA for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe pruritus in hemodialysis patients in December 2020. In February 2021, the FDA accepted the NDA for filing, and in March 2021, the FDA granted Priority Review for our NDA. The PDUFA target action date for KORSUVA (CR845/difelikefalin) injection is August 23, 2021.

Our partner, VFMCRP, submitted a MAA to the EMA in March 2021, which was accepted for review by the EMA. If approved, KORSUVA (CR845/difelikefalin) injection would receive marketing authorization in all member states of the EU, as well as in Iceland, Liechtenstein, and Norway. The EMA's decision on the EU MAA is expected in the second quarter of 2022.

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 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).

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

In April 2021, we announced top-line data from our Phase 2 KARE clinical trial. The KARE Phase 2 trial was a randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of Oral KORSUVA (CR845/difelikefalin) for moderate-to-severe pruritus in 401 adult subjects with AD. Patients were stratified across treatment groups by disease severity. KARE enrolled 64% of patients characterized as mild-to-moderate (BSA<10%)

and 36% falling into the moderate-to-severe category (BSA>10%). Subjects were randomized to three tablet strengths of Oral KORSUVA (CR845/difelikefalin): 0.25 mg, 0.5 mg and 1 mg taken twice daily (BID) versus placebo for 12 weeks followed by 4 weeks of an active extension phase. A prespecified interim conditional power assessment was conducted after approximately 50% of the originally targeted patient number completed the designated 12-week treatment period. Based on the Independent Data Monitoring Committee's recommendation, the sample size for each of the 0.5 mg dose and placebo groups were increased by approximately 60%.

KARE's primary efficacy endpoint was change from baseline in the weekly mean of the daily 24-hour Itch NRS score at week 12 of the treatment period for the intent to treat, or ITT, population. Although no dose group met this endpoint, a statistically significant improvement from baseline was evident as early as week 1 for the 1.0 mg dose group, which was sustained through 75% of the treatment period.

In a prespecified analysis, a statistically significant change in the primary efficacy endpoint was observed in the mild-to-moderate (BSA<10%) patient population (p=0.036, All doses vs placebo), which was evident at week 1 and sustained through the treatment period.

The key secondary endpoint for KARE was the assessment of the proportion of patients achieving an improvement from baseline of ≥4 points with respect to the weekly mean of the daily 24-hour Itch NRS score at week 12 (4-point Responder Analysis). No dose group met this endpoint for the ITT population.

Prespecified analysis by disease severity indicated a statistically significant improvement in the 4-point Responder Analysis in the mild-to-moderate (BSA<10%) patient population with 32% of KORSUVA-treated patients achieving a ≥4 point reduction in NRS at Week 12 versus 19% in the placebo group (p=0.033, All doses vs placebo). A statistically significant improvement was also achieved for the 0.5 mg dose (p=0.046, 0.5 mg vs placebo).

Oral KORSUVA (CR845/difelikefalin) was generally well-tolerated across all doses. Overall, the incidence of treatment-emergent AEs was generally similar across Oral KORSUVA (CR845/difelikefalin) and placebo groups.

We have scheduled an End of Phase 2 Meeting with the FDA in the third quarter of 2021 and, subject to discussions with the FDA, aim to initiate a Phase 3 program in mild-to-moderate AD patients by the end of the year.

Oral KORSUVA (CR845/Difelikefalin) for Treatment of Non-Dialysis Dependent (NDD) 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 NDD–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).

In April 2021, we held an End of Phase 2 Meeting with the FDA to discuss the results of the Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) in NDD CKD-aP and the potential Phase 3 program. The FDA indicated the acceptability of Stage 5 pre-dialysis CKD patients as a viable patient population for a Phase 3 trial. The FDA also indicated the potential to use data from our previous trials of KORSUVA (CR845/difelikefalin) Injection in dialysis patients to support an approval based on a single Phase 3 clinical trial of Oral KORSUVA (CR845/difelikefalin) in the Stage 5 pre-dialysis population. We plan to meet with the FDA in the fourth quarter of 2021 to discuss the potential inclusion of earlier stage CKD patients in a Phase 3 program.

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

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, primarily due to the ongoing effects of the COVID-19 pandemic on patient enrollment, we currently aim to have top-line data in the first half of 2022.

