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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 SEPTEMBER 30, 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 November 3, 2022 was: 53,733,607.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2022

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PART I
FINANCIAL INFORMATION

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

CARA THERAPEUTICS, INC.

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

	September 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 42,806	$ 13,453
Marketable securities	112,806	153,582
Accounts receivable, net - related party	9,623	—
Inventory, net	1,835	2,584
Income tax receivable	697	697
Other receivables	451	455
Prepaid expenses	18,562	2,519
Total current assets	186,780	173,290
Operating lease right-of-use assets	1,918	2,973
Marketable securities, non-current	23,916	69,754
Property and equipment, net	487	631
Restricted cash	408	408
Total assets	$ 213,509	$ 247,056
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 26,316	$ 15,861
Operating lease liabilities, current	1,876	1,755
Total current liabilities	28,192	17,616
Operating lease liabilities, non-current	497	1,918
Commitments and contingencies (Note 16)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at September 30, 2022 and December 31, 2021, zero shares issued and outstanding at September 30, 2022 and December 31, 2021	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at September 30, 2022 and December 31, 2021, 53,733,607 shares and 53,480,812 shares issued and outstanding at September 30, 2022 and December 31, 2021, respectively	53	53
Additional paid-in capital	722,808	708,585
Accumulated deficit	(535,893)	(480,758)
Accumulated other comprehensive loss	(2,148)	(358)
Total stockholders' equity	184,820	227,522
Total liabilities and stockholders' equity	$ 213,509	$ 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		Nine Months Ended	
	September 30, 2022	September 30, 2021	September 30, 2022	September 30, 2021
Revenue:				
Collaborative revenue	$ 7,443	$ —	$ 15,446	$ 706
License and milestone fees	—	20,031	15,000	21,223
Commercial supply revenue	3,370	—	8,160	—
Clinical compound revenue	—	241	—	278
Total revenue	10,813	20,272	38,606	22,207
Operating expenses:				
Cost of goods sold	3,055	—	5,136	—
Research and development	24,691	15,514	65,869	59,870
General and administrative	6,912	5,882	23,829	17,898
Total operating expenses	34,658	21,396	94,834	77,768
Operating loss	(23,845)	(1,124)	(56,228)	(55,561)
Other income, net	665	111	1,093	502
Net loss	$ (23,180)	$ (1,013)	$ (55,135)	$ (55,059)
Net loss per share:				
Basic and Diluted	$ (0.43)	$ (0.02)	$ (1.03)	$ (1.10)
Weighted average shares:				
Basic and Diluted	53,726,123	50,114,710	53,616,753	50,031,615
Other comprehensive income (loss), net of tax of $0:				
Change in unrealized gains (losses) on available-for-sale marketable securities	(101)	6	(1,790)	(72)
Total comprehensive loss	$ (23,281)	$ (1,007)	$ (56,925)	$ (55,131)

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		Common Stock Subscribed in Private Offering		Additional Paid-In Capital	Stock Subscription Receivable	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Equity
	Shares	Amount	Shares	Amount					
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
Stock-based compensation expense	—	—	—	—	4,232	—	—	—	4,232
Shares issued upon exercise of stock options	30,000	—	—	—	182	—	—	—	182
Shares issued upon vesting of restricted stock units	89,075	—	—	—	423	—	—	—	423
Net loss	—	—	—	—	—	—	(4,206)	—	(4,206)
Other comprehensive loss	—	—	—	—	—	—	—	(324)	(324)
Balance at June 30, 2022	53,710,300	$ 53	—	$ —	$ 719,129	$ —	$ (512,713)	$ (2,047)	$ 204,422
Stock-based compensation expense	—	—	—	—	3,520	—	—	—	3,520
Shares issued upon exercise of stock options	15,807	—	—	—	104	—	—	—	104
Shares issued upon vesting of restricted stock units	7,500	—	—	—	55	—	—	—	55
Net loss	—	—	—	—	—	—	(23,180)	—	(23,180)
Other comprehensive loss	—	—	—	—	—	—	—	(101)	(101)
Balance at September 30, 2022	53,733,607	$ 53	—	$ —	$ 722,808	$ —	$ (535,893)	$ (2,148)	$ 184,820

CARA THERAPEUTICS, INC.

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

	Common Stock		Common Stock Subscribed in Private Offering		Additional Paid-In Capital	Stock Subscription Receivable	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2020	49,872,213	$ 50	—	$ —	$ 641,195	$ —	$ (392,317)	$ 73	$ 249,001
Stock-based compensation expense	—	—	—	—	2,744	—	—	—	2,744
Shares issued upon exercise of stock options	45,035	—	—	—	688	—	—	—	688
Shares issued upon vesting of restricted stock units	109,419	—	—	—	1,388	—	—	—	1,388
Net loss	—	—	—	—	—	—	(23,301)	—	(23,301)
Other comprehensive loss	—	—	—	—	—	—	—	(61)	(61)
Balance at March 31, 2021	50,026,667	$ 50	—	$ —	$ 646,015	$ —	$ (415,618)	$ 12	$ 230,459
Stock-based compensation expense	—	—	—	—	3,376	—	—	—	3,376
Shares issued upon exercise of stock options	25,494	—	—	—	293	—	—	—	293
Shares issued upon vesting of restricted stock units	36,000	—	—	—	100	—	—	—	100
Net loss	—	—	—	—	—	—	(30,745)	—	(30,745)
Other comprehensive loss	—	—	—	—	—	—	—	(17)	(17)
Balance at June 30, 2021	50,088,161	$ 50	—	$ —	$ 649,784	$ —	$ (446,363)	$ (5)	$ 203,466
Subscription of common stock in Vifor stock purchase ($15.23 per share)	—	—	3,282,391	3	44,966	(44,969)	—	—	—
Stock-based compensation expense	—	—	—	—	3,487	—	—	—	3,487
Shares issued upon exercise of stock options	43,825	—	—	—	339	—	—	—	339
Shares issued upon vesting of restricted stock units	44,002	—	—	—	906	—	—	—	906
Net loss	—	—	—	—	—	—	(1,013)	—	(1,013)
Other comprehensive income	—	—	—	—	—	—	—	6	6
Balance at September 30, 2021	50,175,988	$ 50	3,282,391	$ 3	$ 699,482	$ (44,969)	$ (447,376)	$ 1	$ 207,191

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Nine Months Ended	
	September 30, 2022	**September 30, 2021**
Operating activities		
Net loss	$ (55,135)	$ (55,059)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	13,933	12,001
Depreciation and amortization	187	186
Amortization expense component of lease expense	1,055	969
Amortization of available-for-sale marketable securities, net	498	590
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, net - related party	(9,623)	—
Inventory, net	749	—
Income tax receivable	—	810
Other receivables	4	(19,793)
Prepaid expenses	(16,043)	5,818
Accounts payable and accrued expenses	10,455	(3,069)
Operating lease liabilities	(1,300)	(1,186)
Net cash used in operating activities	(55,220)	(58,842)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	162,185	134,220
Proceeds from redemptions of available-for-sale marketable securities, at par	—	13,500
Proceeds from sale of available-for-sale marketable securities	—	10,029
Purchases of available-for-sale marketable securities	(77,858)	(108,989)
Purchases of property and equipment	(43)	—
Proceeds from sale of property and equipment	—	70
Net cash provided by investing activities	84,284	48,830
Financing activities		
Proceeds from the exercise of stock options	289	1,320
Net cash provided by financing activities	289	1,320
Net increase (decrease) in cash, cash equivalents and restricted cash	29,353	(8,692)
Cash, cash equivalents and restricted cash at beginning of period	13,861	32,091
Cash, cash equivalents and restricted cash at end of period	$ 43,214	$ 23,399
Noncash investing and financing activities		
Stock subscription receivable from Vifor International	$ —	$ 44,969

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

1. Business

Cara Therapeutics, Inc., or the Company, is a 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.

