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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 MARCH 31, 2022

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 May 5, 2022 was: 53,591,225.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED MARCH 31, 2022

PART I –FINANCIAL INFORMATION

PART I
FINANCIAL INFORMATION

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

CARA THERAPEUTICS, INC.

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

	March 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 21,362	$ 13,453
Marketable securities	119,749	153,582
Accounts receivable - related party	2,496	—
Inventory, net	1,907	2,584
Income tax receivable	697	697
Other receivables	438	455
Prepaid expenses	5,113	2,519
Total current assets	151,762	173,290
Operating lease right-of-use assets	2,629	2,973
Marketable securities, non-current	68,456	69,754
Property and equipment, net	611	631
Restricted cash	408	408
Total assets	$ 223,866	$ 247,056
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 16,501	$ 15,861
Operating lease liabilities, current	1,795	1,755
Total current liabilities	18,296	17,616
Operating lease liabilities, non-current	1,455	1,918
Commitments and contingencies (Note 16)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at March 31, 2022 and December 31, 2021, zero shares issued and outstanding at March 31, 2022 and December 31, 2021	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at March 31, 2022 and December 31, 2021, 53,591,225 shares and 53,480,812 shares issued and outstanding at March 31, 2022 and December 31, 2021, respectively	53	53
Additional paid-in capital	714,292	708,585
Accumulated deficit	(508,507)	(480,758)
Accumulated other comprehensive loss	(1,723)	(358)
Total stockholders' equity	204,115	227,522
Total liabilities and stockholders' equity	$ 223,866	$ 247,056

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Three Months Ended	
	March 31, 2022	March 31, 2021
Revenue:		
Commercial supply revenue	$ 4,790	$ —
License and milestone fees	—	1,192
Collaborative revenue	—	706
Clinical compound revenue	—	37
Total revenue	4,790	1,935
Operating expenses:		
Cost of goods sold	2,081	—
Research and development	21,273	19,131
General and administrative	9,347	6,365
Total operating expenses	32,701	25,496
Operating loss	(27,911)	(23,561)
Other income, net	162	260
Net loss	$ (27,749)	$ (23,301)
Net loss per share:		
Basic and Diluted	$ (0.52)	$ (0.47)
Weighted average shares:		
Basic and Diluted	53,507,060	49,917,990
Other comprehensive loss, net of tax of $0:		
Change in unrealized losses on available-for-sale marketable securities	(1,365)	(61)
Total comprehensive loss	$ (29,114)	$ (23,362)

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	(Loss) Income	Equity
Balance at December 31, 2021	53,480,812	$ 53	$ 708,585	$ (480,758)	$ (358)	$ 227,522
Stock-based compensation expense	—	—	4,266	—	—	4,266
Shares issued upon exercise of stock options	470	—	3	—	—	3
Shares issued upon vesting of restricted stock units	109,943	—	1,438	—	—	1,438
Net loss	—	—	—	(27,749)	—	(27,749)
Other comprehensive loss	—	—	—	—	(1,365)	(1,365)
Balance at March 31, 2022	53,591,225	$ 53	$ 714,292	$ (508,507)	$ (1,723)	$ 204,115

	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

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Three Months Ended	
	March 31, 2022	**March 31, 2021**
Operating activities		
Net loss	$ (27,749)	$ (23,301)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	5,704	4,132
Depreciation and amortization	63	63
Amortization expense component of lease expense	344	316
Amortization of available-for-sale marketable securities, net	292	194
Realized gain on sale of available-for-sale marketable securities	—	(39)
Realized gain on sale of property and equipment	—	(70)
Changes in operating assets and liabilities:		
Accounts receivable - related party	(2,496)	—
Inventory, net	677	—
Other receivables	17	(1,687)
Prepaid expenses	(2,594)	(942)
Accounts payable and accrued expenses	640	(2,001)
Operating lease liabilities	(423)	(386)
Net cash used in operating activities	(25,525)	(23,721)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	44,000	27,655
Proceeds from redemptions of available-for-sale marketable securities, at par	—	2,100
Proceeds from sale of available-for-sale marketable securities	—	8,029
Purchases of available-for-sale marketable securities	(10,526)	(23,985)
Purchases of property and equipment	(43)	—
Proceeds from sale of property and equipment	—	70
Net cash provided by investing activities	33,431	13,869
Financing activities		
Proceeds from the exercise of stock options	3	688
Net cash provided by financing activities	3	688
Net increase (decrease) in cash, cash equivalents and restricted cash	7,909	(9,164)
Cash, cash equivalents and restricted cash at beginning of period	13,861	32,091
Cash, cash equivalents and restricted cash at end of period	$ 21,770	$ 22,927

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 an early commercial-stage biopharmaceutical corporation formed on July 2, 2004. The Company is leading a new treatment paradigm to improve the lives of patients suffering from pruritus. The Company's primary activities to date have been organizing and staffing the Company, developing its lead product and product candidates, including conducting preclinical and clinical trials of difelikefalin-based product candidates, and raising capital.

On August 23, 2021, the Company received U.S. Food and Drug Administration, or FDA, approval for KORSUVA™ (difelikefalin) injection, or KORSUVA injection, for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis. The Company has a license agreement with Vifor (International) Ltd., or Vifor, that provides full commercialization rights of KORSUVA injection to Vifor in dialysis clinics in the United States under a profit-sharing arrangement, whereby total net sales of KORSUVA injection in the U.S., as recorded by Vifor, are reduced by a marketing and distribution fee owed by the Company based on the level of annual net sales, and the resulting amount is shared according to a 60% (Company)/40% (Vifor) profit split (see Note 11, *Collaboration and Licensing Agreements)*. The Company expects commercial launch of KORSUVA injection in the U.S. in April 2022 and associated revenues in the second quarter of 2022.

As of March 31, 2022, 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 $229,710 under its license and supply agreements for difelikefalin, primarily with 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. In October 2021, the Company received net proceeds of $44,969 from the issuance and sale of 3,282,391 shares of the Company's common stock to Vifor in connection with U.S. regulatory approval for KORSUVA injection in August 2021. 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 11, *Collaboration and Licensing Agreements*).

As of March 31, 2022, the Company had unrestricted cash and cash equivalents and marketable securities of $209,567 and an accumulated deficit of $508,507. 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 $27,749 and $23,301 for the three months ended March 31, 2022 and 2021, respectively, and had net cash used in operating activities of $25,525 and $23,721 for the three months ended March 31, 2022 and 2021, 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 FDA and other government regulations. If the Company does not successfully commercialize KORSUVA injection or any of its other product candidates, it will be unable to generate additional recurring product revenue or achieve profitability.

CARA THERAPEUTICS, INC.

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

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, 2021 were derived from audited financial statements, but do not include all disclosures required by GAAP. These unaudited interim condensed financial statements should be read in conjunction with the audited financial statements and accompanying notes thereto included in the Company's Annual Report on Form 10-K for the year ended December 31, 2021.

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 amount and periods over which certain revenues will be recognized, including licensing and collaborative revenue recognized from non-refundable up-front and milestone payments, accounts receivable, inventory valuation and related reserves, 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, the incremental borrowing rate used in lease calculations and the likelihood of realization of deferred tax assets.

The ongoing COVID-19 pandemic and geopolitical tensions, such as Russia's recent incursion into Ukraine, have 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, 2021, except as disclosed below.

CARA THERAPEUTICS, INC.

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

Accounts Receivable – Related Party

Accounts receivable – related party consists of amounts due from sales of KORSUVA injection under the Company's licensing agreement with Vifor. The Company does not obtain collateral for its accounts receivable.

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for credit losses when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company believes that credit risk associated with its licensing partner Vifor is not significant. The Company reviews the need for an allowance for credit losses for any receivable based on various factors including payment history and historical bad debt experience. The Company had no allowance for credit losses as of March 31, 2022.

3. Available-for-Sale Marketable Securities

As of March 31, 2022 and December 31, 2021, the Company's available-for-sale marketable securities consisted of debt securities issued by the U.S. Treasury, U.S. government-sponsored entities and investment grade institutions as well as municipal bonds.

The following tables summarize the Company's available-for-sale marketable securities by major type of security as of March 31, 2022 and December 31, 2021:

As of March 31, 2022

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 15,577	$ —	$ (27)	$ 15,550
U.S. government agency obligations	12,000	—	(370)	11,630
Corporate bonds	66,765	—	(740)	66,025
Commercial paper	72,952	—	(163)	72,789
Municipal bonds	22,634	—	(423)	22,211
Total available-for-sale marketable securities	$ 189,928	$ —	$ (1,723)	$ 188,205

As of December 31, 2021

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 11,573	$ —	$ (3)	$ 11,570
U.S. government agency obligations	17,020	—	(45)	16,975
Corporate bonds	66,495	—	(171)	66,324
Commercial paper	106,914	5	(31)	106,888
Municipal bonds	21,692	—	(113)	21,579
Total available-for-sale marketable securities	$ 223,694	$ 5	$ (363)	$ 223,336

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 March 31, 2022 and December 31, 2021:

CARA THERAPEUTICS, INC.

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

As of March 31, 2022

	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	$ 15,550	$ (27)	$ —	$ —	$ 15,550	$ (27)
U.S. government agency obligations	9,687	(313)	1,943	(57)	11,630	(370)
Corporate bonds	61,610	(644)	4,415	(96)	66,025	(740)
Commercial paper	72,789	(163)	—	—	72,789	(163)
Municipal bonds	21,213	(396)	998	(27)	22,211	(423)
Total	$ 180,849	$ (1,543)	$ 7,356	$ (180)	$ 188,205	$ (1,723)

As of December 31, 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. Treasury securities	$ 11,570	$ (3)	$ —	$ —	$ 11,570	$ (3)
U.S. government agency obligations	9,456	(45)	—	—	9,456	(45)
Corporate bonds	62,704	(170)	2,020	(1)	64,724	(171)
Commercial paper	52,163	(31)	—	—	52,163	(31)
Municipal bonds	20,562	(105)	1,017	(8)	21,579	(113)
Total	$ 156,455	$ (354)	$ 3,037	$ (9)	$ 159,492	$ (363)

As of March 31, 2022 and December 31, 2021, 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 March 31, 2022 and December 31, 2021, the Company held a total of 73 out of 73 positions and 58 out of 76 positions, respectively, that were in an unrealized loss position, four of which had been in an unrealized loss position for 12 months or greater as of March 31, 2022. 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. Treasury and U.S. government agency obligations. The unrealized losses on the Company's investments in direct obligations of U.S. Treasury and government agencies 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 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 6 out of 6 positions for its U.S. Treasury securities, and 4 out of 4 positions for its U.S. government agency obligations, that were in unrealized loss positions as of March 31, 2022.

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

CARA THERAPEUTICS, INC.

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

factors. The credit ratings of these investments in the Company's portfolio have not been downgraded below investment 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 25 out of 25 positions for its corporate bonds, 23 out of 23 positions for its commercial paper, and 15 out of 15 positions for its municipal bonds, that were in unrealized loss positions as of March 31, 2022.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of March 31, 2022, the Company's marketable debt securities mature at various dates through November 2024. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows.