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 Notalgia Paresthetica (NP)

In January 2021, 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 120 adult subjects with NP. Subjects will be randomized to receive Oral KORSUVA (CR845/difelikefalin) 2.0 mg twice daily versus placebo for eight weeks followed by a 4-week active extension period and follow up visit approximately 14 days after the last dose of the study. The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour worst itching NRS score at week 8 of the treatment period. Secondary endpoints include improvement in itch-related quality of life assessed by the change from baseline to Week 8

and a change from baseline in itch-related sleep disturbance subscale measured by the itch medical outcomes study at week 8. We currently plan to complete enrollment in the trial by year-end 2021.

Intravenous CR845/Difelikefalin for Treatment of Acute Postoperative Pain (PONV)

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 (International) Ltd.

In October 2020, we entered into a license agreement, or the Vifor Agreement, with Vifor under which we granted Vifor an exclusive license solely in the United States to use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA (CR845/difelikefalin) injection for all therapeutic uses relating to the inhibition, prevention or treatment of itch associated with pruritus in hemodialysis and peritoneal dialysis patients in the United States. Under the Vifor Agreement, we retain all rights with respect to the clinical development of, and activities to gain regulatory approvals of, KORSUVA (CR845/difelikefalin) injection in the United States.

Under the terms of the Vifor Agreement, we received from Vifor an upfront payment of $100.0 million and an additional payment of $50.0 million for the purchase of an aggregate of 2,939,552 shares of our common stock at a price of $17.0094 per share, which represents a premium over a pre-determined average closing price of our common stock. Upon U.S. regulatory approval of KORSUVA (CR845/difelikefalin) injection, we will also be eligible to receive an additional $50.0 million common stock investment at a 20% premium to the 30-day trailing average price of our common stock as of such date. In addition, pursuant to the Vifor Agreement, we are eligible to receive payments of up to $240.0 million upon the achievement of certain sales-based milestones.

The Vifor Agreement provides full commercialization rights in dialysis clinics to Vifor in the United States under a profit-sharing arrangement. Pursuant to the profit-sharing arrangement, we will generally be entitled to 60% of the net profits (as defined in the Vifor Agreement) from sales of KORSUVA (CR845/difelikefalin) injection in the United States (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by the VFMCRP Agreement) and Vifor is entitled to 40% of such net profits, subject to potential temporary adjustment in future years based on certain conditions. Under the Vifor Agreement, in consideration of Vifor's conduct of the marketing, promotion, selling and distribution of KORSUVA (CR845/difelikefalin) injection in the United States, we will pay a marketing and distribution fee to Vifor based on the level of annual net sales. This fee will be deducted from product sales in calculating the net profits that are subject to the profit-sharing arrangement under the Vifor Agreement.

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.

Upon entry into the VFMCRP Agreement, VFMCRP made a non-refundable, non-creditable $50.0 million upfront payment to us and Vifor purchased 1,174,827 shares of our common stock for $20.0 million, at a premium for the price of $17.024 per share. We are eligible to receive from VFMCRP 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, 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 received a non-refundable and non-creditable upfront license fee of $15.0 million and are eligible to receive up to an aggregate of $10.5 million in clinical development and regulatory milestones (before contractual foreign currency exchange adjustments). In January 2021, we met the milestone criteria, as set forth in the Maruishi Agreement, for Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan. As a result, we received the $2.0 million milestone payment ($1.9 million after contractual foreign currency exchange adjustments) in May 2021. As of June 30, 2021, we have received $4.5 million (before contractual foreign currency exchange adjustments) of clinical development and regulatory milestones from Maruishi. 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 received a non-refundable and non-creditable $0.6 million upfront payment and are eligible to receive up to an aggregate of $3.8 million in development and regulatory milestones (before South Korean withholding taxes). As of June 30, 2021, 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 a license agreement with Enteris, or 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. Based on a successful End of Phase 2 Meeting with the FDA in April 2021, we paid a $10.0 million milestone to Enteris during the second quarter of 2021, which was recorded in R&D expense for the three and six months ended June 30, 2021. During the three and six months ended June 30, 2020, no milestone payments or royalties were paid to Enteris in relation to the Enteris License Agreement.

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. Substantially all of our revenue recognized to date has consisted of upfront payments under license agreements with Vifor, 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. Through June 30, 2021, we have earned a total of $8.6 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 Vifor or VFMCRP agreements 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 or milestone payments, 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 2021 will be consistent with 2020. 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, or IT, 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 2021 will be consistent with 2020 to support our continued R&D activities and for 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 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. Because our revenue in 2020 exceeded $70.0 million, we are not eligible to exchange our 2021 R&D tax credit for cash, therefore there was no benefit from income taxes for the three and six months ended June 30, 2021.