In August 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 International, that provides full commercialization rights of KORSUVA injection to Vifor in dialysis clinics in the U.S. under a profit-sharing arrangement, whereby total net sales of KORSUVA injection in the U.S., as recorded by Vifor International, are reduced by Vifor International's cost of goods sold, or COGS, as well as 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 International) profit split (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by the agreement with Vifor Fresenius Medical Care Renal Pharma Ltd., or Vifor), subject to potential temporary adjustment in future years based on certain conditions (see Note 11, *Collaboration and Licensing Agreements)*. Commercial launch of KORSUVA injection began in the U.S. in April 2022 and the Company began recording the associated profit-sharing revenues in the second quarter of 2022. In May 2022, as permitted by the agreements with Vifor International, Vifor International assigned its rights and obligations under the license agreement and a related supply agreement to Vifor. The Company's rights and obligations under these agreements were unaffected by this assignment and the assignment does not affect the Company's economic rights under the agreements. Throughout the Notes to Condensed Financial Statements, unless the context requires otherwise, references to Vifor's commercialization of KORSUVA injection pursuant to this license agreement, and the Company's provision of KORSUVA injection under this supply agreement, should be understood to refer to Vifor International prior to the assignment and to Vifor following the assignment, as applicable. Vifor International was acquired by CSL Limited in August 2022. The acquisition of Vifor International by CSL did not affect any of the Company's rights or obligations pursuant to its agreements with Vifor.

In April 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 member states of the European Union, or EU, as well as Iceland, Liechtenstein, and Norway. Kapruvia was also approved in the UK in April 2022. In addition, as part of the Access Consortium, the product was approved in August 2022 in Switzerland as Kapruvia, as well as Singapore and Canada as KORSUVA. In 2018, the Company entered into a license agreement with Vifor that provides full commercialization rights of Kapruvia, and where applicable KORSUVA, to Vifor worldwide (excluding the U.S., Japan and South Korea). In markets outside of the U.S., the Company is eligible to receive tiered double-digit royalty payments based on annual net sales, as defined in the agreement with Vifor, of difelikefalin injection in the licensed territories. In the U.S. market, the agreement with Vifor provides that Vifor will promote difelikefalin injection in the dialysis clinics of Fresenius Medical Care North America, or FMCNA, under a profit-sharing arrangement, whereby the Company is generally entitled to 50% of the annual net profits (as defined in the agreement with Vifor) based on net FMCNA clinic sales (as defined in the agreement with Vifor) and Vifor is entitled to 50% of such net profits, subject to potential adjustments in a calendar year based on certain conditions (see Note 11,

CARA THERAPEUTICS, INC.

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

Collaboration and Licensing Agreements). Commercial launch of Kapruvia in the EU commenced in September 2022 in Austria and shortly thereafter in Germany. Launches in additional EU countries are planned in the coming months.

The Company also has a license agreement with Maruishi Pharmaceutical Co. Ltd., or Maruishi, 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. In September 2022, Maruishi submitted a New Drug Application in Japan for approval of difelikefalin injection for the treatment of pruritus in hemodialysis patients (see Note 11, *Collaboration and Licensing Agreements)*.

As of September 30, 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. Including profit share revenue, the Company had also earned approximately $263,500 under its license and supply agreements for difelikefalin, primarily with Vifor International, Vifor, 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 International 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 International in connection with the Company's license agreement with Vifor International. 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 International in connection with the Company's license agreement with Vifor (see Note 11, *Collaboration and Licensing Agreements*).

As of September 30, 2022, the Company had unrestricted cash and cash equivalents and marketable securities of $179,528 and an accumulated deficit of $535,893. 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 $23,180 and $1,013 for the three months ended September 30, 2022 and 2021, respectively, and $55,135 and $55,059 for the nine months ended September 30, 2022 and 2021, respectively, and had net cash used in operating activities of $55,220 and $58,842 for the nine months ended September 30, 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, Kapruvia or any of its other product candidates, it will be unable to generate additional recurring product revenue or achieve profitability.

2. Basis of Presentation

The unaudited interim condensed financial statements included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission, or SEC. Accordingly, they do not include all information and disclosures necessary for a presentation of the Company's financial position, results of operations and cash flows in conformity with generally accepted accounting principles in the United States of America, or GAAP. In the opinion of management, these unaudited interim financial statements reflect all adjustments, consisting primarily of normal recurring accruals, necessary for a fair presentation of results for the periods presented. The results of operations for interim periods are not necessarily indicative of the results for the full year. Certain information and footnote disclosures

CARA THERAPEUTICS, INC.

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

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, revenue recognition associated with profit-sharing arrangements, 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, net – related party, 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 COVID-19 pandemic and geopolitical tensions, such as Russia's incursion into Ukraine, resulted in a global slowdown of economic activity, decades-high inflation, rising interest rates, and a potential recession in the U.S. 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.

Accounts Receivable, Net – Related Party

Accounts receivable, net – related party consists of amounts due from sales of KORSUVA injection under the Company's supply agreements with Vifor, as well as revenues earned from its profit-sharing agreement from sales of KORSUVA injection in the U.S. under the licensing agreements 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 an insignificant allowance for credit losses as of September 30, 2022.

Revenue Recognition – Profit-Sharing Arrangement

The Company receives its share of the net profits from Vifor's sale of KORSUVA injection to third parties in the U.S. under its existing license agreements. The Company has adopted a policy to recognize revenue net of tax withholdings, as applicable.

The Company determined that Vifor is a customer under Accounting Standards Update, or ASU, 2014-09, *Revenue from Contracts with Customers (Topic 606)*, as amended by ASU 2016-08, 2016-10, 2016-12 and 2016-20, or ASC 606, in relation to its profit share arrangement with Vifor. The Company sells commercial product to Vifor, who ultimately sells the commercial product to third parties. The Company's profit share arrangement revenues generated from sales of KORSUVA injection in the U.S. are considered akin to sales-based royalties. In accordance with the sales-based royalty exception, the Company recognizes its share of the pre-tax commercial net profit generated from the sales of KORSUVA injection in the U.S. in the period the product sales are earned, as reported by Vifor. The related COGS for Vifor associated with the net profit share arrangement as well as the marketing and distribution fee for the applicable period reduces the Company's profit share revenue for the period. The net sales amounts are determined based on amounts provided by Vifor and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees, product returns, and co-payment assistance costs, which could be adjusted based on actual results in the future. The Company is dependent on Vifor for timely and accurate information regarding the net revenues from sales of KORSUVA injection in the U.S. in accordance with ASC 606 to accurately report its results of operations. If the Company does not receive timely and accurate information or incorrectly estimates activity levels associated with the profit share arrangement at a given point in time, the Company could be required to record adjustments in future periods.

In accordance with ASC 606-10-55, *Principal Agent Considerations*, the Company records revenue transactions as net product revenue if it is deemed the principal in the transaction, which includes being the primary obligor, retaining inventory risk, and control over pricing. Given that the Company is not the primary obligor and does not have the inventory risks in the license agreement with Vifor, it records its share of the net profits from the sales of KORSUVA injection in the U.S. on a net basis and presents the settlement payments from Vifor as Collaborative revenue. The Company and Vifor settle the profit sharing quarterly (see Note 11, *Collaboration and Licensing Agreements)*.

3. Available-for-Sale Marketable Securities

As of September 30, 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.

CARA THERAPEUTICS, INC.