	As of March 31, 2022		As of December 31, 2021	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 120,070	$ 119,749	$ 153,631	$ 153,582
One year to three years	69,858	68,456	70,063	69,754
Total	$ 189,928	$ 188,205	$ 223,694	$ 223,336

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.

There were no sales of available-for-sale marketable securities during the three months ended March 31, 2022. During the three months ended March 31, 2021, the Company sold certain shares of its available-for-sale debt securities with a total fair value of $8,029, which resulted in realized gains of $39 for the three months ended March 31, 2021.

As of March 31, 2022 and December 31, 2021, accrued interest receivables on our available-for-sale debt securities were $438 and $455, respectively.

CARA THERAPEUTICS, INC.

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

4. Accumulated Other Comprehensive (Loss) Income

The following table summarizes the changes in accumulated other comprehensive (loss) income, net of tax, from unrealized gains (losses) on available-for-sale marketable securities, the Company's only component of accumulated other comprehensive (loss) income, for the three months ended March 31, 2022 and 2021, respectively.

	Total Accumulated Other Comprehensive (Loss) Income
Balance, December 31, 2021	$ (358)
Other comprehensive loss before reclassifications	(1,365)
Amount reclassified from accumulated other comprehensive loss	—
Net current period other comprehensive loss	(1,365)
Balance, March 31, 2022	$ (1,723)
Balance, December 31, 2020	$ 73
Other comprehensive loss before reclassifications	(22)
Amount reclassified from accumulated other comprehensive income	(39)
Net current period other comprehensive loss	(61)
Balance, March 31, 2021	$ 12

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

Component of Accumulated Other Comprehensive (Loss) Income	Three Months Ended March 31, 2022	Three Months Ended March 31, 2021	Affected Line Item in the Condensed Statements of Comprehensive Loss
Unrealized gains (losses) on available-for-sale marketable securities:			
Realized gains on sales of securities	$ —	$ 39	Other income, net
Income tax effect	—	—	Benefit from income taxes
Realized gains on sales of securities, net of tax	$ —	$ 39	

5. Fair Value Measurements

As of March 31, 2022 and December 31, 2021, the Company's financial instruments consisted of cash, cash equivalents, available-for-sale marketable securities, accounts receivable – related party, prepaid expenses, restricted cash, accounts payable and accrued liabilities. The fair values of cash, cash equivalents, accounts receivable – related party, 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.

The Company validates the prices provided by its third-party pricing services by reviewing their pricing methods, obtaining market values from other pricing sources, and comparing them to the share prices presented by the third-party pricing services. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by its third-party pricing services as of March 31, 2022 or December 31, 2021.

CARA THERAPEUTICS, INC.

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

The following tables summarize the Company's financial assets measured at fair value on a recurring basis as of March 31, 2022 and December 31, 2021.

Fair value measurement as of March 31, 2022:

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	$ 21,362	$ 21,362	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	15,550	—	15,550	—
U.S. government agency obligations	11,630	—	11,630	—
Corporate bonds	66,025	—	66,025	—
Commercial paper	72,789	—	72,789	—
Municipal bonds	22,211	—	22,211	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 209,975	$ 21,770	$ 188,205	$ —

Fair value measurement as of December 31, 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	$ 13,453	$ 13,453	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	11,570	—	11,570	—
U.S. government agency obligations	16,975	—	16,975	—
Corporate bonds	66,324	—	66,324	—
Commercial paper	106,888	—	106,888	—
Municipal bonds	21,579	—	21,579	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 237,197	$ 13,861	$ 223,336	$ —

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 months ended March 31, 2022 and 2021, respectively. There were no transfers of financial assets into or out of Level 3 classification during the three months ended March 31, 2022 and 2021, 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 16, *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 March 31, 2022, the restricted cash balance for the Stamford Lease was invested in a commercial money market account.

As of March 31, 2022 and December 31, 2021, 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.

	March 31, 2022	December 31, 2021
Cash and cash equivalents	$ 21,362	$ 13,453
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 21,770	$ 13,861

7. Inventory, net

Inventories consist of the following:

	March 31, 2022	December 31, 2021
Raw materials	$ 1,095	$ 927
Work-in-process	812	1,657
Total	$ 1,907	$ 2,584

As of March 31, 2022 and December 31, 2021, inventory balances include inventory costs subsequent to regulatory approval of KORSUVA injection on August 23, 2021. There were no write-downs of commercial supply inventory during the three months ended March 31, 2022.

8. Prepaid expenses

As of March 31, 2022, prepaid expenses were $5,113, consisting of $2,167 of prepaid R&D clinical costs, $2,134 of prepaid insurance and $812 of other prepaid costs. As of December 31, 2021, prepaid expenses were $2,519, consisting of $1,481 of prepaid R&D clinical costs, $369 of prepaid insurance, and $669 of other prepaid costs.

9. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	March 31, 2022	December 31, 2021
Accounts payable	$ 5,594	$ 5,625
Accrued research projects	6,444	4,648
Accrued compensation and benefits	2,412	4,959
Accrued professional fees and other	2,051	629
Total	$ 16,501	$ 15,861

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10. Stockholders' Equity

In March 2022, as a result of the achievement of certain performance targets, an aggregate of 37,999 performance-based restricted stock units of certain employees vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation*).

In March 2022, as a result of the completion of the first year of the three-year vesting period for restricted stock units granted in March 2021 and the full vesting of the Chief Executive Officer's, or CEO's, second tranche of restricted stock units granted in October 2021, an aggregate of 39,278 time-based restricted stock units vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation*).

In March 2022, the Company filed a universal shelf registration statement, or the Shelf Registration Statement, which provides for aggregate offerings of up to $300,000 of common stock, preferred stock, debt securities, warrants or any combination thereof. The Shelf Registration Statement has not yet been declared effective by the Securities and Exchange Commission. The securities registered under the Shelf Registration Statement include $154,525 of unsold securities that had been registered under the Company's previous Registration Statement on Form S-3 (File No. 333-230333) that was declared effective on April 4, 2019.

The Company may offer additional securities under its Shelf Registration Statement, when declared effective, from time to time in response to market conditions or other circumstances if it believes such a plan of financing is in the best interests of its stockholders. Also in March 2022, the Company entered into an open market sales agreement, or the Sales Agreement, with Jefferies LLC, as sales agent, pursuant to which it may, subject to the effectiveness of the Shelf Registration Statement, from time to time, issue and sell common stock with an aggregate value of up to $80,000 in an at-the-market offering. Jefferies is acting as sole sales agent for any sales made under the Sales Agreement for a 3% commission on gross proceeds. The common stock will be sold at prevailing market prices at the time of the sale, and, as a result, prices may vary. Unless otherwise terminated earlier, the Sales Agreement continues until all shares available under the Sales Agreement have been sold.

In February 2022, as a result of the completion of the second year of the three-year vesting period for restricted stock units granted in February 2020, an aggregate of 32,666 time-based restricted stock units vested and were settled in shares of the Company's common stock (see Note 14, *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 vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation*).

In February 2021, as a result of the completion of the first year of the three-year vesting period for restricted stock units granted in February 2020, an aggregate of 32,669 time-based restricted stock units vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation*).

11. Collaboration and Licensing Agreements

Vifor (International) Ltd. (Vifor)

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 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

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Vifor Agreement, the Company retains all rights with respect to the clinical development of, and activities to gain regulatory approvals of, 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 is generally entitled to 60% of the net profits (as defined in the Vifor Agreement) from sales of 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 difelikefalin injection in the United States, the Company pays a marketing and distribution fee to Vifor based on the level of annual net sales. This fee is 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, or the Vifor Stock Purchase Agreement.

After U.S. regulatory approval of KORSUVA injection in August 2021, the Company received an additional $50,000 in October 2021 for the purchase of an aggregate of 3,282,391 shares of the Company's common stock at a price of $15.23 per share, which represents a 20% premium to the 30-day trailing average price of the Company's common stock as of the date of the achievement of the milestone. The purchase of the Company's common stock was governed by the Vifor Stock Purchase Agreement.

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 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, which was executed in September 2021. The supply price is the Company's cost of goods sold, or COGS, as calculated under GAAP, plus an agreed upon margin. The Vifor Supply Agreement will co-terminate with the Vifor Agreement.

The Vifor 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 Vifor Supply Agreement is the Company's COGS plus an agreed upon margin, which is commensurate with the "COGS 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 commercial supply 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.

Vifor Fresenius Medical Care Renal Pharma Ltd. (VFMCRP)

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

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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 Company is eligible to receive from VFMCRP additional regulatory and commercial milestone payments in the aggregate of up to $455,000, consisting of up to $15,000 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 difelikefalin injection in the licensed territories. The Company retained full commercialization rights for difelikefalin injection for the treatment of chronic kidney disease associated pruritus, or 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 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. Subsequently, the remaining commercialization rights in the U.S. were granted to Vifor as part of the Vifor Agreement in 2020, as discussed above.

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 COGS, 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 COGS plus an agreed upon margin, which is commensurate with the "COGS 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 compound to VFMCRP is not a performance obligation under the VFMCRP Agreement but rather the VFMCRP Supply Agreement is a separate agreement from the VFMCRP Agreement. The only performance obligation under the VFMCRP Supply Agreement is the delivery of the Licensed Product to VFMCRP for commercialization.

Maruishi Pharmaceutical Co., Ltd. (Maruishi)

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 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 difelikefalin in the United States and Japan, respectively. In addition, the Company provided Maruishi specific clinical development services for difelikefalin used in Maruishi's field of use.

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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.

Chong Kun Dang Pharmaceutical Corporation (CKDP)

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 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 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 difelikefalin in South Korea, if any, and share in any sub-license fees.

12. Revenue Recognition

The Company currently recognizes revenue for the Vifor, VFMCRP, Maruishi and CKDP agreements (see Note 11, *Collaboration and Licensing Agreements*). Under each of these agreements, the Company has recognized revenue from (1) commercial supply sales to Vifor under the Vifor Supply Agreement; (2) upfront payments; (3) regulatory milestone payments under the Vifor and VFMCRP agreements; and (4) clinical development milestone payments under the Maruishi and CKDP agreements. 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 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 March 31, 2022, the Company recorded accounts receivable – related party of $2,496 which related to sales of KORSUVA injection to Vifor during the three months ended March 2022. There were no material balances of receivables as of December 31, 2021, and no other contract assets or contract liabilities related to the Vifor, VFMCRP, Maruishi and CKDP agreements as of March 31, 2022 and December 31, 2021.

The Company routinely assesses the creditworthiness of its license and collaboration partners. The Company has not experienced any losses related to receivables from its license and collaboration partners as of March 31, 2022 and December 31, 2021.

Performance obligations

Under the Vifor Agreement, the Company’s only performance obligation is granting a license to allow Vifor to commercialize difelikefalin in the United States, which occurred at inception of the contract in October 2020 (see Note 11, *Collaboration and Licensing Agreements*).

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Under the Vifor Supply Agreement, the Company's only performance obligation is the delivery of KORSUVA injection to Vifor in accordance with the receipt of purchase orders. Revenue from the sale of the Licensed Product to Vifor is recognized as delivery of the Licensed Product occurs. The Company had commercial supply revenue of $4,790 for the three months ended March 31, 2022, of which $2,295 was recognized in January 2022 with no associated COGS since these inventory costs were incurred prior to regulatory approval on August 23, 2021, and $2,495 was recognized in March 2022 with associated COGS of $2,081 since these inventory costs were capitalized as inventory subsequent to regulatory approval.