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2021 and 2020

Revenue

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	% change	2021	2020	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
License and milestone fees	$ —	$ 5,099	-100%	$ 1,192	$ 13,120	-91%
Collaborative revenue	—	—	N/A	706	—	N/A
Clinical compound revenue	—	535	-100%	37	607	-94%
Total revenue	$ —	$ 5,634	-100%	$ 1,935	$ 13,727	-86%

License and milestone fees revenue

There were no license and milestone fees revenue during the three months ended June 30, 2021. License and milestone fees revenue of $5.1 million for the three months ended June 30, 2020 was related to license fees of $4.5 million earned by us in connection with the VFMCRP Agreement, as well as $0.6 million (net of South Korean withholding taxes) earned by us for achieving a development milestone under the CKDP Agreement (see Notes 10 and

11 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements* and *Revenue Recognition*, respectively, in this Quarterly Report on Form 10-Q).

License and milestone fees revenue of $1.2 million for the six months ended June 30, 2021 was related to the milestone payment we earned in January 2021 from Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan that was allocated to the license fee performance obligation under the Maruishi Agreement. License and milestone fees revenue of $13.1 million for the six months ended June 30, 2020 was related to license fees of $12.5 million earned by us in connection with the VFMCRP Agreement, as well as $0.6 million (net of South Korean withholding taxes) earned by us for achieving a development milestone under the CKDP Agreement (see Notes 10 and 11 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements* and *Revenue Recognition*, respectively, in this Quarterly Report on Form 10-Q).

Collaborative Revenue

Collaborative revenue of $0.7 million for the six months ended June 30, 2021 was related to the milestone payment we earned in January 2021 from Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan that was allocated to the R&D services performance obligation under the Maruishi Agreement. There were no collaborative revenues for the three months ended June 30, 2021, and for the three and six months ended June 30, 2020 (see Notes 10 and 11 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements* and *Revenue Recognition*, respectively, in this Quarterly Report on Form 10-Q).

Clinical compound revenue

There was no clinical compound revenue for the three months ended June 30, 2021. Clinical compound revenue of $535,000 for the three months ended June 30, 2020 was related to the sales of clinical compound to VFMCRP for $88,000 and to Maruishi for $447,000.

Clinical compound revenue of $37,000 for the six months ended June 30, 2021 was related to the sale of clinical compound to Maruishi. Clinical compound revenue of $607,000 for the six months ended June 30, 2020 was related to the sales of clinical compound to VFMCRP for $88,000 and to Maruishi for $519,000.

Research and Development Expense

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	% change	2021	2020	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 6,718	$ 17,063	-61%	$ 16,719	$ 42,802	-61%
Consultant services in support of clinical trials	1,059	1,398	-24%	2,230	2,673	-17%
Stock-based compensation	1,902	2,803	-32%	4,060	4,426	-8%
Depreciation and amortization	31	27	14%	62	55	15%
Other R&D operating expenses	15,515	4,817	222%	21,285	9,688	120%
Total R&D expense	$ 25,225	$ 26,108	-3%	$ 44,356	$ 59,644	-26%

For the three months ended June 30, 2021 compared to the three months ended June 30, 2020, the net decrease in direct clinical trial costs and related consultant costs primarily resulted from decreases totaling $14.0 million, mainly from activities related to the KALM-2 Phase 3 efficacy trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the Phase 3 (up to 12 weeks) safety trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the KALM-1 Phase 3 efficacy trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the Phase 2 efficacy trial for pruritus associated with AD, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients, costs associated with supportive Phase 1 studies, and costs associated with preparing for our NDA submission. These decreases were partially offset by an increase of $2.6 million, mainly from the Phase 2 efficacy and safety trial for pruritus associated with NP, and start-up costs related to Oral CKD Phase 3 programs in non-hemodialysis patients. There was also an increase of $0.7 million in

clinical and commercial drug manufacturing costs The decrease in stock-based compensation expense was primarily related to the vesting of performance-based restricted stock units, for which performance conditions were achieved during the three months ended June 30, 2020, as compared to the three months ended June 30, 2021. The increase in other R&D operating expenses primarily resulted from a $10.0 million milestone earned by Enteris during the three months ended June 30, 2021, increases in payroll and related costs, and increases in travel and related costs, partially offset by a decrease in cost of compound sales.