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

The following tables summarize the Company's available-for-sale marketable securities by major type of security as of September 30, 2022 and December 31, 2021:

As of September 30, 2022

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 4,004	$ —	$ (7)	$ 3,997
U.S. government agency obligations	9,500	—	(646)	8,854
Corporate bonds	39,955	—	(838)	39,117
Commercial paper	62,884	—	(64)	62,820
Municipal bonds	22,527	—	(593)	21,934
Total available-for-sale marketable securities	$ 138,870	$ —	$ (2,148)	$ 136,722

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

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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 September 30, 2022 and December 31, 2021:

As of September 30, 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	$ 3,997	$ (7)	$ —	$ —	$ 3,997	$ (7)
U.S. government agency obligations	4,646	(354)	4,208	(292)	8,854	(646)
Corporate bonds	23,606	(606)	15,511	(232)	39,117	(838)
Commercial paper	62,820	(64)	—	—	62,820	(64)
Municipal bonds	7,912	(204)	14,022	(389)	21,934	(593)
Total	$ 102,981	$ (1,235)	$ 33,741	$ (913)	$ 136,722	$ (2,148)

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 September 30, 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 September 30, 2022 and December 31, 2021, the Company held a total of 57 out of 57 positions and 58 out of 76 positions, respectively, that were in an unrealized loss position, 18 of which had been in an unrealized loss position for 12 months or greater as of September 30, 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 two out of two positions for its U.S. Treasury securities, and

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three out of three positions for its U.S. government agency obligations, that were in unrealized loss positions as of September 30, 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 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 15 out of 15 positions for its corporate bonds, 22 out of 22 positions for its commercial paper, and 15 out of 15 positions for its municipal bonds, that were in unrealized loss positions as of September 30, 2022.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of September 30, 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 September 30, 2022		As of December 31, 2021	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 113,967	$ 112,806	$ 153,631	$ 153,582
One year to three years	24,903	23,916	70,063	69,754
Total	$ 138,870	$ 136,722	$ 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 and nine months ended September 30, 2022. During the three and nine months ended September 30, 2021, the Company sold certain shares of its available-for-sale debt securities with a total fair value of $1,000 and $10,029, respectively, which resulted in no realized gains or losses for the three months ended September 30, 2021, and $39 of realized gains for the nine months ended September 30, 2021, respectively.

As of September 30, 2022 and December 31, 2021, accrued interest receivables on the Company's available-for-sale debt securities were $451 and $455, respectively.

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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 nine months ended September 30, 2022 and 2021, respectively.

	Total Accumulated Other Comprehensive (Loss) Income
Balance, December 31, 2021	$ (358)
Other comprehensive loss before reclassifications	(1,790)
Amount reclassified from accumulated other comprehensive loss	—
Net current period other comprehensive loss	(1,790)
Balance, September 30, 2022	$ (2,148)
Balance, December 31, 2020	$ 73
Other comprehensive loss before reclassifications	(33)
Amount reclassified from accumulated other comprehensive income	(39)
Net current period other comprehensive loss	(72)
Balance, September 30, 2021	$ 1

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 September 30,		Nine Months Ended September 30,		Affected Line Item in the Condensed Statements of Comprehensive Loss
	2022	2021	2022	2021	
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 September 30, 2022 and December 31, 2021, the Company's financial instruments consisted of cash, cash equivalents, available-for-sale marketable securities, accounts receivable, net – related party, prepaid expenses, restricted cash, accounts payable and accrued liabilities. The fair values of cash, cash equivalents, accounts receivable, net – 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

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pricing services. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by its third-party pricing services as of September 30, 2022 or December 31, 2021.

The following tables summarize the Company's financial assets measured at fair value on a recurring basis as of September 30, 2022 and December 31, 2021.

Fair value measurement as of September 30, 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	$ 42,806	$ 42,806	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	3,997	—	3,997	—
U.S. government agency obligations	8,854	—	8,854	—
Corporate bonds	39,117	—	39,117	—
Commercial paper	62,820	—	62,820	—
Municipal bonds	21,934	—	21,934	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 179,936	$ 43,214	$ 136,722	$ —

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 and nine months ended September 30, 2022 and 2021, respectively. There were no transfers of financial assets into or out of Level 3 classification during the three and nine months ended September 30, 2022 and 2021, respectively.

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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 balance to serve as collateral for the letter of credit issued to the landlord by the bank. As of September 30, 2022, the restricted cash balance for the Stamford Lease was invested in a commercial money market account.

As of September 30, 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.

	September 30, 2022	December 31, 2021
Cash and cash equivalents	$ 42,806	$ 13,453
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 43,214	$ 13,861

7. Inventory, net

Inventory, net consists of the following:

	September 30, 2022	December 31, 2021
Raw materials	$ 1,833	$ 927
Work-in-process	2	1,657
Total	$ 1,835	$ 2,584

As of September 30, 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 and nine months ended September 30, 2022.

8. Prepaid expenses

As of September 30, 2022, prepaid expenses were $18,562, consisting of $17,090 of prepaid R&D clinical costs, $858 of prepaid insurance and $614 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.

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9. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	September 30, 2022	December 31, 2021
Accounts payable	$ 15,218	$ 5,625
Accrued research projects	5,149	4,648
Accrued compensation and benefits	4,228	4,959
Accrued professional fees and other	1,721	629
Total	$ 26,316	$ 15,861

10. Stockholders' Equity

In September 2022, as a result of the appointment of the Company's new Chief Financial Officer, or CFO, 7,500 time-based restricted stock units held by the Company's interim principal financial and accounting officer vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation*).

In June 2022, as a result of the accelerated vesting of restricted stock units associated with the former Chief Executive Officer's, or CEO's, modification of equity awards, an aggregate of 33,999 restricted stock units vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation*).

In June 2022, as a result of the completion of the one-year vesting period, an aggregate of 43,200 restricted stock units of members of the Board of Directors vested and were settled in shares of the Company's common stock. Also in June 2022, the Company granted 11,876 fully vested restricted stock units, which were immediately settled in shares of common stock, to the Company's chairman in consideration of his effort in connection with the Company's CEO transition in 2021 (see Note 14, *Stock-Based Compensation*).

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 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 was declared effective on May 11, 2022. 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 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, 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

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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. No shares were sold under the Sales Agreement during the nine months ended September 30, 2022.

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 August 2021, the Company earned a $50,000 regulatory milestone from Vifor for the purchase of the Company's common stock at a price of $15.23 per share. As of September 30, 2021, the Company recorded a stock subscription receivable of $44,969 in connection with the U.S. regulatory approval of KORSUVA injection, representing $15.23 per share, as well as license and milestone fees revenue of $5,031 representing the excess of the stock purchase price over the cost of the purchased shares, based on the closing price of the Company's common stock on the date of the achievement of the milestone. In October 2021, after the expiration of the requisite waiting period under the Hart-Scott-Rodino Antitrust Improvement Act of 1976, or the HSR Act, the Company received the $50,000 payment and issued 3,282,391 shares of its common stock in connection with U.S. regulatory approval of KORSUVA injection on August 23, 2021 (see Note 11, *Collaboration and Licensing Agreements*).

In August 2021, as a result of the achievement of certain performance targets, an aggregate of 44,002 performance-based restricted stock units of various executive officers vested and were settled in shares of the Company's common stock (see Note 14, *Stock-Based Compensation)*.

In June 2021, as a result of the completion of the one-year vesting period, an aggregate of 36,000 restricted stock units held by members of the Board of Directors 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 International)

In October 2020, the Company entered into a license agreement with Vifor International, or Vifor Agreement No. 1, under which the Company granted Vifor International an exclusive license solely in the U.S. 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 U.S. Under Vifor Agreement No. 1, the Company retains all rights with respect to the clinical development of, and activities to gain regulatory approvals of, difelikefalin injection in the U.S.