Under the VFMCRP Agreement, the Company's performance obligations of granting a license to allow VFMCRP to commercialize 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 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 11, *Collaboration and Licensing Agreements*).

The Company's only performance obligation under the VFMCRP Supply Agreement is to deliver difelikefalin injection to VFMCRP in accordance with the receipt of purchase orders. Revenue from the sale of the Licensed Product to VFMCRP is recognized as delivery of the Licensed Product occurs. There were no sales of clinical or commercial compound to VFMCRP during the three months ended March 31, 2022 and 2021.

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 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 difelikefalin and to conduct Phase 1 and proof-of-concept Phase 2 clinical trials of an intravenous formulation of 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 11, *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. There were no sales of clinical compound to Maruishi during the three months ended March 31, 2022. The Company had clinical compound revenue of $37 during the three months ended March 31, 2021, for the sale of clinical compound to Maruishi.

Under the CKDP Agreement, the Company's only performance obligation is to transfer the license to the Company's IP related to difelikefalin, which occurred at inception of the contract in 2012 (see Note 11, *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.

Variable Consideration

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

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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).

There were no license and milestone fees revenue or collaborative revenue recognized under the Maruishi Agreement during the three months ended March 31, 2022. During the three months ended March 31, 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.

There were no revenues recognized under the CKDP Agreement during the three months ended March 31, 2022 and 2021.

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.

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13. Net Loss Per Share

The Company computes basic net loss per share by dividing net loss by the weighted-average number of shares of common stock outstanding. Diluted net income per share includes the potential dilutive effect of common stock equivalents as if such securities were exercised during the period, when the effect is dilutive. Common stock equivalents may include outstanding stock options or restricted stock units, which are included using the treasury stock method when dilutive. For the three months ended March 31, 2022 and 2021, the Company excluded the effects of potentially dilutive shares that were outstanding during those respective periods from the denominator as their inclusion would be anti-dilutive due to the Company's net losses during those periods.

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

	Three Months Ended March 31,	
	2022	2021
Basic:		
Weighted average common shares outstanding	53,507,060	49,917,990
Diluted:		
Weighted average common shares outstanding - Basic	53,507,060	49,917,990
Common stock equivalents*	—	—
Denominator for diluted net loss per share	53,507,060	49,917,990

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

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

	Three Months Ended March 31,	
	2022	2021
Net loss - basic and diluted	$ (27,749)	$ (23,301)
Weighted-average common shares outstanding:		
Basic and diluted	53,507,060	49,917,990
Net loss per share, Basic and Diluted:	$ (0.52)	$ (0.47)

As of March 31, 2022, 7,430,629 stock options and 736,272 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.

As of March 31, 2021, 5,918,808 stock options and 401,831 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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14. 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 generally 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, 2022, the aggregate number of shares of common stock that may be issued pursuant to Stock Awards under the 2014 Plan automatically increased from 8,984,679 to 10,589,103. 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

On February 25, 2022, the Compensation Committee of the Company's Board of Directors, or the Compensation Committee, approved and granted a total of 243,000 restricted stock units to certain employees under the 2014 Plan with a grant date fair value of $10.46 per share. Vesting of the restricted stock units is contingent on the achievement of certain performance targets related to commercial milestones, subject to the recipient's continuous service through each

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performance target. Recognition of compensation expense associated with these awards begins when, and to the extent, the performance criteria are probable of achievement and the employee has met the service conditions. For the three months ended March 31, 2022, no stock compensation expense relating to these restricted stock units was recognized. As of March 31, 2022, none of the restricted stock units were vested or settled in shares of the Company's common stock.

Additionally on February 25, 2022, the Compensation Committee also approved and granted a total of 145,170 time-based restricted stock units to certain employees under the 2014 Plan with a grant date fair value of $10.46 per share. The restricted stock units vest in three equal installments annually from the date of the grant. As a result, the Company recognizes compensation expense associated with these restricted stock units ratably over the three-year vesting period following the grant date. For the three months ended March 31, 2022, the Company recognized $50 of stock compensation expense associated with these awards, with $18 recorded in R&D expense and $32 in general and administrative, or G&A, expense. As of March 31, 2022, none of the restricted stock units were vested or settled in shares of the Company's common stock.

On December 17, 2021, the Compensation Committee approved and granted a total of 63,573 time-based restricted stock units to certain employees under the 2014 Plan with a grant date fair value of $12.45 per share. The restricted stock units vest in two equal installments on December 15, 2022 and June 15, 2023. As a result, the Company recognizes compensation expense associated with these restricted stock units ratably over the 18-month vesting period following the grant date. For the three months ended March 31, 2022, the Company recognized $131 of stock compensation expense associated with these awards, with $52 recorded in R&D expense and $79 in G&A expense. As of March 31, 2022, none of the restricted stock units were vested or settled in shares of the Company's common stock.

On October 29, 2021, the Compensation Committee also approved and granted 147,942 time-based restricted stock units in connection with the appointment of the Company's new CEO under the 2014 Plan with a grant date fair value of $16.83 per share. The first tranche of 142,000 restricted stock units vests 25% on the first anniversary of the date of grant and the balance quarterly over the next 36 months. The second tranche of 5,942 restricted stock units fully vested on March 31, 2022. As a result, the Company recognizes compensation expense associated with these two restricted stock unit tranches ratably over their respective vesting periods following the grant date. For the three months ended March 31, 2022, stock compensation expense associated with these awards of $206 was recognized in G&A expense. As of March 31, 2022, 5,942 of the 147,942 restricted stock units were vested and settled in shares of the Company's common stock.

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 2022 Annual Meeting of Stockholders, 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 the three months ended March 31, 2022, stock compensation expense associated with these awards of $139 was recognized in G&A expense. As of March 31, 2022, none of the restricted stock units were vested or settled in shares of the Company's common stock.

On March 30, 2021, the Compensation Committee approved and granted a total of 176,000 restricted stock units to certain employees under the 2014 Plan with a grant date fair value of $20.59 per share. Vesting of the restricted stock units was 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

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employee has met the service conditions. In February 2022, performance targets relating to 37,999 restricted stock units had been achieved and thus restricted stock units vested and the awards were settled in shares of common stock. For the three months ended March 31, 2022, the Company recognized $729 of stock compensation expense associated with these awards in G&A expense. G&A amounts recorded for the three months ended March 31, 2022 included $303 of stock compensation expense relating to the modification of certain of these restricted stock units on November 1, 2021 (see *Stock Award Modifications* below). As of March 31, 2022, 82,001 of the 176,000 restricted stock units vested and were settled in shares of the Company's common stock, while the remaining 93,999 restricted stock units were forfeited as a result of not achieving certain defined performance targets of the awards.

Additionally on March 30, 2021, the Compensation Committee also approved and granted a total of 100,000 time-based restricted stock units to certain employees 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. In March 2022, 33,336 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 March 31, 2022, the Company recognized $284 of stock compensation expense associated with these awards, with $54 recorded in R&D expense and $230 in G&A expense. For the three months ended March 31, 2021, the Company recognized an immaterial amount of stock compensation expense for the one day of outstanding time-based restricted stock units. G&A amounts recorded for the three months ended March 31, 2022 included $203 of stock compensation expense relating to the modification of certain of these restricted stock units on November 1, 2021 (see *Stock Award Modifications* below). As of March 31, 2022, 33,336 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 months ended March 31, 2021, stock compensation expense of $139 was recognized in G&A expense. All of the restricted stock units were vested and settled in shares of the Company's common stock as of June 2021.

In February 2020, the Compensation Committee approved and granted a total of 138,000 restricted stock units to certain employees under the 2014 Plan with a grant date fair value of $16.36 per share. Vesting of the restricted stock units was 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, were achieved and thus restricted stock units vested and the awards were settled in shares of common stock. For the three months ended March 31, 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. As of March 31, 2022, 113,500 of the 138,000 restricted stock units vested and were settled in shares of the Company's common stock, while the remaining 24,500 restricted stock units were forfeited as a result of not achieving certain defined performance targets of the awards.

Additionally in February 2020, the Compensation Committee also approved and granted a total of 98,000 time-based restricted stock units to certain employees 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

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following the grant date. In February 2022, 32,666 of these restricted stock units vested and were settled in shares of the Company's common stock in satisfaction of the second year of vesting. 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 March 31, 2022, the Company recognized $219 of stock compensation expense associated with these awards, with $43 recorded in R&D expense and $176 in G&A expense. G&A amounts recorded for the three months ended March 31, 2022 included $155 of stock compensation expense relating to the modification of certain of these restricted stock units on November 1, 2021 (see *Stock Award Modifications* below). For the three months ended March 31, 2021, the Company recognized $132 of stock compensation expense associated with these awards, with $43 recorded in R&D expense and $89 in G&A expense. As of March 31, 2022, 65,335 of the 98,000 restricted stock units vested and were settled in shares of the Company's common stock.

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 three months ended March 31, 2022 is presented below:

	Number of Units	Weighted Average Grant Date Fair Value
Outstanding, December 31, 2021	576,544	$ 17.50
Awarded	388,170	10.46
Vested and released	(109,943)	19.13
Forfeited	(118,499)	19.72
Outstanding, March 31, 2022	736,272	$ 13.19
Restricted stock units exercisable (vested and deferred), March 31, 2022	—	

Stock Options

Under the 2014 Plan, the Company granted 977,438 and 673,200 stock options during the three months ended March 31, 2022 and 2021, respectively. No stock options were granted under the 2019 Inducement Plan during the three months ended March 31, 2022 and 2021. The fair values of stock options granted during the three months ended March 31, 2022 and 2021 were estimated as of the dates of grant using the Black-Scholes option pricing model with the following assumptions:

	Three Months Ended March 31,	
	2022	2021
Risk-free interest rate	1.70% - 2.35%	0.66% - 1.21%
Expected volatility	81.4% - 81.9%	71.6% - 71.8%
Expected dividend yield	0%	0%
Expected life of employee and Board options (in years)	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 March 31, 2022 and 2021 was $7.55 and $12.49, respectively. No options were granted to non-employee members of the Company's Board of Directors for their Board service or to non-employee consultants during the three months ended March 31, 2022 and 2021.

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During the three months ended March 31, 2022 and 2021, the Company recognized compensation expense relating to stock options as follows:

	Three Months Ended March 31,	
	2022	2021
Research and development	$ 1,917	$ 1,590
General and administrative	2,030	1,014
Total stock option expense	$ 3,947	$ 2,604

The following were excluded from the table above as they are not related to stock options: compensation expense for (i) the vesting of certain employees' restricted stock units for $167 in R&D expense and $1,452 in G&A expense for the three months ended March 31, 2022; (ii) the vesting of certain employees' restricted stock units for $568 in R&D expense and $822 in G&A expense for the three months ended March 31, 2021; and (iii) compensation expense relating to the Board of Directors' restricted stock units for $139 in G&A expense for each of the three months ended March 31, 2022 and 2021.