For the six months ended June 30, 2021 compared to the six months ended June 30, 2020, the net decrease in direct clinical trial costs and related consultant costs primarily resulted from decreases totaling $33.7 million, mainly from activities related to the KALM-2 Phase 3 efficacy trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, the Phase 3 (up to 12 weeks) safety trial of KORSUVA (CR845/difelikefalin) injection in CKD patients undergoing hemodialysis, 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 for pruritus associated with AD, the Phase 2 efficacy trial of Oral CR845 in CKD-aP patients, costs associated with supportive Phase 1 studies, and costs associated with preparing for our NDA submission. These decreases were partially offset by an increase of $5.0 million, mainly from the Phase 2 efficacy and safety trial for pruritus associated with NP, start-up costs related to Oral CKD Phase 3 programs in non-hemodialysis patients, and other general costs. There was also an increase of $2.3 million in clinical and commercial drug manufacturing costs. The decrease in stock-based compensation expense was primarily related to lower stock-based compensation expense associated with the vesting of performance-based restricted stock units during the three months ended June 30, 2021, as compared to the comparable period in 2020. The increase in other R&D operating expenses primarily resulted from a $10.0 million milestone earned by Enteris during the six months ended June 30, 2021, and increases in payroll and related costs, partially offset by a decrease in cost of compound sales.

The following table summarizes our R&D expenses by programs for the three and six months ended June 30, 2021 and 2020:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	% change	2021	2020	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
I.V. CR845 - Pruritus	$ 2,381	$ 12,160	-80%	$ 5,376	$ 31,151	-83%
I.V. CR845 - Pain	—	25	-100%	12	56	-78%
Oral CR845 - Pruritus	5,384	6,225	-14%	13,454	14,195	-5%
Oral CR845 - Pain	1	6	-79%	5	15	-67%
Internal research and development expenses/milestone payments[1]	17,459	7,692	127%	25,509	14,227	79%
Total research and development expenses	$ 25,225	$ 26,108	-3%	$ 44,356	$ 59,644	-26%

[1] Includes a $10.0 million milestone payment to Enteris for each of the three and six months ended June 30, 2021.

General and Administrative Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	% change	2021	2020	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 1,358	$ 1,306	4%	$ 2,235	$ 2,437	-8%
Stock-based compensation	1,574	1,815	-13%	3,548	3,039	17%
Depreciation and amortization	31	21	50%	62	41	50%
Other G&A operating expenses	2,688	2,268	19%	6,171	4,451	39%
Total G&A expense	$ 5,651	$ 5,410	4%	$ 12,016	$ 9,968	21%

For the three months ended June 30, 2021 compared to the three months ended June 30, 2020, the increase in professional fees and public/investor relations expenses was primarily the result of an increase legal fees, partially offset by a decrease in consultants' costs. The decrease in stock-based compensation expense was primarily related to the vesting of performance-based restricted stock units, for which performance conditions were achieved during the three months ended June 30, 2020, as compared to the three months ended June 30, 2021. The increase in other G&A operating expenses was primarily the result of increases in payroll and related costs and commercial costs.

For the six months ended June 30, 2021 compared to the six months ended June 30, 2020, the decrease in professional fees and public/investor relations expenses was primarily the result of a decrease in consultants' costs, partially offset by an increase in legal fees. The increase in stock-based compensation expense was primarily related to higher stock-based compensation expense associated with the vesting of performance-based restricted stock units during the three months ended June 30, 2021, as compared to the comparable period in 2020. The increase in other G&A operating expenses was primarily the result of increases in payroll and related costs, commercial costs, insurance costs, and IT related costs.

Other Income, Net

	Three Months Ended June 30,			Six Months Ended June 30,		
	2021	2020	% change	2021	2020	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other income, net	$ 131	$ 634	-79%	$ 391	$ 1,591	-75%

For the three months ended June 30, 2021 compared to the three months ended June 30, 2020, the decrease in other income, net was primarily due to a decrease in interest income resulting from a lower yield on our higher average balance of our portfolio of investments in the 2021 period.

For the six months ended June 30, 2021 compared to the six months ended June 30, 2020, the decrease in other income, net was primarily due to a decrease in interest income and a decrease in net accretion income resulting from a lower yield on our higher average balance of our portfolio of investments in the 2021 period.

Benefit from Income Taxes

For the three months ended June 30, 2021 and 2020, pre-tax losses were $30.7 million and $25.3 million, respectively, and we recognized a benefit from income taxes of $182,000 for the three months ended June 30, 2020.