Vifor Agreement No. 1 provides full commercialization rights in dialysis clinics to Vifor International in the U.S. under a profit-sharing arrangement. Pursuant to the profit-sharing arrangement, the Company is generally entitled to

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60% of the net profits (as defined in Vifor Agreement No. 1) from sales of difelikefalin injection in the U.S. and Vifor International is entitled to 40% of such net profits (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by Vifor Agreement No. 2, as defined below), subject to potential temporary adjustment in future years based on certain conditions. Under Vifor Agreement No. 1, in consideration of Vifor's conduct of the marketing, promotion, selling and distribution of difelikefalin injection in the U.S., the Company pays a marketing and distribution fee to Vifor based on the level of annual net sales. This fee as well as Vifor's COGS are deducted from net sales in calculating the net profits that are subject to the profit-sharing arrangement under Vifor Agreement No. 1.

Under the terms of Vifor Agreement No. 1, the Company received from Vifor International 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 Vifor Agreement No. 1, 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 U.S. 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 International under the terms of a supply agreement, or the Vifor International Supply Agreement, which was executed in September 2021. The supply price is the Company's COGS, as calculated under GAAP, plus an agreed upon margin. The Vifor International Supply Agreement will co-terminate with Vifor Agreement No. 1.

The Vifor International 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 International 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 International is not a performance obligation under Vifor Agreement No. 1 but rather the Vifor International Supply Agreement is a separate agreement from Vifor Agreement No. 1. The only performance obligation under the Vifor International Supply Agreement is the delivery of the Licensed Product to Vifor International for commercialization.

In May 2022, as permitted by Vifor Agreement No. 1 and the Vifor International Supply Agreement, Vifor International assigned its rights and obligations under these agreements to Vifor. The Company's rights and obligations under these agreements were unaffected by this assignment, and the assignment does not affect the Company's economic rights under the agreements. Throughout the Notes to Condensed Financial Statements, unless the context requires otherwise, references to Vifor's commercialization of KORSUVA injection pursuant to the license agreement, and the Company's provision of KORSUVA injection under this supply agreement, should be understood to refer to Vifor International prior to the assignment and to Vifor following the assignment, as applicable. Vifor International was

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acquired by CSL Limited in August 2022. The acquisition of Vifor International by CSL did not affect any of the Company's rights and obligations pursuant to these agreements.

Vifor Fresenius Medical Care Renal Pharma Ltd. (Vifor)

In May 2018, the Company entered into a license agreement, or Vifor Agreement No. 2, with Vifor under which the Company granted Vifor an exclusive, royalty-bearing license, or the Vifor License, to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize the Licensed Product for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in the Field worldwide (excluding the U.S., Japan and South Korea), or the Territory.

Upon entry into Vifor Agreement No. 2, Vifor made a non-refundable, non-creditable $50,000 upfront payment to the Company and Vifor International 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.

As a result of the European Commission's regulatory approval of Kapruvia in April 2022, the Company received a $15,000 regulatory milestone payment from Vifor under Vifor Agreement No. 2 during the nine months ended September 30, 2022. In addition, after U.S. regulatory approval of KORSUVA injection in August 2021, the Company earned a $15,000 regulatory milestone payment from Vifor under Vifor Agreement No. 2 during the three and nine months ended September 30, 2021.

The Company is eligible to receive from Vifor commercial milestone payments in the aggregate of up to $440,000, 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 Vifor Agreement No. 2, 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 U.S. except in the dialysis clinics of FMCNA, where Vifor will promote difelikefalin injection under a profit-sharing arrangement, whereby the Company is generally entitled to 50% of the annual net profits (as defined in Vifor Agreement No. 2) based on net FMCNA clinic sales (as defined in Vifor Agreement No. 2) and Vifor is entitled to 50% of such net profits, subject to potential adjustments in a calendar year based on certain conditions. Subsequently, the remaining commercialization rights in the U.S. were assigned to Vifor by Vifor International, as permitted by Vifor Agreement No. 1, as discussed above.

The Company retains the rights to make and have made the Licensed Product in the Territory for commercial sale by Vifor in the Field in or outside the Territory and for supply of Licensed Product to Vifor under the terms of a supply agreement, or the Vifor 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 Vifor Supply Agreement will co-terminate with Vifor Agreement No. 2.

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 compound to Vifor is not a performance obligation under Vifor Agreement No. 2 but rather the Vifor Supply Agreement is a separate agreement from Vifor Agreement No. 2. The only performance obligation under the Vifor Supply Agreement is the delivery of the Licensed Product to Vifor for commercialization. Vifor International was acquired by CSL Limited in August 2022. The

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acquisition of Vifor International by CSL did not affect any of the Company's rights or obligations pursuant to these agreements.

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

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

In September 2022, Maruishi submitted a New Drug Application in Japan for approval of difelikefalin injection for the treatment of pruritus in hemodialysis patients.

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 U.S. 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 has primarily recognized revenue under its license and collaboration agreements from (1) profit-sharing revenue following its commercial launch of KORSUVA injection in April 2022; (2) upfront license fees and milestone payments, including development and regulatory milestones; (3) commercial supply revenue from Vifor; and (4) clinical compound sales from certain license agreements. As of September 30, 2022, the Company has not yet received any royalty payments or earned any sales-based milestones under its collaboration agreements.

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As of September 30, 2022, the Company had license and collaboration agreements with Vifor, Maruishi and CKDP. The following table provides amounts included in the Company's Condensed Statements of Comprehensive Loss as revenue for the three and nine months ended September 30, 2022 and 2021:

	Three Months Ended		Nine Months Ended	
	September 30, 2022	September 30, 2021	September 30, 2022	September 30, 2021
Collaborative revenue				
Vifor (KORSUVA injection profit sharing)	$ 7,443	$ —	$ 15,446	$ —
Maruishi	—	—	—	706
Total collaborative revenue	$ 7,443	$ —	$ 15,446	$ 706
License and milestone fees				
Vifor	$ —	$ 20,031	$ 15,000	$ 20,031
Maruishi	—	—	—	1,192
Total license and milestone fees	$ —	$ 20,031	$ 15,000	$ 21,223
Commercial supply revenue				
Vifor (KORSUVA injection)	$ 3,370	$ —	$ 8,160	$ —
Total commercial supply revenue	$ 3,370	$ —	$ 8,160	$ —
Clinical compound revenue				
Vifor (difelikefalin injection)	$ —	$ 241	$ —	$ 241
Maruishi	—	—	—	37
Total clinical compound revenue	$ —	$ 241	$ —	$ 278

Collaborative revenue

Beginning in April 2022, the Company began recording its profit-sharing revenue from the sales of KORSUVA injection by Vifor to third parties in the U.S. Under the license agreements with Vifor, KORSUVA injection net sales are calculated and recorded by Vifor in accordance with U.S. GAAP and include gross sales net of discounts, rebates, allowances, sales taxes, freight and insurance charges, and other applicable deductions. These amounts include the use of estimates and judgments, which could be adjusted based on actual results in the future. The Company records its share of the net profits from the sales of KORSUVA injection in the U.S. on a net basis and presents the revenue earned each period as Collaborative revenue. This treatment is in accordance with the Company's revenue recognition policy, given that the Company is not the primary obligor and does not have the inventory risks in the collaboration agreement with Vifor in the U.S. The Company relies on Vifor to provide accurate and complete information related to the profit-sharing calculation of sales of KORSUVA injection in order to record its collaborative revenue (see Note 2, *Basis of Presentation – Revenue Recognition – Profit-Sharing Arrangement*). During the three and nine months ended September 30, 2022, the Company recorded $7,443 and $15,446, respectively, as collaborative revenue for its profit-share from the sales of KORSUVA injection in the U.S. There was no profit share revenue recorded during the three and nine months ended September 30, 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 (considered license and milestone fees revenue), and performance of R&D services, which occurred from 2013 to 2015 (considered collaborative revenue), 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

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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 and are included as collaborative revenue (see Note 11, *Collaboration and Licensing Agreements*).