A summary of stock option award activity related to employees, non-employee members of the Company's Board of Directors and non-employee consultants as of and for the three months ended March 31, 2022 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2021	6,512,280	$ 15.58
Granted	977,438	10.63
Exercised	(470)	6.50
Forfeited	(37,241)	15.22
Expired	(21,378)	25.16
Outstanding, March 31, 2022	7,430,629	$ 14.91
Options exercisable, March 31, 2022	4,357,399	

The Company does not expect to realize any tax benefits from its stock option activity or the recognition of stock-based compensation expense because the Company currently has net operating losses and has a full valuation allowance against its deferred tax assets. Accordingly, no amounts related to excess tax benefits have been reported in cash flows from operations for the three months ended March 31, 2022 and 2021.

Stock Award Modifications

In November 2021, the Company and the former President and CEO mutually agreed to a transition from CEO to a consulting role through June 30, 2022, if not terminated earlier per the terms of the consulting agreement. As a result, the Company modified the terms of its former CEO's outstanding Stock Awards to (1) automatically vest any unvested stock options or time-based restricted stock units that would have vested in the twelve month period following the end of the consulting period if continuous service is achieved with the Company during such twelve-month period; (2) extend the period during which the vested stock options may be exercised through the earlier of (i) eighteen months following the separation date (November 8, 2021); or (ii) the original expiration date applicable to each of the stock options, unless terminated earlier in accordance with the 2014 Plan, if continuous service is achieved with the Company; and (3) extend the period in which performance-based vesting milestones for restricted stock units may be achieved through March 31, 2022, if continuous service is achieved with the Company.

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The Company determined that vested Stock Awards which had modifications due to the extension of the exercise period were Type 1 modifications pursuant to Financial Accounting Standards Board Accounting Standards Codification 718, or ASC 718, because those Stock Awards would have vested before and after the modification. Acceleration of vesting for the Stock Awards that would have vested in the twelve-month period following the consulting term was determined to be a Type 3 modification requiring stock compensation expense pursuant to ASC 718 because absent the modification terms, those Stock Awards would have been forfeited as of the last day that the former CEO provided continuous service as a consultant. In addition, Type 4 performance-based restricted stock units were not considered probable of achieving performance targets on the modification date, but 17,333 performance-based restricted stock units were achieved in February 2022, which resulted in additional stock compensation expense being recorded during the three months ended March 31, 2022.

During the three months ended March 31, 2022, total incremental stock compensation expense relating to modifications of stock options, time-based and performance-based restricted stock units of the former CEO was $1,564, which is included in G&A expense for the three months ended March 31, 2022. Of this total amount, $903 is included in G&A expense in the stock option compensation expense table above.

15. Income Taxes

The Company has recognized a full tax valuation allowance against its deferred tax assets as of March 31, 2022 and December 31, 2021. 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. As such, the Company's effective tax rate is zero for both periods.

Historically, the Company's 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 the Company's revenue in 2020 exceeded $70,000, it was not eligible to exchange its 2021 R&D tax credit for cash, therefore there was no benefit from income taxes for the three months ended March 31, 2021. As of March 31, 2022, the Company does not qualify to receive a refund of the 2022 credit, therefore no receivable or benefit from income taxes have been recorded for the 2022 credit.

16. 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

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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. The Company did not exercise its Royalty Buyout right and such right expired in August 2021. During the three months ended March 31, 2022 and 2021, no milestone payments or royalties were paid to Enteris by the Company in relation to the Enteris License Agreement.

Manufacturing Agreements

In July 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 ingredient difelikefalin, or API, for the 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 KORSUVA 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.

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 difelikefalin injection, the Company's lead product candidate. Pursuant to the Product Agreements, Patheon and Patheon Greenville will manufacture commercial supplies of difelikefalin injection at the Monza, Italy and Greenville, North Carolina manufacturing sites, respectively, from active pharmaceutical ingredient supplied by the Company. Patheon and Patheon Greenville will be responsible for supplying the other required raw materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

Leases

Lease expense is recognized on a straight-line basis over the lease term of the Company's lease agreements for its original headquarters, and additional office space, in Stamford, Connecticut. As a result, $406 of operating lease cost, or lease expense, was recognized for each of the three months ended March 31, 2022 and 2021, consisting of $284 relating to R&D lease expense and $122 relating to G&A lease expense in each of the periods.

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Other information related to the leases was as follows:

	Three Months Ended March 31,	
	2022	2021
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash outflows relating to operating leases	$ 485	$ 476
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ —
Remaining lease term - operating leases (years)	1.8	2.8
Discount rate - operating leases	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 liabilities as of March 31, 2022, were as follows:

Year Ending December 31,	
2022 (Excluding the three months ended March 31, 2022)	$ 1,473
2023	1,991
Total future minimum lease payments, undiscounted	3,464
Less imputed interest	(214)
Total	$ 3,250
Operating lease liabilities reported as of March 31, 2022:	
Operating lease liabilities - current	$ 1,795
Operating lease liabilities - non-current	1,455
Total	$ 3,250

17. Related Party Transactions

As of March 31, 2022, Vifor owned 7,396,770, or 13.8%, of the Company's common stock. Both Vifor and VFMCRP are considered related parties as of March 31, 2022 and December 31, 2021 (see Note 11, *Collaboration and Licensing Agreements*).

Sales of KORSUVA injection to Vifor of $4,790 were included within Commercial supply revenue on the Company's Condensed Statement of Comprehensive Loss for the three months ended March 31, 2022.

Amounts due from Vifor of $2,496 relating to sales of KORSUVA injection to Vifor during the three months ended March 31, 2022 were included within Accounts receivable – related party on the Company's Condensed Balance Sheet as of March 31, 2022.

18. Subsequent Events

On April 27, 2022, the European Commission granted marketing authorization to difelikefalin injection under the brand name Kapruvia® (difelikefalin), or Kapruvia, for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adult hemodialysis patients. The marketing authorization approves Kapruvia for use in all

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member states of the European Union, as well as Iceland, Liechtenstein and Norway. The Company expects commercial launch of Kapruvia in these markets in the second half of 2022.

As a result of the European Commission's regulatory approval of Kapruvia in April 2022, the Company achieved a $15,000 regulatory milestone payment from VFMCRP under the VFMCRP Agreement, which will be recorded as license and milestone fees revenue in the second quarter of 2022.

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," "seek," "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:

- our ability to successfully commercialize KORSUVA™ (difelikefalin) injection, or KORSUVA injection, and Kapruvia® (difelikefalin), our difelikefalin injection product which was granted marketing authorization by the European Commission, or Kapruvia, including the timing of associated revenues and additional regulatory submissions and approvals, and execute on our marketing plans for any other drugs or indications that may be approved in the future;
- our ability to obtain and maintain coverage and adequate reimbursement for KORSUVA injection;
- 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;
- risks that KORSUVA injection revenue, expenses and costs may not be as expected;
- the performance of third-party manufacturers and clinical research organizations, or CROs;
- risks relating to KORSUVA injection's market acceptance, competition, reimbursement and regulatory actions;
- the size and growth of the potential markets for pruritus management, including chronic kidney disease associated pruritus, or CKD-aP, in hemodialysis and non-dialysis markets, chronic liver disease associated pruritus, or CLD-aP, pruritus associated with atopic dermatitis, or AD-aP, and pruritus associated with notalgia paresthetica, or NP, markets;
- the success and timing of our clinical trials and reporting of our results from these trials, including our clinical trial programs for Oral KORSUVA (difelikefalin) in NDD-CKD-aP, CLD-aP, AD-aP, and NP;
- our plans to develop and commercialize Oral KORSUVA (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 rate and degree of market acceptance of any other future approved products;

- our ability to obtain and maintain additional regulatory approval of our product candidates, and the labeling under any approval we may obtain;
- the anticipated use of Enteris Biopharma, Inc.'s, or Enteris's, Peptelligence® technology to develop, manufacture and commercialize Oral KORSUVA (difelikefalin);
- 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 for any other future approved products;
- 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 other future approved products;
- our planned use of our cash and cash equivalents and marketable securities and the clinical milestones we expect to fund with such proceeds;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;
- our ability to obtain funding for our operations;
- our ability to obtain and maintain intellectual property protection for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others;
- the success of competing drugs that are or may become available; and
- the potential effects of the ongoing COVID-19 pandemic and geopolitical tensions on our business, operations and clinical development and regulatory timelines and plans as well as commercial and clinical drug supply chain continuity and the commercial launch of KORSUVA injection.

You should refer to the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2021 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, 2021.

Overview

We are an early commercial-stage biopharmaceutical company leading a new treatment paradigm to improve the lives of patients suffering from pruritus. Our novel KORSUVA injection is the first and only U.S. Food and Drug Administration, or FDA, approved treatment for moderate-to-severe pruritus associated with CKD in adults undergoing hemodialysis. We are developing an Oral KORSUVA (difelikefalin) formulation and initiated Phase 3 programs in the first quarter of 2022 for the treatment of pruritus in patients with AD and NDD-CKD. Phase 2 trials of Oral KORSUVA (difelikefalin) are ongoing in PBC and NP patients with moderate-to-severe pruritus.

On August 23, 2021, our lead product, KORSUVA injection, was approved by the FDA for the treatment of moderate-to-severe pruritus associated with CKD in adults undergoing hemodialysis in the United States. In December 2021, the U.S. Centers for Medicare & Medicaid Services, or CMS, granted Transition Drug Add-on Payment Adjustment, or TDAPA, to KORSUVA injection in the anti-pruritic functional category. TDAPA began applying to KORSUVA injection on April 1, 2022, for two years. Commercial launch of KORSUVA injection began in April 2022 and we expect that associated revenues will be recorded in the second quarter of 2022.

We have partnered with VFMCRP, a joint venture between Vifor Pharma Group and Fresenius Medical Care, and Vifor to commercialize KORSUVA 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). VFMCRP is a leading nephrology commercial organization with a significant presence in nephrology offices and dialysis centers. We are launching KORSUVA injection into a highly concentrated market. The dialysis market in the U.S. is dominated by two key providers, Fresenius and Davita, which combined control about 75% of the market. In addition, about 80% of the CKD hemodialysis patients are insured by Medicare.

We have built a pipeline around an oral formulation of difelikefalin, the active compound in KORSUVA injection. We are developing Oral KORSUVA (difelikefalin) in programs to create potential opportunities across all three disease categories (systemic, dermatological, and neurological) with chronic pruritus. This platform of Oral KORSUVA (difelikefalin) programs is designed to significantly expand the addressable market and patient populations that might benefit from our compound. We have four clinical programs in disease areas with about 16 million potential patients: NDD-CKD associated pruritus, AD, CLD, and NP.

Based on our completed Phase 2 trials and FDA End of Phase 2 meetings, in the first quarter of 2022, we initiated two Phase 3 registrational programs of Oral KORSUVA (difelikefalin) for the treatment of pruritus, one in NDD-CKD and the other in AD.

In earlier-stage programs, we have a Phase 2 study ongoing for Oral KORSUVA (difelikefalin) in the treatment of NP, a neurologic pruritus in which chronic pruritus is the key manifestation of sensory neuropathic syndrome. This condition has no FDA-approved treatments nor robust data to support the use of any single therapy. We currently anticipate a readout on this trial in the second quarter of 2022. We believe this program could provide insight on Oral KORSUVA's (difelikefalin) potential in other chronic neurologic pruritus conditions. In addition, we have an ongoing Phase 2 study of Oral KORSUVA (difelikefalin) for the treatment of PBC for which we currently anticipate a readout in the second half of 2022. This program could provide insight into whether Oral KORSUVA (difelikefalin) has utility in other chronic liver diseases.