For the six months ended June 30, 2021 and 2020, pre-tax losses were $54.0 million and $54.3 million, respectively, and we recognized a benefit from income taxes of $304,000 for the six months ended June 30, 2020.

Because our revenue in 2020 exceeded $70.0 million, we are not eligible to exchange our 2021 R&D tax credit for cash, therefore there was no benefit from income taxes for the three and six months ended June 30, 2021.

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, 2021 and December 31, 2020.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception and through June 30, 2021, we have raised an aggregate of approximately $776.4 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 $203.8 million under our license agreements, primarily with Vifor, VFMCRP, Maruishi, CKDP and an earlier product candidate for which development efforts ceased in 2007; and (4) net proceeds of $53.0 million from the purchase of our common stock in relation to the license agreements with Vifor and 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, 2021, we had $207.4 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 2023, without giving effect to any potential milestone payments or potential product revenue we may receive under our licensing and collaboration agreements with Vifor, 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 Vifor Agreement, we are eligible to receive regulatory and commercial milestone payments in the aggregate of up to $290.0 million, consisting of a $50.0 million common stock investment for a regulatory milestone and up to $240.0 million upon the achievement of certain sales-based milestones. As of June 30, 2021, we have not received any milestone payments under the Vifor Agreement.

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, 2021, 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. In January 2021, we met the milestone criteria, as set forth in the Maruishi Agreement, for Maruishi’s first initiation of a Phase 3 trial for uremic pruritus in

Japan. As a result, we received the $2.0 million milestone payment ($1.9 million after contractual foreign currency exchange adjustments) in May 2021. As of June 30, 2021, we have received $4.5 million (before contractual foreign currency exchange adjustments) of clinical development and regulatory milestones from Maruishi.

Under the CKDP Agreement, we are potentially eligible to earn up to an aggregate of $2.3 million in clinical development milestones and $1.5 million in regulatory milestones, before South Korean withholding tax, as well as tiered royalties with percentages ranging from the high single digits to the high teens, based on net sales of products containing CR845/difelikefalin in South Korea, if any, and share in any sub-license fees. As of June 30, 2021, we have received $2.3 million (before South Korean withholding tax) of development and regulatory milestones from CKDP.

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 $30.7 million and $25.1 million for the three months ended June 30, 2021 and 2020, respectively, and $54.0 million for each of the six months ended June 30, 2021 and 2020, respectively. As of June 30, 2021, we had an accumulated deficit of $446.4 million. Although we generated net income for the year ended December 31, 2020 as a result of a commercial license transaction, we expect to continue to incur significant expenses and operating and net losses in the foreseeable future, as we continue to develop and seek marketing approval for I.V. and Oral CR845/difelikefalin. Our financial results 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 Vifor, 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 Vifor, 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 disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic and its variants. 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 conducting supportive Phase 1 trials, Phase 2 trials, and Phase 3 trials of Oral KORSUVA (CR845/difelikefalin) in patients with pruritus associated with CKD, CLD, AD, and NP, we expect that our existing cash and cash equivalents and available-for-sale marketable securities as of June 30, 2021 will be sufficient for us to fund our currently anticipated operating expenses and capital expenditures into 2023, without giving effect to any potential milestone payments or potential product revenue we may receive under our collaboration agreements with Vifor, 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, 2021 and 2020:

	Six Months Ended	
	June 30, 2021	June 30, 2020
	Dollar amounts in thousands	
Net cash used in operating activities	$ (44,726)	$ (65,955)
Net cash provided by investing activities	34,397	104,341
Net cash provided by financing activities	981	276
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (9,348)	$ 38,662

Net cash used in operating activities

Net cash used in operating activities for the six months ended June 30, 2021 consisted primarily of a net loss of $54.0 million, partially offset by an $8.6 million cash inflow from net non-cash charges and a $0.7 million cash inflow from net changes in operating assets and liabilities. Net non-cash charges primarily consisted of stock-based compensation expense of $7.6 million and the amortization expense component of lease expense of $0.6 million relating to our Stamford operating leases. The change in operating assets and liabilities primarily consisted of a cash inflow of $3.8 million from a decrease in prepaid expenses, primarily related to an decrease in prepaid clinical costs and a cash inflow of $0.8 million due to a decrease in income tax receivable, partially offset by a cash outflow of $3.4 million from a decrease in accounts payable and accrued expenses and a cash outflow of $0.8 million relating to operating lease liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, or the Stamford operating leases.