There was no collaborative revenue recognized under the Maruishi Agreement during the three and nine months ended September 30, 2022, or during the three months ended September 30, 2021. During the nine months ended September 30 2021, the criteria for revenue recognition for a milestone event set forth in the Maruishi Agreement was achieved, and the Company recorded $706 as collaborative revenue based on the relative standalone selling prices described above at contract inception.

License and milestone fees revenue

Under Vifor Agreement No. 2, the Company's performance obligations of granting a license to allow Vifor to commercialize difelikefalin injection worldwide, except in the U.S., 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 were shared with Vifor 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*).

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.

As a result of the European Commission's regulatory approval of Kapruvia in April 2022, the Company received a $15,000 regulatory milestone payment from Vifor under Vifor Agreement No. 2, which was recorded as license and milestone fees revenue for the nine months ended September 30, 2022. In addition, after U.S. regulatory approval of KORSUVA injection in August 2021, the Company achieved a $15,000 regulatory milestone payment which was received in October 2021 and was recorded as license and milestone fees revenue for the three and nine months ended September 30, 2021. These regulatory milestone payments were considered variable consideration due to the uncertainty of occurrence of these events as specified at inception of the agreement. Therefore, these potential regulatory milestone payments were not included in the transaction price at the inception of the agreement. There were no license and milestone fees recognized under Vifor Agreement No. 2 for the three months ended September 30, 2022.

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. The excess of the stock purchase price over the cost of the purchased shares at the closing price of the Company's common stock on the date of the achievement of the milestone of $5,031 was included as license and milestone fees revenue for accounting purposes for the three and nine months ended September 30, 2021.

There were no license and milestone fees revenue recognized under the Maruishi Agreement during the three and nine months ended September 30, 2022, or the three months ended September 30, 2021. During the nine months ended

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September 30, 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 based on the relative standalone selling prices described above at contract inception.

Commercial supply revenue

Under the Vifor International 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 $3,370 for the three months ended September 30, 2022 with associated COGS of $3,055. The Company has commercial supply revenue of $8,160 for the nine months ended September 30, 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 $5,865 was recognized with associated COGS of $5,136 since these inventory costs were capitalized as inventory subsequent to regulatory approval.

Clinical compound revenue

The Company's only performance obligation under the Vifor Supply Agreement is to deliver clinical compound to Vifor in accordance with the receipt of purchase orders. There were no sales of clinical compound under the Vifor Supply Agreement during the three and nine months ended September 30, 2022. During each of the three and nine months ended September 30, 2021, the Company recognized clinical compound revenue of $241 from the sale of clinical compound to Vifor and as a result, the Company incurred R&D expense of $228 during these periods.

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 and nine months ended September 30, 2022, or during the three months ended September 30, 2021. During the nine months ended September 30, 2021, the Company recognized clinical compound revenue of $37 from the sale of clinical compound to Maruishi and as a result, the Company incurred R&D expense of $33 during this period.

Contract balances

As of September 30, 2022, the Company recorded accounts receivable, net – related party of $9,623 which related to its profit-sharing revenue from sales of KORSUVA injection in the U.S. by Vifor and its commercial supply of KORSUVA injection to Vifor during the three months ended September 30, 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, Vifor International, Maruishi and CKDP agreements as of September 30, 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 September 30, 2022 and December 31, 2021.

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

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dilutive. For the three and nine months ended September 30, 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 September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Basic:				
Weighted average common shares outstanding	53,726,123	50,114,710	53,616,753	50,031,615
Diluted:				
Weighted average common shares outstanding - Basic	53,726,123	50,114,710	53,616,753	50,031,615
Common stock equivalents*	—	—	—	—
Denominator for diluted net loss per share	53,726,123	50,114,710	53,616,753	50,031,615

* 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 September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Net loss - basic and diluted	$ (23,180)	$ (1,013)	$ (55,135)	$ (55,059)
Weighted-average common shares outstanding:				
Basic and diluted	53,726,123	50,114,710	53,616,753	50,031,615
Net loss per share, basic and diluted:	$ (0.43)	$ (0.02)	$ (1.03)	$ (1.10)

As of September 30, 2022, 7,654,523 stock options and 640,950 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 September 30, 2021, 5,974,549 stock options and 365,029 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 June 15, 2022, the Compensation Committee of the Company's Board of Directors, or the Compensation Committee, approved and granted a total of 7,500 time-based restricted stock units under the 2014 Plan, with a grant date fair value of $7.94 per share, to the Company's interim principal financial and accounting officer, in connection with his assuming the responsibilities of the Company's former Chief Financial Officer, or CFO, on an interim basis.

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The Company accelerated the recognition of compensation expense and the restricted stock units vested fully on September 12, 2022, when the appointment of the Company's new CFO occurred. For the three and nine months ended September 30, 2022, the Company recognized $55 and $60, respectively, of stock compensation expense associated with these awards, all of which was recorded within general and administrative, or G&A, expense. As of September 30, 2022, all of the 7,500 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 59,380 restricted stock units were granted to non-employee directors on June 2, 2022, the date of the Company's 2022 Annual Meeting of Stockholders, under the 2014 Plan with a grant date fair value of $8.42 per share. The restricted stock units will vest on the earlier of (i) June 2, 2023 and (ii) immediately prior to the Company's next Annual Meeting of Stockholders following the grant date, subject to the recipient's continued service through such date. As a result, the Company recognizes compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the three and nine months ended September 30, 2022, stock compensation expense of $126 and $164, respectively, was recognized in G&A expense. As of September 30, 2022, none of the 59,380 restricted stock units were vested or settled in shares of the Company's common stock. Also in June 2022, the Company granted 11,876 fully vested restricted stock units, which were immediately settled in shares of common stock, to the Company's chairman in consideration of his effort in connection with the Company's CEO transition in 2021. For the nine months ended September 30, 2022, stock compensation expense of $100 was recognized in G&A expense associated with this award.

On February 25, 2022, the Compensation Committee also 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 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 and nine months ended September 30, 2022, no stock compensation expense relating to these restricted stock units was recognized. In June 2022, 29,000 of these restricted stock units were forfeited as a result of the resignation of the Company's former CFO. As of September 30, 2022, none of the remaining 214,000 outstanding 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 and nine months ended September 30, 2022, the Company recognized $116 and $274, respectively, of stock compensation expense associated with these awards, with $48 recorded in R&D expense and $68 recorded in G&A expense for the three months ended September 30, 2022, and $113 recorded in R&D expense and $161 recorded in G&A expense for the nine months ended September 30, 2022. In June 2022, 20,000 of these restricted stock units were forfeited as a result of the resignation of the Company's former CFO. As of September 30, 2022, none of the remaining 125,170 outstanding 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 and nine months ended September 30, 2022, the Company recognized $110 and $323,

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respectively, of stock compensation expense associated with these awards, with $53 recorded in R&D expense and $57 recorded in G&A expense for the three months ended September 30, 2022, and $157 recorded in R&D expense and $166 recorded in G&A expense for the nine months ended September 30, 2022. In June 2022, 11,170 of these restricted stock units were forfeited as a result of the resignation of the Company's former CFO. As of September 30, 2022, none of the remaining 52,403 outstanding 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 and nine months ended September 30, 2022, stock compensation expense associated with these awards of $151 and $506, respectively, was recognized in G&A expense. As of September 30, 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 vested on June 3, 2022. As a result, the Company recognized compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the nine months ended September 30, 2022, stock compensation expense associated with these awards of $239 was recognized in G&A expense. For the three and nine months ended September 30, 2021, stock compensation expense of $142 and $184, respectively, was recognized in G&A expense. All of the 43,200 restricted stock units vested and were settled in shares of the Company's common stock as of September 30, 2022.