We were incorporated and commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our lead product and product candidates, including conducting preclinical studies and clinical trials of 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. KORSUVA injection was approved in the U.S. in August 2021, with commercial launch occurring in April 2022.

Recent Developments

COVID-19 Update

The extent of the impact of the ongoing COVID-19 pandemic on our business, operations and clinical development and regulatory timelines and plans remains uncertain, and will depend on certain developments, including the duration and outbreak and spread of 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 timing of our submission of our New Drug Application, or NDA, to the FDA for KORSUVA injection was not affected, as we submitted the NDA in December 2020. The COVID-19 pandemic, however, has affected, and may in the future affect, the initiation of certain trial sites and patient enrollment for our ongoing Phase 2 clinical trials of Oral KORSUVA (difelikefalin) for moderate-to-severe pruritus in patients with NP, and for the treatment of pruritus in patients with hepatic impairment due to PBC. While we currently do not expect any significant delays in our clinical development or commercial timelines, the ultimate impact of the evolving COVID-19 pandemic remains difficult to predict.

To the extent possible, we are conducting business as usual, with necessary or advisable modifications to employee travel and employee work locations. We are continuing to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees, partners and other third-parties with whom we do business. The extent to which the ongoing and evolving COVID-19 pandemic may affect our business, operations and clinical development and regulatory timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain.

Overview of our Product Candidates

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

Program	Product Candidate	Primary Indication	Status	Commercialization Rights
Pruritus	KORSUVA (difelikefalin) injection	Pruritus CKD - Hemodialysis	• FDA approved in August 2021 • TDAPA application granted in December 2021 by CMS, effective April 2022 • EMA MAA granted in April 2022 • U.S. commercial launch in April 2022	VFMCRP/Vifor (United States); Maruishi (Japan); CKDP (South Korea); VFMCRP (Worldwide, other than United States, Japan and South Korea)
	Oral KORSUVA (difelikefalin)	Pruritus Atopic Dermatitis (AD-aP)	• Phase 2 trial completed; top-line data reported • Phase 3 trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (difelikefalin)	Pruritus NDD-CKD	• Phase 2 trial completed; top-line data reported • Phase 3 trial ongoing	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral KORSUVA (difelikefalin)	Pruritus CLD - Primary Biliary Cholangitis (PBC)	• Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral KORSUVA (difelikefalin)	Notalgia Paresthetica (NP)	• KOMFORT Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)

Difelikefalin – Our Lead Product

Our product candidate, difelikefalin, is a new chemical entity, which is designed to selectively stimulate kappa, rather than mu, and delta opioid receptors. Difelikefalin has been designed with specific chemical characteristics to restrict its entry into the central nervous system, or CNS, and further limit its mechanism of action to kappa opioid receptors, or 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 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). 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 KORSUVA injection and Oral KORSUVA (difelikefalin) for our other product candidates, if approved, would be attractive to both patients and physicians as a treatment for chronic pruritus across the spectrum of systemic, neurological, and dermatological variations of the disease.

KORSUVA Injection for Moderate-to-Severe Pruritus Associated with CKD in Adults Undergoing Hemodialysis

Chronic kidney disease, or CKD, is a clinical condition wherein progressive kidney damage leads to an impairment of kidney function over time. Primary risk factors culminating into CKD include diabetes, hypertension, cardiovascular disease, or hereditary renal disease. Early-stage disease is generally associated with few mild clinical manifestations; however, CKD can progress to kidney failure or end-stage renal disease, or ESRD, which is fatal without dialysis or

transplantation. According to the National Kidney Foundation, ESRD is estimated to affect approximately 750,000 individuals per year in the U.S., of which approximately 500,000 patients undergo regular dialysis.

Chronic pruritus is one of the many comorbidities of CKD, characterized by a highly unpleasant and irritating sensation that triggers an urge to scratch the skin. CKD-aP adversely affects patient quality of life and can result in infections, sleep-deprivation, depression, and even increased risk of mortality.

CKD-aP's intractable systemic itch has a high prevalence. According to Fresenius Medical Care, a world leading provider of products and medical care for dialysis patients, there were approximately 3.2 million patients globally undergoing dialysis in 2017. According to the Dialysis Outcomes and Practice Patterns Study published in December 2017 in the Clinical Journal of the American Society of Nephrologists, it is estimated that nearly 70% of these patients suffer from some form of CKD-aP with approximately 40% of these patients experiencing moderate to severe pruritus.

KORSUVA Injection Approved by the FDA in August 2021

KORSUVA injection was approved by the FDA on August 23, 2021 and is the first and only product approved by the FDA for the treatment of moderate-to-severe pruritus associated with CKD in adult patients undergoing hemodialysis. KORSUVA injection is not scheduled as a controlled substance. The clinical development program was the largest in CKD-aP patients undergoing hemodialysis with over 1,300 patients participating.

In June 2017, the FDA granted Breakthrough Therapy Designation to KORSUVA injection for the treatment of CKD-aP in hemodialysis patients. The KORSUVA injection NDA received Priority Review by the FDA, which is granted to therapies that, if approved, would offer significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

KORSUVA injection is the first and only FDA-approved product in the United States to treat CKD-aP in adults undergoing hemodialysis. There are no approved products in Europe to treat CKD-aP. Patients are generally managed with a multitude of products including corticosteroids, gabapentin, antihistamines, antidepressants and others with limited efficacy and tolerability. There is one product, nalfurafine (Remitch®) marketed by Toray Industries, approved to treat CKD-aP in Japan, but not approved in either the U.S. or Europe.

In October 2020, we entered into a license agreement with Vifor pursuant to which we granted Vifor an exclusive license solely in the United States to use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA 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.

Our U.S. commercial partner, Vifor Pharma Group, submitted the payment reimbursement application for TDAPA and HCPCS to CMS in September 2021. In December 2021, CMS granted TDAPA to KORSUVA injection in the anti-pruritic functional category. TDAPA began applying to KORSUVA injection on April 1, 2022 for two years. CMS expressed in its written communication to us and Vifor Pharma, a continuing interest in engaging with the companies regarding potential post-TDAPA support to ensure all beneficiaries with ESRD have access to innovative products such as KORSUVA injection.

Commercialization of KORSUVA injection in the U.S began in April 2022 and we expect that associated revenues will be recorded in the second quarter of 2022.

Clinical Results

KORSUVA injection was approved by the FDA on August 23, 2021 and is the first and only product approved for the treatment of moderate-to-severe pruritus associated with CKD in adult patients undergoing hemodialysis.

It was approved based on the NDA filing that was supported by positive data from two pivotal Phase 3 trials – KALM™-1, conducted in the U.S., and the global KALM-2 trial, as well as supportive data from an additional 32 clinical studies. KORSUVA injection was found to be generally well tolerated in the pivotal studies highlighted below.

In April 2020, we announced positive top-line results from our KALM-2 pivotal Phase 3 trial of KORSUVA 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 study met the primary efficacy endpoint with 54% of the patients receiving 0.5 mcg/kg of KORSUVA 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, Table of Contents 11 score at week 12 (p= 0.02). The study also met the key secondary endpoint with 41% of patients receiving KORSUVA 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 injection was generally well-tolerated with a safety profile consistent with that seen in KALM-1 and the KORSUVA clinical program in patients with CKD-aP.

Overall, the incidence of adverse effects, or AEs, and serious AEs were similar across both KORSUVA 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), falls (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 of KORSUVA 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 study met the primary efficacy endpoint with 51% of the patients receiving 0.5 mcg/kg of KORSUVA injection versus 28% of patients receiving placebo achieving at least a 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 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 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 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).

Update on KORSUVA injection outside the U.S.

Our partner, VFMCRP, submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, in March 2021, which was subsequently accepted for review by the EMA. On April 27, 2022, the European Commission granted marketing authorization to Kapruvia for the treatment of moderate-to-severe pruritus associated with CKD in adult hemodialysis patients. The marketing authorization approves Kapruvia for use in all member states of the European Union, or EU, as well as Iceland, Liechtenstein and Norway. We expect commercial launch of Kapruvia in these markets in the second half of 2022.

In addition, our partner in Japan, Maruishi, announced positive Phase 3 top-line data in January 2022. Maruishi and its sublicensee Kissei confirmed the primary endpoint was achieved in a Japanese Phase 3 clinical study (double-blind, placebo-controlled period) of difelikefalin injection for the treatment of pruritus in hemodialysis patients. In the Phase 3 study, 178 patients were administered difelikefalin or placebo for 6 weeks followed by an open-label extension period of difelikefalin administration for 52 weeks. The primary endpoint, change in itch NRS score, and the secondary endpoint, change in itching scores of Shiratori severity criteria, were significantly improved from baseline compared to the placebo group. Difelikefalin was well-tolerated.

VFMCRP has submitted a marketing application for KORSUVA injection via the Access Consortium (which also includes applications to Canada, Switzerland, Australia, and Singapore) in the second quarter of 2021. Decision on this application is expected in the second quarter of 2022.

Oral KORSUVA (difelikefalin) Programs

Oral KORSUVA (difelikefalin) for Treatment of Non-Dialysis-Dependent Chronic Kidney Disease (NDD-CKD) Associated Pruritus

CKD-aP (also known as uremic pruritus) is a frequent and wearisome symptom in patients with NDD-CKD (Stage I – V). We are initiating a Phase 3 program with Oral KORSUVA (difelikefalin) for the treatment of pruritus in NDD-CKD, specifically in patients diagnosed with Stage IV and V CKD. There are approximately 1.2 million patients diagnosed with Stage IV and Stage V CKD in the United States and approximately 300,000 of these patients suffer from moderate-to-severe pruritus.

There are no FDA-approved treatment options specifically for this indication in the U.S. or Europe. Patients are generally managed with a multitude of products including corticosteroids, gabapentin, antihistamines, antidepressants, and others with varying degrees of success. There is one product, nalfurafine (Remitch®) marketed by Toray Industries, approved to treat CKD-aP in Japan, but not approved in either the U.S. or Europe.

In December 2019, we announced top-line data from our Phase 2 trial of Oral KORSUVA (difelikefalin) for the treatment of pruritus in NDD–CKD patients diagnosed with Stage III – V CKD. The Phase 2, multicenter, randomized, double-blind, placebo-controlled 12-week trial was 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 (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 mg tablet strength of Oral KORSUVA (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 difelikefalin 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 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 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 (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 difelikefalin and placebo groups. The most common AEs reported in >5% of patients in the 1 mg difelikefalin group vs. placebo were dizziness (7.5% difelikefalin vs. 0% placebo), fall (6% difelikefalin vs. 0% placebo), diarrhea (6% difelikefalin vs. 1.5% placebo) and constipation (6% difelikefalin 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 (difelikefalin) in NDD CKD-aP and the potential Phase 3 program. The FDA indicated the acceptability of Stage V pre-dialysis CKD patients as a viable patient population for a program. In November 2021, the FDA provided written guidance indicating the patient population can be expanded to include the group of Stage IV pre-dialysis patients with advanced CKD in a registration program consisting of two pivotal Phase 3 clinical trials.