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 provided by investing activities

Net cash provided by investing activities was $34.4 million for the six months ended June 30, 2021, which primarily included cash inflows of $89.1 million from maturities and redemptions of available-for-sale marketable securities and

proceeds of $9.0 million from the sales of available-for-sale marketable securities, partially offset by cash outflows of $63.8 million for the purchases of available-for-sale marketable securities.

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 financing activities

Net cash provided by financing activities for the six months ended June 30, 2021 and 2020 consisted of proceeds of $981,000 and $276,000, respectively, received from the exercise of stock options.

Contractual Obligations and Commitments

Contractual obligations and commitments as of June 30, 2021 consisted of operating lease obligations in connection with the Stamford operating leases 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. Based on our manufacturing service agreement with Patheon, we have a non-cancelable purchase capacity reservation of approximately $6.5 million through 2022. We expect the majority of this capacity reservation will be reimbursed upon the execution of the supply agreement with Vifor. We have no other material non-cancelable purchase commitments with any other 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 Notes 15 and 16 of Notes to Condensed Financial Statements, *Commitments and Contingencies*, and *Subsequent Event*, respectively, in this Quarterly Report on Form 10-Q for details about our contractual obligations and commitments, and Note 6 of Notes to Condensed Financial Statements, *Restricted Cash*, in this Quarterly Report on Form 10-Q for details about our letter of credit associated with our Stamford operating leases.

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

Our management’s discussion and analysis of financial condition and results of operations is based upon our condensed financial statements, which have been prepared in accordance with GAAP. The preparation of these condensed financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the condensed balance sheets and the reported amounts of revenues and expenses during the reporting periods. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments, and assumptions. We periodically review our estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates are reflected in the condensed financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles.

During the three and six months ended June 30, 2021, 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, 2020.

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

Interest Rate Risk

As of June 30, 2021, 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, 2021, we had invested $185.1 million of our cash reserves in such marketable securities. Those marketable securities included $185.1 million of investment grade debt instruments with a yield of approximately 0.25% and maturities through May 2024. As of December 31, 2020, we had invested $219.8 million of our cash reserves in such marketable securities. Those marketable securities included $219.8 million of investment grade debt instruments with a yield of approximately 0.32% and maturities through December 2023.

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, we do not believe we are materially exposed to changes in interest rates related to our investments. As a result, we do not currently use interest rate derivative instruments to manage exposure to interest rate changes.

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 100 basis point, or 1%, increase in interest rates as of June 30, 2021 and December 31, 2020, would have resulted in immaterial decreases in the fair values of our portfolio of marketable securities at those dates.

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. For the three and six months ended June 30, 2021 and 2020, we did not record any charges to credit loss expense for our available-for-sale securities. (Refer to Note 3 of Notes to Condensed Financial Statements, *Available-for-Sale Marketable Securities*, in this Quarterly Report on Form 10-Q.

As of June 30, 2021 and December 31, 2020, we did not have material balances of receivables on our Condensed Balance Sheets.

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

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of June 30, 2021. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2021, 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

There were no changes in our internal control over financial reporting that occurred during the quarter ended June 30, 2021 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Controls and Procedures

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

PART II

OTHER INFORMATION

Item 1. ***Legal Proceedings***

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

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

There have been no material changes in risk factors discussed in Part I. Item 1A. *Risk Factors* in our Annual Report on Form 10-K for the year ended December 31, 2020.

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
31.1†	Certification of Chief Executive Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
31.2†	Certification of Chief Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
32.1†*	Certifications of Chief Executive Officer and Chief Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.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).				

† Filed herewith.

* This certification is furnished and will not be deemed 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, irrespective of any general incorporation language contained in such filing.

SIGNATURES

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

CARA THERAPEUTICS, INC.

Date: August 9, 2021

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

Date: August 9, 2021

By /s/ THOMAS REILLY
Thomas Reilly
Chief Financial Officer
(Principal Financial and Accounting Officer)

EXHIBIT 31.1

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

I, Derek Chalmers, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 9, 2021

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

EXHIBIT 31.2

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

I, Thomas Reilly, 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 9, 2021

By: /s/ Thomas Reilly
THOMAS REILLY
CHIEF FINANCIAL OFFICER

EXHIBIT 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended June 30, 2021, 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 Thomas Reilly, as Chief Financial Officer of the Company, each hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his 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 9, 2021

/s/ THOMAS REILLY
Name: Thomas Reilly
Title: Chief Financial Officer
Date: August 9, 2021