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 employee has met the service conditions. In February 2022 and August 2021, performance targets relating to 37,999 and 44,002 restricted stock units, respectively, had been achieved and thus restricted stock units vested and the awards were settled in shares of common stock. For the nine months ended September 30, 2022, the Company recognized $729 of stock compensation expense associated with these awards in G&A expense. G&A amounts recorded for the nine months ended September 30, 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). For each of the three and nine months ended September 30, 2021, the Company recognized $906 of stock compensation expense, with $329 recorded in R&D expense and $577 recorded in G&A expense. As of September 30, 2022, 82,001 of the 176,000 restricted stock units had vested and were settled in shares of the Company's common stock, while the remaining 93,999 restricted stock units were forfeited during the three months ended March 31, 2022 as a result of not achieving certain defined performance targets of the awards. As a result, there were no outstanding restricted stock units as of September 30, 2022 under this grant.

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

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following the grant date. On June 30, 2022, 17,333 of these restricted stock units vested and were settled in shares of the Company's common stock in accordance with the acceleration of vesting provisions relating to the modification of certain of these restricted stock units on November 1, 2021 (see *Stock Award Modifications* below). 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 and nine months ended September 30, 2022, the Company recognized $83 and $563, respectively, of stock compensation expense associated with these awards, with $55 recorded in R&D expense and $28 in G&A expense for the three months ended September 30, 2022, and $164 recorded in R&D expense and $399 in G&A expense for the nine months ended September 30, 2022. G&A amounts recorded for the nine months ended September 30, 2022 included $317 of stock compensation expense relating to the modification of certain of these restricted stock units on November 1, 2021. For the three and nine months ended September 30, 2021, the Company recognized $173 and $344, respectively of stock compensation expense, with $55 recorded in R&D expense and $118 in G&A expense for the three months ended September 30, 2021, and $110 recorded in R&D expense and $234 recorded in G&A expense for the nine months ended September 30, 2021. As of September 30, 2022, 50,669 of the 100,000 outstanding restricted stock units were vested and settled in shares of the Company's common stock, while 17,333 restricted stock units were forfeited in June 2022 as a result of the completion of the consulting agreement in relation to the modification of certain of these restricted stock units on November 1, 2021.

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 recognized compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the nine months ended September 30, 2021, stock compensation expense of $239 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 30, 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 nine months ended September 30, 2021, the Company recognized $1,256 of stock compensation expense relating to the vesting of these restricted stock units, with $524 recorded in R&D expense and $732 in G&A expense. As of September 30, 2022, 113,500 of the 138,000 restricted stock units had vested and were settled in shares of the Company's common stock, while the remaining 24,500 restricted stock units had been forfeited as a result of not achieving certain defined performance targets of the awards. As a result, there were no outstanding restricted stock units as of September 30, 2022 under this grant.

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 following the grant date. On June 30, 2022, 16,666 of these restricted stock units vested and were settled in shares of the Company's common stock in accordance with the acceleration of vesting provisions relating to the modification of certain of these restricted stock units on November 1, 2021 (see *Stock Award Modifications* below). 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

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the Company's common stock in satisfaction of the first year of vesting. For the three and nine months ended September 30, 2022, the Company recognized $66 and $460, respectively, of stock compensation expense associated with these awards, with $44 recorded in R&D expense and $22 in G&A expense for the three months ended September 30, 2022, and $131 recorded in R&D expense and $329 in G&A expense for the nine months ended September 30, 2022. G&A amounts recorded for the nine months ended September 30, 2022 included $264 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 and nine months ended September 30, 2021, the Company recognized $135 and $400, respectively, of stock compensation expense, with $44 recorded in R&D expense and $91 in G&A expense for the three months ended September 30, 2021, and $130 recorded in R&D expense and $270 in G&A expense for the nine months ended September 30, 2021. As of September 30, 2022, 82,001 of the 98,000 restricted stock units were vested and 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 nine months ended September 30, 2022 is presented below:

	Number of Units	Weighted Average Grant Date Fair Value
Outstanding, December 31, 2021	576,544	$ 17.50
Awarded	466,926	10.11
Vested and released	(206,518)	16.74
Forfeited	(196,002)	17.06
Outstanding, September 30, 2022	640,950	$ 12.50
Restricted stock units exercisable (vested and deferred), September 30, 2022	—	

Stock Options

Under the 2014 Plan, the Company granted 437,500 and 30,000 stock options during the three months ended September 30, 2022 and 2021, respectively, and 1,739,919 and 819,250 stock options during the nine months ended September 30, 2022 and 2021, respectively. No stock options were granted under the 2019 Inducement Plan during the three and nine months ended September 30, 2022 and 2021. The fair values of stock options granted during the three and nine months ended September 30, 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 September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Risk-free interest rate	2.65% - 4.09%	0.92% - 1.01%	1.70% - 4.09%	0.66% - 1.23%
Expected volatility	77.7% - 78.2%	83.0% - 83.4%	77.7% - 81.9%	71.6% - 83.5%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee and Board options (in years)	6.25	6.25	6.25	6.25

The weighted-average grant date fair value per share of options granted to employees and non-employee members of the Company's Board of Directors for their Board service during the three months ended September 30, 2022 and 2021 was $7.37 and $9.24, respectively, and during the nine months ended September 30, 2022 and 2021 was $7.27 and

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$12.14, respectively. No options were granted to non-employee consultants during the three and nine months ended September 30, 2022 and 2021.

During the three and nine months ended September 30, 2022 and 2021, the Company recognized compensation expense relating to stock options as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Research and development	$ 1,719	$ 1,833	$ 5,380	$ 5,228
General and administrative	1,149	1,205	5,137	3,444
Total stock option expense	$ 2,868	$ 3,038	$ 10,517	$ 8,672

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 $200 in R&D expense and $381 in G&A expense for the three months ended September 30, 2022, and $565 in R&D expense and $2,350 in G&A expense for the nine months ended September 30, 2022; (ii) the vesting of certain employees' restricted stock units for $429 in R&D expense and $785 in G&A expense for the three months ended September 30, 2021, and $1,094 in R&D expense and $1,812 in G&A expense for the nine months ended September 30, 2021; (iii) compensation expense relating to the Board of Directors' restricted stock units for $126 and $503 in G&A expense for the three and nine months ended September 30, 2022, respectively; and (iv) compensation expense relating to the Board of Directors' restricted stock units for $142 and $423 in G&A expense for the three and nine months ended September 30, 2021, respectively.

A summary of stock option award activity related to employees, non-employee members of the Company's Board of Directors and non-employee consultants as of and for the nine months ended September 30, 2022 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2021	6,512,280	$ 15.58
Granted	1,739,919	10.28
Exercised	(46,277)	6.26
Forfeited	(356,819)	14.50
Expired	(194,580)	16.21
Outstanding, September 30, 2022	7,654,523	$ 14.47
Options exercisable, September 30, 2022	4,764,271	

The Company does not expect to realize any tax benefits from its stock option activity or the recognition of stock-based compensation expense because the Company currently has net operating losses and has a full valuation allowance against its deferred tax assets. Accordingly, no amounts related to excess tax benefits have been reported in cash flows from operations for the nine months ended September 30, 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

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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. The consulting agreement ended on June 30, 2022.

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 through June 30, 2022.