We initiated the Phase 3 NDD CKD-aP program in the first quarter of 2022. The Phase 3 program consists of two identical studies (U.S. and global study), KICK 1 and KICK 2. Each study is expected to enroll approximately 400

patients, who will be randomized 1:1 to either oral difelikefalin 1 mg once daily or matching placebo. The study population will include adult patients suffering from moderate-to-severe pruritus with advanced CKD in Stages 4 or 5, not on dialysis. The primary endpoint will be the proportion of patients with a ≥4-point improvement at Week 12 from baseline in the worst-itch numerical rating scale, or WI-NRS, after which patients will be re-randomized to either oral difelikefalin or placebo for 52-weeks. We expect to report top-line results in the second half of 2024.

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

AD is a chronic, pruritic inflammatory dermatosis that affects up to 25% of children and 2% to 5% of adults. Chronic pruritus is one of the defining features of AD. The itch is so common in AD that AD is often described as the itch that rashes. The point prevalence of chronic pruritus ranges between 87% to 100% in AD. According to a study published in Allergy in 2018, the point prevalence in adults in the U.S. is 4.9%, or approximately 12 million adults. Both quality of life and psychosocial well-being are known to negatively correlate with itch severity. The associated psychosocial morbidity of this distressing symptom includes sleep disruption, depression, agitation, anxiety, altered eating habits, reduced self-esteem and difficulty concentrating.

Additionally, AD patients can be segmented into groups based on the severity of their skin lesions as well as the severity of their itch. In a study published in *Annals of Allergy, Asthma Immunology* in 2021, it was found that nearly 25% of AD patients had mild-to-moderate lesions but still had severe pruritus. This “itch dominant” AD phenotype has a significant unmet medical need as their skin lesions have been controlled, but their severe itch has persisted. Most times, these patients have tried available agents (i.e., topical therapies, including corticosteroids, antihistamines) to control pruritus related to their AD unsuccessfully resulting in a significant patient population that needs a new oral agent for pruritus relief.

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 (difelikefalin) for moderate-to-severe pruritus in 401 adult subjects with AD-aP. KARE enrolled 64% of patients characterized as mild-to-moderate (Body Surface Area, or BSA, <10%) and 36% falling into the moderate-to-severe category (BSA>10%). Subjects were randomized to three tablet strengths of Oral KORSUVA (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, taking the total trial size up by 28%.

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 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 33% of difelikefalin-treated patients achieving a ≥4-point reduction in NRS at Week 12 versus 19% in the placebo group for the 0.5 mg dose (p=0.046). All doses performed similarly (0.25 mg, 0.5 mg, and 1 mg) versus placebo.

Oral KORSUVA (difelikefalin) was generally well-tolerated across all doses.

We initiated a Phase 3 program for the treatment of pruritus in AD patients in the first quarter of 2022. The pivotal Phase 3 program for difelikefalin in AD will comprise of two studies: KIND 1 and KIND 2 and will investigate the use of oral difelikefalin as adjunctive treatment to topical corticosteroids. The KIND 1 study will be composed of two parts: Part A and Part B.

KIND 1 and KIND 2 will be double-blind, controlled, 12-week studies with patients allowed to roll-over into open label 52-week extensions. Part A is expected to include 280 patients who will be randomized equally to four arms. At the end of the 12-week treatment period in Part A, we expect to have an internal data read out in the second half of 2023, which will provide key information, specifically the dose and the sample size to initiate Part B and KIND 2. Part B and KIND 2 will be identical in design. They will be double-blind, controlled, 12-week studies with patients randomized 1:1 to either difelikefalin or matching placebo as adjunct treatment to topical corticosteroids. The difelikefalin dose is expected to be based on the results from Part A of KIND 1. The primary endpoint will be the proportion of patients with a ≥4-point improvement at Week 12 from baseline in the WI-NRS.

The studies will include adult patients with AD whose pruritus has not been adequately controlled by topical therapy alone, with chronic pruritus for ≥6 weeks with moderate-to-severe pruritus (WI-NRS of ≥ 5). Patients must have an Investigator Global Assessment ≥ 2 and a BSA ≤20% and we will stratify patients to a BSA <10% or ≥ 10% with the aim to enroll 85% of patients with a BSA <10%.

Oral KORSUVA (difelikefalin) for Treatment of Moderate-to-Severe Pruritus Associated with Notalgia Paresthetica (NP)

NP is a common, neurosensory condition caused by alteration and damage to thoracic spinal nerves and is characterized by chronic pruritus in the upper back. It is estimated that chronic pruritus affects up to 13% of the United States population. NP falls within the subcategory of chronic neuropathic pruritus which comprises approximately 8% of all cases of chronic pruritus. According to the IQVIA study, an estimated 1 million patients were diagnosed by dermatologists with ICD10 codes commonly used for NP in the United States.

There are no FDA-approved treatments for NP. The management of NP is challenging and conventional treatments for pruritus, such as antihistamines and topical steroids, are largely ineffective.

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 (difelikefalin) for moderate-to-severe pruritus in approximately 120 adult subjects with NP. Subjects were randomized to receive Oral KORSUVA (difelikefalin) 2 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 aim to have top-line data in the second quarter of 2022.

Oral KORSUVA (difelikefalin) for Treatment of Chronic Liver Disease-Associated Pruritus (CLD-aP)

Pruritus develops in association with chronic liver diseases including hepatitis, liver cirrhosis, and PBC. It is estimated that approximately 6 million patients were diagnosed with CLD in 2019 in the United States and approximately 3 million patients received a prescription for an anti-pruritic. There are no FDA-approved therapies for pruritus associated with CLD, including PBC. Current antipruritic therapies, primarily antihistamines and corticosteroids as well as other therapies tried off-label, are largely ineffective in treating the disease and/or can produce significant side effects.

We are currently evaluating Oral KORSUVA (difelikefalin) in PBC for which it has been estimated that 70% of patients experience pruritus to initially establish the proof-of-concept in CLD-aP.

In June 2019, we announced the initiation of a Phase 2 trial of Oral KORSUVA (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 a 1 mg tablet of Oral KORSUVA (difelikefalin) taken twice daily 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 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 second half of 2022.

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 (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 (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 represented a premium over a pre-determined average closing price of our common stock. The purchase of our common stock was governed by a separate stock purchase agreement, or the Vifor Stock Purchase Agreement.

After U.S. regulatory approval of KORSUVA injection in August 2021, we received an additional $50.0 million in October 2021 for the purchase of an aggregate of 3,282,391 shares of our common stock at a price of $15.23 per share, which represents a 20% premium to the 30-day trailing average price of our common stock. The purchase of our common stock was governed by the Vifor Stock Purchase Agreement. 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.

We retain the right to make and have made KORSUVA injection, on a non-exclusive basis, in the United States for commercial sale of KORSUVA injection for use in all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients anywhere in the world and for supply of Licensed Product to Vifor under the terms of a supply agreement, or the Vifor Supply Agreement, which was executed in September 2021. The supply price is our cost of goods sold, or COGS, as calculated under GAAP, plus an agreed upon margin. The Vifor Supply Agreement will co-terminate with the Vifor Agreement.

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 are generally entitled to 60% of the net profits (as defined in the Vifor Agreement) from sales of KORSUVA 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 injection in the United States, we pay a marketing and distribution fee to Vifor based on the level of annual net sales. This fee is 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 (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 retained 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. Subsequently, the remaining commercialization rights in the U.S. were granted to Vifor as part of the Vifor Agreement in 2020, as discussed above.

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, which represented a premium over a pre-determined average closing price of our common stock.

We are eligible to receive from VFMCRP additional regulatory and commercial milestone payments in the aggregate of up to $455.0 million, consisting of up to $15.0 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 (difelikefalin) injection in the licensed territories. In the United States, we and VFMCRP will promote KORSUVA (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 (see Note 18 of Notes to Condensed Financial Statements, *Subsequent Events*, in this Quarterly Report on Form 10-Q).

We retain the right to make and have made KORSUVA (difelikefalin) injection worldwide (excluding the United States, Japan and South Korea), or the Territory, for commercial sale by VFMCRP in or outside the Territory, and for supply of KORSUVA (difelikefalin) injection to VFMCRP under the terms of a supply agreement, or the VFMCRP Supply Agreement, which was executed in May 2020. The supply price is our COGS, as calculated under GAAP, plus an agreed upon margin. The VFMCRP Supply Agreement will co-terminate with the VFMCRP Agreement.

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 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 difelikefalin and, under certain conditions, Maruishi may substitute another pruritus indication for the uremic pruritus indication originally included in its license from us. Maruishi is required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize difelikefalin in Japan. We are required to use commercially reasonable efforts, at our expense, to develop, obtain regulatory approval for and commercialize difelikefalin in the United States.

In January 2022, Maruishi and its sublicensee Kissei confirmed the primary endpoint was achieved in a Japanese Phase 3 clinical study (double-blind, placebo-controlled period) of difelikefalin injection for the treatment of pruritus in hemodialysis patients. In the Phase 3 study, 178 patients were administered difelikefalin or placebo for 6 weeks followed by an open-label extension period of difelikefalin administration for 52 weeks. The primary endpoint, change in itch NRS score, and the secondary endpoint, change in itching scores of Shiratori severity criteria, were significantly improved from baseline compared to the placebo group. Difelikefalin was well-tolerated.

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 March 31, 2022, 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.

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 difelikefalin in South Korea. CKDP is required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize difelikefalin in South Korea. We are required to use commercially reasonable efforts, at our expense, to develop, obtain regulatory approval for and commercialize 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 March 31, 2022, 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.

Manufacturing and License Agreements

Polypeptide Laboratories S.A. (PPL)

In July 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 active pharmaceutical ingredient, or API, for the 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 NDA for KORSUVA 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.

Enteris Biopharma, Inc. (Enteris)

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 had 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. We did not exercise our Royalty Buyout right and such right expired in August 2021.

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 (Patheon)

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

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

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 difelikefalin injection, our lead product candidate. Pursuant to the Product Agreements, Patheon and Patheon Greenville will manufacture commercial supplies of difelikefalin injection at the Monza, Italy and Greenville, North Carolina manufacturing sites, respectively, from API 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

Substantially all of our revenue recognized to date has consisted of upfront and milestone payments under license agreements with Vifor, VFMCRP, Maruishi and CKDP, some of or all of which was deferred upon receipt, sub-license payments under our license agreement with Maruishi for difelikefalin, as well as license agreements for CR665, our first-generation drug program for which development efforts have ceased, clinical compound sales from certain license agreements, and commercial supply revenue from Vifor. To date, we have earned a total of $94.4 million in clinical development or regulatory milestone payments, including the $15.0 million regulatory milestone earned upon the European Commission approval of Kapruvia in April 2022, and clinical compound and commercial sales from certain license agreements. We have not yet received any royalties under any of our collaborations.

Commercial launch of KORSUVA injection began in April 2022 and we expect that associated revenues will be recorded in the second quarter of 2022.

Revenue from sales of KORSUVA injection in future periods is subject to uncertainties and will depend on several factors, including the success of our and our commercial partners' commercialization efforts in the U.S., the number of new patients switching to KORSUVA injection, patient retention and demand, the number of physicians prescribing KORSUVA injection, the rate of monthly prescriptions, reimbursement from third-party payors, the conversion of patients from our clinical trials to commercial customers, and market trends. More specifically, in December 2021, CMS granted TDAPA to KORSUVA injection in the anti-pruritic functional category. TDAPA began applying to KORSUVA injection on April 1, 2022, for two years. CMS expressed in its written communication to us and Vifor Pharma, a continuing interest in engaging with the companies regarding potential post-TDAPA support to ensure all beneficiaries with ESRD have access to innovative products such as KORSUVA injection. However, there is no assurance that KORSUVA injection will be able to maintain its price established in the TDAPA period in the post-TDAPA timeframe, which could significantly impact our revenues in future periods. We will continue to monitor and analyze this data during the initial launch period in 2022.

As of March 31, 2022, Vifor owned 7,396,770, or 13.8%, of our common stock. Both Vifor and VFMCRP are considered related parties as of March 31, 2022 and December 31, 2021 (see Note 17 of Notes to Condensed Financial Statements, *Related Party Transactions*, in this Quarterly Report on Form 10-Q).

Cost of Goods Sold (COGS)

COGS includes costs related to sales of our commercial product, KORSUVA injection, to Vifor. Costs related to the sales of KORSUVA injection are generally recognized upon receipt of shipment by Vifor. Our COGS for KORSUVA injection include the cost of producing commercial product that correspond with commercial supply revenue, such as third-party supply and overhead costs, as well as certain period costs related to freight, packaging, stability, and quality testing. Through February 2022, we had not recorded any COGS related to our commercial supply revenue as all inventory costs were incurred prior to receipt of regulatory approval of KORSUVA injection and, accordingly, were expensed as incurred. In March 2022, we recorded commercial supply revenue of $2.5 million, with associated COGS of $2.1 million as these inventory costs were incurred subsequent to the receipt of regulatory approval of KORSUVA injection and, accordingly, were capitalized as inventory. As a result, we recognized $2.5 million in Accounts receivable – related party on our Condensed Balance Sheet as of March 31, 2022. We expect our COGS to increase as Vifor generates additional sales of KORSUVA injection in the future.

Research and Development (R&D)

Our R&D expenses relate primarily to the development of 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 2022 will be higher than 2021. 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 (G&A)

General and administrative, or G&A, 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 2022 will be consistent with 2021 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 KORSUVA (difelikefalin) or any future product candidate obtains regulatory approval for marketing, we expect to incur expenses associated with building a sales and marketing team.

Our license agreement with Vifor provides full commercialization rights of KORSUVA injection to Vifor under a profit-sharing arrangement. Under this profit-sharing arrangement, in consideration of Vifor's conduct of the marketing, promotion, selling and distribution of KORSUVA injection in the U.S., we pay a marketing and distribution fee to Vifor based on the level of annual net sales. This fee is deducted from product sales in calculating the net profits that are subject to the profit-sharing arrangement (see Note 11 of Notes to Condensed Financial Statements, C*ollaboration and Licensing Arrangements*, in this Quarterly Report on Form 10-Q).

Other Income, Net

Other income, net consists of interest and dividend income earned on our cash, cash equivalents, and marketable securities, 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.

Income Taxes

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

Results of Operations

Comparison of the Three Months Ended March 31, 2022 and 2021

Revenue

	Three Months Ended March 31,		
	2022	2021	% change
	Dollar amounts in thousands		
Commercial supply revenue	$ 4,790	$ —	N/A
License and milestone fees	—	1,192	-100%
Collaborative revenue	—	706	-100%
Clinical compound revenue	—	37	-100%
Total revenue	$ 4,790	$ 1,935	148%

Commercial Supply Revenue

Commercial supply revenue of $4.8 million for the three months ended March 31, 2022 was related to sales of KORSUVA injection to Vifor. There was no commercial supply revenue for the three months ended March 31, 2021 as commercial launch began in April 2022.

License and milestone fees revenue

There was no license and milestone fees revenue for the three months ended March 31, 2022. License and milestone fees revenue of $1.2 million for the three months ended March 31, 2021 was related to the milestone payment we earned 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 (see Notes 11 and 12 of Notes to Condensed Financial Statements, *Collaboration and Licensing Agreements* and *Revenue Recognition*, respectively, in this Quarterly Report on Form 10-Q).

Collaborative Revenue

There was no collaborative revenue for the three months ended March 31, 2022. Collaborative revenue of $0.7 million for the three months ended March 31, 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 (see Notes 11 and 12 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 March 31, 2022. Clinical compound revenue of $37,000 for the three months ended March 31, 2021 was related to the sale of clinical compound to Maruishi.

Research and Development Expense

	Three Months Ended March 31,		
	2022	2021	% change
	Dollar amounts in thousands		
Direct clinical trial costs	$ 11,566	$ 10,000	16%
Consultant services in support of clinical trials	1,349	1,170	15%
Stock-based compensation	2,084	2,158	-3%
Depreciation and amortization	31	31	0%
Other R&D operating expenses	6,243	5,772	8%
Total R&D expense	$ 21,273	$ 19,131	11%

For the three months ended March 31, 2022 compared to the three months ended March 31, 2021, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $3.1 million, mainly from increases of other general costs associated with our oral programs. There were also increases of $0.4 million in clinical and manufacturing costs. These increases were partially offset by decreases of $1.7 million, mainly from the Phase 2 efficacy trial for pruritus associated with AD-aP, and costs associated with preparing for our NDA submission in 2021. 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 March 31, 2022, as compared to the comparable period in 2021, partially offset by an increase in stock-based compensation expense primarily relating to additional stock option and time-based restricted stock unit grants to new and existing employees. The increase in other R&D operating expenses primarily resulted from increases in payroll related costs.

The following table summarizes our R&D expenses by programs for the three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,		
	2022	2021	% change
	Dollar amounts in thousands		
External research and development expenses:			
KORSUVA (difelikefalin) injection - Pruritus	$ 3,103	$ 2,995	4%
Oral KORSUVA (difelikefalin) - Pruritus	10,011	8,070	24%
Other	—	16	-100%
Internal research and development expenses/milestone payments	8,159	8,050	1%
Total research and development expenses	$ 21,273	$ 19,131	11%

General and Administrative Expenses

	Three Months Ended March 31,		
	2022	2021	% change
	Dollar amounts in thousands		
Professional fees and public/investor relations	$ 1,935	$ 877	121%
Stock-based compensation	3,620	1,974	83%
Depreciation and amortization	32	31	3%
Other G&A operating expenses	3,760	3,483	8%
Total G&A expense	$ 9,347	$ 6,365	47%

For the three months ended March 31, 2022 compared to the three months ended March 31, 2021, the increase in professional fees and public/investor relations expenses was primarily the result of an increase in consultants' costs and legal fees. The increase in stock-based compensation expense was primarily related to the modification of our former CEO's equity awards in November 2021 resulting in additional compensation expense of approximately $1.6 million during the three months ended March 31, 2022 for the continuation of the consulting period through June 30, 2022, and additional stock option and time-based restricted stock unit grants to existing employees. The increase in other G&A operating expenses was primarily the result of increases in payroll related costs.

Other Income, Net

	Three Months Ended March 31,		
	2022	2021	% change
	Dollar amounts in thousands		
Other income, net	$ 162	$ 260	-38%

For the three months ended March 31, 2022 compared to the three months ended March 31, 2021, the decrease in other income, net was primarily due to an increase in net amortization expense of available-for-sale marketable securities and realized gains on sales of available-for-sale securities and property and equipment during the three months ended March 31, 2021, partially offset by an increase in interest income resulting from a higher yield on our portfolio of investments in the 2022 period.

Income Taxes

Because our revenue in 2020 exceeded $70.0 million, we were not eligible to exchange our 2021 R&D tax credit for cash, therefore there was no benefit from income taxes for the three months ended March 31, 2021. As of March 31, 2022, we did not qualify to receive a refund of the 2022 credit, therefore no receivable or benefit from income taxes was recorded for the 2022 credit.

We recognized a full valuation allowance against deferred tax assets at March 31, 2022 and December 31, 2021. 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. As such, our effective tax rate is zero for both the three months ended March 31, 2022 and 2021.

Capital Requirements, Liquidity, and Capital Resources

Short-Term and Long-Term Cash 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 related to the Oral KORSUVA (difelikefalin) program.

As of March 31, 2022, we have no commitments for capital expenditures in either the short-term or long-term. The following discussion summarizes our current and long-term material cash requirements as of March 31, 2022, which we expect to fund primarily with current unrestricted cash and cash equivalents and available-for-sale marketable securities:

	Material Cash Requirements		
	Total	Less than 1 Year	1-2 Years
Operating lease obligations[1]	$ 3,464	$ 1,966	$ 1,498
Manufacturing purchase obligations[2]	2,104	2,104	—
Other obligations[3]	408	—	408
Total	$ 5,976	$ 4,070	$ 1,906

(1) Operating lease obligations relate to our Stamford operating leases entered into in December 2015 and amended in June 2020 and continue through December 2023. See Note 16 of Notes to Condensed Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q for details about our operating lease obligations.

(2) Based on our MSA with Patheon that we entered into in July 2019, we have a purchase capacity reservation through 2022. We expect the majority of this capacity reservation will be reimbursed in accordance with the supply agreement with Vifor. See Note 16 of Notes to Condensed Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q for details about our MSA with Patheon. 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.

(3) We are required to maintain a stand-by letter of credit as a security deposit under our leases for office space in Stamford, Connecticut. See 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.

As we anticipate revenue increasing in the short-term and long-term with the commercialization of KORSUVA injection, our costs of manufacturing will also increase.

Based on the Enteris License Agreement that we entered into in August 2019, we are obligated to pay (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. As these milestone payments may or may not be achieved, and royalties may or may not be owed depending on our future commercial success, there were no future payments that were considered cash requirements in the table above as of March 31, 2022. See Note 16 of Notes to Condensed Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q for details about our Enteris License Agreement.

We do not have any other requirements or off-balance sheet arrangements that have or are reasonably likely to have a material current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, cash requirements or capital resources.

Since inception, we have incurred significant operating and net losses. We incurred net losses of $27.7 million and $23.3 million for the three months ended March 31, 2022 and 2021, respectively. As of March 31, 2022, we had an accumulated deficit of $508.5 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 and our partner Vifor Pharma begin the commercial launch of KORSUVA injection and to develop and seek marketing approval for Oral KORSUVA (difelikefalin). However, we will not incur any material commercial costs on KORSUVA injection due to the licensing agreement with Vifor. Our financial results may fluctuate significantly from quarter to quarter and year to year, depending on the success of our commercialization efforts, 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 Oral KORSUVA (difelikefalin) for AD-aP, NDD-CKD, CLD-PBC and NP;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any other 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 commercialization of KORSUVA injection and the successful development of any of our other 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 successfully commercialize KORSUVA injection, complete the development of I.V. difelikefalin, oral 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 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. difelikefalin, oral 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.

Although commercial launch of KORSUVA injection began in April 2022, and our other 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 commercialization of KORSUVA injection and the development and commercialization of our other 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 continuing 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 and geopolitical tensions, such as Russia's recent incursion into Ukraine. 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.