As of the result of the consulting period ending on June 30, 2022, there was no incremental stock compensation expense relating to the modifications of stock options, time-based and performance-based restricted stock units recorded during the three months ended September 30, 2022. During the nine months ended September 30, 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 $2,563, which is included in G&A expense for the nine months ended September 30, 2022. Of this total amount, $1,679 is included in G&A expense in the stock option compensation expense table above for the nine months ended September 30, 2022.

15. Income Taxes

The Company has recognized a full tax valuation allowance against its deferred tax assets as of September 30, 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 the three and nine months ended September 30, 2022 and 2021.

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 and nine months ended September 30, 2021. As of September 30, 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 during the three and nine months ended September 30, 2022.

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-

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bearing license, including the right to grant sublicenses, under certain proprietary technology and patent rights related to or covering formulations for oral delivery of peptide active pharmaceutical ingredients with functional excipients to enhance permeability and/or solubility, known as Enteris's Peptelligence® technology, to develop, manufacture and commercialize products using such technology worldwide, excluding Japan and South Korea.

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

The Company is also obligated, pursuant to the Enteris License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. Until the second anniversary of the entry into the Enteris License Agreement, the Company had 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 September 30, 2022, Enteris earned a $5,000 milestone payment based on the first patient dosing in a Phase 3 trial, which was subsequently paid in October 2022. This milestone payment to Enteris was recorded in R&D expense for the three and nine months ended September 30, 2022. In June 2021, the Company paid a $10,000 milestone payment to Enteris based on a successful End of Phase 2 Meeting with the FDA in April 2021, which was recorded in R&D expense for the nine months ended September 30, 2021.

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

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materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

Leases

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 September 30, 2022 and 2021, consisting of $284 relating to R&D lease expense and $122 relating to G&A lease expense in both periods. For each of the nine months ended September 30, 2022 and 2021, $1,218 of operating lease cost, or lease expense, was recognized, consisting of $853 relating to R&D lease expense and $365 relating to G&A lease expense in both periods.

Other information related to the leases was as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Cash paid for amounts included in the measurement of lease liabilities:				
Operating cash outflows relating to operating leases	$ 491	$ 482	$ 1,463	$ 1,436
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ —	$ —	$ —
Remaining lease term - operating leases (years)	1.3	2.3	1.3	2.3
Discount rate - operating leases	7.0 %	7.0 %	7.0 %	7.0 %

Future minimum lease payments under non-cancellable operating leases, as well as a reconciliation of these undiscounted cash flows to the operating lease liabilities as of September 30, 2022, were as follows:

Year Ending December 31,	
2022 (Excluding the nine months ended September 30, 2022)	$ 494
2023	1,992
Total future minimum lease payments, undiscounted	2,486
Less imputed interest	(113)
Total	$ 2,373
Operating lease liabilities reported as of September 30, 2022:	
Operating lease liabilities - current	$ 1,876
Operating lease liabilities - non-current	497
Total	$ 2,373

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17. Related Party Transactions

As of September 30, 2022, Vifor International owned 7,396,770, or 13.8%, of the Company's common stock. Both Vifor and Vifor International are considered related parties as of September 30, 2022 and December 31, 2021 (see Note 11, *Collaboration and Licensing Agreements*).

As of September 30, 2022, amounts due from Vifor of $9,623 relating to the Company's profit-share revenue from sales of KORSUVA injection in the U.S. by Vifor and its commercial supply of KORSUVA injection to Vifor were included within Accounts receivable, net – related party on the Company's Condensed Balance Sheet.

The Company's profit-share revenue of $7,443 and $15,446 from sales of KORSUVA injection in the U.S. by Vifor were included within Collaborative revenue on the Company's Condensed Statements of Comprehensive Loss for the three and nine months ended September 30, 2022, respectively.

Sales of KORSUVA injection to Vifor of $3,370 and $8,160 were included within Commercial supply revenue on the Company's Condensed Statements of Comprehensive Loss for the three and nine months ended September 30, 2022, respectively.

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, the UK, and Switzerland, or Kapruvia, as well as Singapore and Canada as KORSUVA, 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 in markets around the world;

- the potential approval of the U.S. Centers for Medicare & Medicaid Services, or CMS's, end-stage renal disease, or ESRD, Prospective Payment System, or PPS, proposed rule to update Medicare payment policies and rates for renal dialysis services;

- the performance of our current and future collaborators and licensees, including Vifor Fresenius Medical Care Renal Pharma 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 and Kapruvia 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 and Kapruvia'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, pruritus associated with atopic dermatitis, or AD-aP, pruritus associated with notalgia paresthetica, or NP, and chronic liver disease associated pruritus, or CLD-aP, including primary biliary cholangitis, or PBC, markets;

- the success and timing of our clinical trials and reporting of our results from these trials, including our clinical trial programs for oral difelikefalin in non-dialysis dependent, or NDD, CKD-aP, AD-aP, NP and PBC;

- our plans to develop and commercialize oral difelikefalin and any future indication or 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 indications or 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 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 indications or products;
- regulatory developments in the U.S. and foreign countries;
- our ability to obtain and maintain coverage and adequate reimbursement from third-party payers for any other future approved indications or 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;
- our ability to maintain proper and effective internal controls, especially due to our high dependence on Vifor for timely and accurate information;
- the success of competing drugs that are or may become available; and
- the potential effects of the COVID-19 pandemic, geopolitical tensions and macroeconomic conditions 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 and Kapruvia.

You should refer to the "Risk Factors" section of our Annual Report on Form 10-K for the year ended December 31, 2021 and in this Quarterly Report on Form 10-Q 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 a 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 formulation of difelikefalin and have initiated Phase 3 programs for the treatment of pruritus in patients with advanced NDD chronic kidney disease and AD. We have completed a Phase 2 proof-of-concept trial of oral difelikefalin for the treatment of moderate-to-severe pruritus in patients with NP.

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 U.S. In December 2021, CMS granted Transition Drug Add-on Payment Adjustment, or TDAPA, to KORSUVA injection in the anti-pruritic functional category. TDAPA went into effect on April 1, 2022, for a minimum of two years. Commercial launch of KORSUVA injection began in April 2022 and we began recording the associated profit-sharing revenues in the second quarter of 2022.

In April 2022, the European Commission granted marketing authorization to difelikefalin injection under the brand name 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 member states of the European Union, or EU, as well as Iceland, Liechtenstein, and Norway. Kapruvia was also approved in the UK in April 2022. In August 2022, as part of the Access Consortium, difelikefalin injection was approved in Switzerland under the brand name Kapruvia, as well as in Singapore and Canada under the brand name KORSUVA. Commercial launches in Austria and Germany have commenced and we expect the commercial launch of Kapruvia to commence in other countries in the coming months.

We have partnered with Vifor, a joint venture between CSL Vifor Pharma Group and Fresenius Medical Care, and Vifor International to commercialize KORSUVA injection in dialysis patients with CKD-aP worldwide, excluding Japan (Maruishi/sub-licensee Kissei), and South Korea (CKDP). CSL Vifor Pharma Group is a leading nephrology commercial organization with a significant presence in nephrology offices and dialysis centers. In the U.S., we are launching KORSUVA injection into a highly concentrated market. The dialysis market is dominated by two key dialysis organizations, Fresenius and DaVita, which combined control about 75% of the market. In addition, about 80% of the CKD hemodialysis patients are insured by Medicare. Outside the U.S., the dialysis market is not dominated by large corporate dialysis companies and is a much more fragmented market than the U.S. Each country will have its own unique reimbursement system for hemodialysis patients.

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

Based on our completed Phase 2 trials and successful End of Phase 2 meetings with the FDA, we initiated two Phase 3 clinical programs of oral difelikefalin for the treatment of chronic pruritus, one in NDD-CKD and the other in AD, in the first quarter of 2022.