Sources of Liquidity

Since our inception to date, we have raised an aggregate of $862.3 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 $244.7 million under our license and supply agreements, primarily with Vifor, VFMCRP, Maruishi, CKDP, which include the $15.0 million regulatory milestone earned upon European Commission approval of Kapruvia in April 2022, and an earlier product candidate for which development efforts ceased in 2007; and (4) net proceeds of $98.0 million from the purchase of our common stock in relation to the license agreements with Vifor and VFMCRP (see Note 11 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, on March 1, 2022, we filed a universal shelf registration statement, or the Shelf Registration Statement, which provides for aggregate offerings of up to $300.0 million of common stock, preferred stock, debt securities, warrants or any combination thereof. The Shelf Registration Statement has not yet been declared effective by the Securities and Exchange Commission. The securities registered under the Shelf Registration Statement include $154.5 million of unsold securities that had been registered under our previous Registration Statement on Form S-3 (File No. 333-230333) that was declared effective on April 4, 2019. We believe that our Shelf Registration Statement, once effective, will provide us with the flexibility to raise additional capital to finance our operations as needed.

We may offer additional securities under our Shelf Registration Statement, when declared effective, 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. On March 1, 2022, we entered into an open market sales agreement, or the Sales Agreement, with Jefferies LLC, as sales agent, pursuant to which we may, subject to the effectiveness of the Shelf Registration Statement, from time to time, issue and sell common stock with an aggregate value of up to $80.0 million in an at-the-market offering. Jefferies is acting as sole sales agent for any sales made under the Sales Agreement for a 3% commission on gross proceeds. The common stock will be sold at prevailing market prices at the time of the sale, and, as a result, prices may vary. Unless otherwise terminated earlier, the Sales Agreement continues until all shares available under the Sales Agreement have been sold.

As of March 31, 2022, we had $209.6 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, including the $15.0 million regulatory milestone payment earned in April 2022 upon European Commission approval of Kapruvia, will be sufficient to fund our currently anticipated operating expenses and capital requirements into the first half of 2024, without giving effect to any additional 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 commercial milestone payments in the aggregate of up to $240.0 million upon the achievement of certain sales-based milestones. In October 2021, we received a $50.0 million milestone payment from Vifor in exchange for the issuance of 3,282,391 shares of our common stock to Vifor as a result of the regulatory approval of KORSUVA injection in August 2021. As of March 31, 2022, we have received $50.0 million of regulatory milestones from Vifor.

Under the VFMCRP Agreement, we are eligible to receive additional regulatory and commercial milestone payments in the aggregate of up to $455.0 million, consisting of up to $15.0 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 difelikefalin injection in the licensed territories. In October 2021, we received a $15.0 million milestone payment from VFMCRP as a result of the regulatory approval of KORSUVA injection in August 2021. As of March 31, 2022, we have received $15.0 million of regulatory milestones from VFMCRP (see Note 18 of Notes to Condensed Financial Statements, *Subsequent Events*, in this Quarterly Report on Form 10-Q).

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 difelikefalin in Japan, if any, and share in any sub-license fees. In May 2021, we received a $2.0 million milestone payment ($1.9 million after contractual foreign currency exchange adjustments) for Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan in January 2021. As of March 31, 2022, we have received $4.5 million (before contractual foreign currency exchange adjustments) of clinical development and regulatory milestone 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 difelikefalin in South Korea, if any, and share in any sub-license fees. As of March 31, 2022, $2.3 million (before South Korean withholding tax) of development and regulatory milestones have been received under the CKDP Agreement.

In December 2021, CMS granted TDAPA to KORSUVA injection in the anti-pruritic functional category. TDAPA began applying to KORSUVA injection on April 1, 2022, for two years. CMS expressed in its written communication to us and Vifor Pharma, a continuing interest in engaging with the companies regarding potential post-TDAPA support to ensure all beneficiaries with ESRD have access to innovative products such as KORSUVA injection. Commercial launch of KORSUVA injection began in April 2022 and we expect that associated revenues will be recorded in the second quarter of 2022.

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

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 (difelikefalin) in patients with pruritus associated with CKD, CLD, AD, and NP, we expect that our current unrestricted cash and cash equivalents and available-for-sale marketable securities, including the $15.0 million regulatory milestone payment earned in April 2022 upon European Commission approval of Kapruvia, will be sufficient for us to fund our currently anticipated operating expenses and capital requirements into the first half of 2024, 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 three months ended March 31, 2022 and 2021:

	Three Months Ended March 31,	
	2022	2021
	Dollar amounts in thousands	
Net cash used in operating activities	$ (25,525)	$ (23,721)
Net cash provided by investing activities	33,431	13,869
Net cash provided by financing activities	3	688
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 7,909	$ (9,164)

Net cash used in operating activities

Net cash used in operating activities for the three months ended March 31, 2022 consisted primarily of a net loss of $27.7 million and a $4.2 million cash outflow from net changes in operating assets and liabilities, partially offset by a $6.4 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of an increase in prepaid expenses of $2.6 million, primarily related to an increase in prepaid clinical costs, an increase of $2.5 million in accounts receivable – related party relating to amounts due from Vifor for sales of KORSUVA injection during the three months ended March 31, 2022, and a cash outflow of $0.4 million relating to operating lease liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, partially offset by a decrease in inventory of $0.7 million and a cash inflow of $0.6 million from an increase in accounts payable and accrued expenses. Net non-cash charges primarily consisted of stock-based compensation expense of $5.7 million, which includes incremental expense related to the modification of our former CEO's equity awards in 2021 of $1.6 million, the amortization expense component of lease expense of $0.3 million relating to our Stamford operating leases, and the amortization of available-for-sale marketable securities, net of $0.3 million.

Net cash used in operating activities for the three months ended March 31, 2021 consisted primarily of a net loss of $23.3 million and a $5.0 million cash outflow from net changes in operating assets and liabilities, partially offset by a $4.6 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of a cash outflow of $2.0 million from a decrease in accounts payable and accrued expenses, a cash outflow of $1.7 million from an increase in Other receivables due to the milestone payment we earned from Maruishi during the three months ended March 31, 2021, a cash outflow of $0.9 million from an increase in prepaid expenses, primarily related to an increase in prepaid clinical costs, and a cash outflow of $0.4 million relating to operating lease liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, or the Stamford operating leases. Net non-cash charges primarily consisted of stock-based compensation expense of $4.1 million and the amortization expense component of lease expense of $0.3 million relating to our Stamford operating leases.

Net cash provided by investing activities

Net cash provided by investing activities was $33.4 million for the three months ended March 31, 2022, which primarily included cash inflows of $44.0 million from maturities of available-for-sale marketable securities, partially offset by cash outflows of $10.5 million for the purchases of available-for-sale marketable securities.

Net cash provided by investing activities was $13.9 million for the three months ended March 31, 2021, which primarily included cash inflows of $29.8 million from maturities and redemptions of available-for-sale marketable securities and proceeds of $8.0 million from the sales of available-for-sale marketable securities, partially offset by cash outflows of $24.0 million for the purchases of available-for-sale marketable securities.

Net cash provided by financing activities

Net cash provided by financing activities for the three months ended March 31, 2022 and 2021 consisted of proceeds of $3,000 and $688,000, respectively, received from the exercise of stock options.

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.

Critical Accounting Estimates

The preparation of our condensed financial statements and related disclosures in conformity with GAAP and our discussion and analysis of financial condition and results of operations require us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the condensed financial statements and the reported amounts of revenues and expenses during the reporting period. 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. Note 2 of Notes to Financial Statements, *Summary of Significant Accounting Policies*, in our Annual Report on Form 10-K for the year ended December 31, 2021 describes the significant accounting policies and methods used in the preparation of our condensed financial statements.

We define our critical accounting estimates as those 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 GAAP.

During the three months ended March 31, 2022, there were no significant changes to our critical accounting estimates from those described in our Annual Report on Form 10-K for the year ended December 31, 2021.

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

Interest Rate Risk

As of March 31, 2022, 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 March 31, 2022, we had invested $188.2 million of our cash reserves in such marketable securities. Those marketable securities included $188.2 million of investment grade debt instruments with a yield of approximately 0.36% and maturities through November 2024. As of December 31, 2021, we had invested $223.3 million of our cash reserves in such marketable securities. Those marketable securities included $223.3 million of investment grade debt instruments with a yield of approximately 0.28% and maturities through November 2024.

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 March 31, 2022 and December 31, 2021, 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 months ended March 31, 2022 and 2021, 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 March 31, 2022, we had $2.5 million in Accounts receivable – related party relating to sales of KORSUVA injection to Vifor. We did not identify any credit risks associated with our licensing partner Vifor during the three months ended March 31, 2022. As of December 31, 2021, we did not have a material balance of receivables.

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 March 31, 2022. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of March 31, 2022, 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 March 31, 2022 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, 2021.

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

None.

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

None.

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

Not applicable.

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

None.

Item 6. ***Exhibits.***

Exhibit No.	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit No.	Date Filed
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-36279	3.1	February 7, 2014
3.2	Amended and Restated Bylaws.	8-K	001-36279	3.2	February 7, 2014
10.1+†	Amended and Restated Non-Employee Director Compensation Policy				
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).				

\+ Indicates management contract or compensatory plan.

† Filed herewith.

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

SIGNATURES

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

CARA THERAPEUTICS, INC.

Date: May 9, 2022

By /s/ CHRISTOPHER POSNER
Christopher Posner
President, Chief Executive Officer, and Director
(Principal Executive Officer)

Date: May 9, 2022

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

CARA THERAPEUTICS, INC.
AMENDED AND RESTATED NON-EMPLOYEE DIRECTOR COMPENSATION POLICY
(EFFECTIVE UPON THE 2022 ANNUAL MEETING OF STOCKHOLDERS)

Equity:

- Initial option grant upon joining the board: Black-Scholes value of $350,000
- Annual equity awards granted on the date of each annual meeting of stockholders (for directors continuing as directors following the annual meeting):

  For the Chairperson or Lead Independent Director:

  - Option: Black-Scholes value of $200,000
  - Restricted stock units: grant date fair value of $200,000

  For each other member of the Board:

  - Option: Black-Scholes value of $100,000
  - Restricted stock units: grant date fair value of $100,000

The initial option grant will vest over three years in 12 equal quarterly installments, from the date of appointment, subject to the director's continued service as a director through each such vesting date.

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

Cash Comp:

- Annual board retainer fee - $45,000
- Chairperson or Lead Independent Director (if any) fee - $35,000
- Audit Committee
  - Chairperson fee (including member fee) - $20,000
  - Member fee - $10,000
- Compensation Committee
  - Chairperson fee (including member fee) - $15,000
  - Member fee - $7,500
- Nominating and Corporate Governance Committee
  - Chairperson fee (including member fee) - $10,000
  - Member fee - $5,000

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

Reimbursement of Expenses:

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

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, Christopher Posner, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: May 9, 2022

By: /s/ Christopher Posner
CHRISTOPHER POSNER
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: May 9, 2022

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 March 31, 2022, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Christopher Posner, 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/ CHRISTOPHER POSNER
Name: Christopher Posner
Title: Chief Executive Officer
Date: May 9, 2022

/s/ THOMAS REILLY
Name: Thomas Reilly
Title: Chief Financial Officer
Date: May 9, 2022