In June 2022, we announced positive topline results from the proof-of-concept Phase 2 KOMFORT trial of oral difelikefalin for the treatment of pruritus in patients with NP (a neurologic condition in which chronic pruritus is the key manifestation). In September 2022, we announced positive results from the extension phase of the Phase 2 KOMFORT trial. This condition currently has no FDA-approved treatments nor robust data to support the use of any single therapy.

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 and clinical studies 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.

Recent Developments

KORSUVA Injection Launch Progress

In April 2022, we started the commercialization of KORSUVA injection in the U.S. through the collaboration with Vifor. The commercial launch is in the early stages but tracking to our expectations. KORSUVA injection's uptake was initially driven by independent and mid-size organizations. In the third quarter of 2022, large dialysis organizations, or LDOs, started to order driving an acceleration in volume sales. Given the highly concentrated market, we expect LDOs to be the main contributor to product demand long-term. In the third quarter of 2022, Vifor also contracted the sales force of Fresenius Renal Pharmaceuticals, a division of Fresenius Medical Care North America, to complement Vifor's sales force in selling into Fresenius clinics in the U.S.

Appointments

We appointed Ryan Maynard to the position of Chief Financial Officer, or CFO, in September 2022. As a member of our Executive Leadership Team, Mr. Maynard leads our financial operations.

We appointed Lisa von Moltke, M.D., to our Board of Directors in November 2022.

COVID-19 Update

The extent of the impact of the COVID-19 pandemic, including the resulting adverse macroeconomic conditions, 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 COVID-19 pandemic, however, affected the initiation of certain trial sites and patient enrollment for our ongoing Phase 2 clinical trial of oral difelikefalin 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 constantly 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 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 (Kapruvia) • UK MAA granted in April 2022 (Kapruvia) • Switzerland (Kapruvia), Canada (KORSUVA) and Singapore (KORSUVA) MAAs granted in August 2022 • Japan New Drug Application filed in September 2022 • U.S. commercial launch commenced in April 2022	Vifor (Worldwide, other than Japan and South Korea)*; Maruishi (Japan); CKDP (South Korea)
	Oral difelikefalin	Pruritus Atopic Dermatitis (AD-aP)	• Phase 2 trial completed; data reported • Phase 3 trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral difelikefalin	Pruritus advanced NDD-CKD	• Phase 2 trial completed; data reported • Phase 3 trial ongoing	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral difelikefalin	Notalgia Paresthetica (NP)	• Phase 2 trial completed; data reported	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral difelikefalin	Pruritus Primary Biliary Cholangitis (PBC)	• Phase 2 trial discontinued based on slow enrollment due primarily to COVID-19	Cara (Worldwide, other than South Korea); CKDP (South Korea)

* Reflects Vifor International's assignment, as permitted under the agreements with Vifor International, of its rights and obligations under a license agreement, and a related supply agreement, to Vifor in May 2022. Our rights and obligations under these agreements were unaffected by this assignment, and the assignment does not affect our economic rights under the agreements with Vifor International. Throughout this Quarterly Report, unless the context requires otherwise, references to Vifor's commercialization of KORSUVA injection pursuant to this license agreement, and our provision of KORSUVA injection under this supply agreement, should be understood to refer to Vifor International prior to the assignment and to Vifor following the assignment, as applicable.

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.

Based on the non-clinical and clinical studies we have completed to date, we believe that oral difelikefalin, if approved for any or multiple indications, would be attractive to both patients and healthcare providers as a potential treatment for chronic pruritus across the spectrum of systemic, neurologic, and dermatologic disease categories.

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 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 New Drug Application 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 U.S., Canada, and Singapore to treat CKD-aP in adults undergoing hemodialysis. Kapruvia is the only approved drug 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 it is not approved in either the U.S. or Europe.

In October 2020, we entered into a license agreement with Vifor International pursuant to which we granted Vifor International an exclusive license solely in the U.S. 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.

Our U.S. commercial partner, Vifor Pharma Group (now CSL Vifor Pharma Group), submitted the payment reimbursement application for TDAPA and HCPCS to CMS in September 2021. In December 2021, CMS granted TDAPA designation to KORSUVA injection in the anti-pruritic functional category. TDAPA became effective for KORSUVA injection on April 1, 2022 for a minimum of two years. CMS expressed in its written communication to us

and Vifor, 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. commenced in April 2022 and we began recording associated profit-sharing revenues 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 KALM-2 conducted globally, 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 the double blinded KALM-2 pivotal Phase 3 trial of KORSUVA injection in hemodialysis patients with moderate-to-severe CKD-aP. The study met the primary efficacy endpoint with 54% of the patients receiving 0.5 mcg/kg of KORSUVA injection vs. 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 itch intensity numeric rating scale, or NRS, score at week 12 (p= 0.02). The study also met the key secondary endpoint with 41% of patients receiving KORSUVA injection achieving a four-point or greater improvement from baseline in the weekly mean of the daily 24-hour worst itch NRS score at week 12 vs. 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 trial of KORSUVA injection in hemodialysis patients with moderate-to-severe CKD-aP. The study met the primary efficacy endpoint with 51% of the patients receiving 0.5 mcg/kg of KORSUVA injection vs. 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 itch 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 vs. patients receiving placebo, p= 0.0004) and 5-D Itch scales (patients receiving KORSUVA experienced 35% improvement vs. 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 itch NRS score at week 12 vs. 18% of 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, Vifor, 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 EU, as well as Iceland, Liechtenstein, and Norway. On April 28, 2022, Kapruvia was also approved in the UK. The commercial launch of Kapruvia in the EU commenced in September 2022 in Austria and shortly thereafter in Germany. Launches in additional EU countries are planned in the coming months.

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 itch scores of Shiratori severity criteria, were significantly improved from baseline compared to the placebo group. Difelikefalin was well-tolerated.

In September 2022, Maruishi submitted a New Drug Application in Japan for the approval of difelikefalin injection for the treatment of pruritus in hemodialysis patients. A final decision on the application is expected in the second half of 2023.

Vifor has submitted a marketing application for difelikefalin injection via the Access Consortium (which includes applications to Canada, Switzerland, Australia, and Singapore) in the second quarter of 2021. In August 2022, the product was approved in Switzerland under the brand name Kapruvia, as well as Canada and Singapore under the brand name KORSUVA. A regulatory decision in Australia is expected by the end of 2022.

Oral difelikefalin Programs

Oral difelikefalin for the 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 initiated a Phase 3 program with oral difelikefalin for the treatment of pruritus in NDD-CKD, specifically in patients diagnosed with Stage IV and V advanced CKD. There are approximately 1.2 million patients diagnosed with Stage IV and V CKD in the U.S. 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 other therapies with varying degrees of success. There is one product, nalfurafine (Remitch®) marketed by Toray Industries, approved to treat CKD-aP in Japan, but it is not approved in either the U.S. or Europe.

In December 2019, we announced top-line data from our Phase 2 trial of oral 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 dosage strengths (0.25 mg, 0.5 mg and 1 mg, once daily administration) of oral difelikefalin vs. 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 itch NRS score at week 12 of the treatment period. Secondary endpoints included change from baseline in itch-related quality of life scores at the end of week 12, as assessed by the total Skindex-10 and 5-D itch scores, as well as the proportion of patients achieving an improvement from baseline ≥3 points with respect to the weekly mean of the daily 24-hour worst itch NRS score at week 12.

Patients treated with the 1 mg dosage strength of oral difelikefalin achieved the primary endpoint of statistically significant reduction in weekly mean of the daily worst itch 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 itch NRS score at week 12 was 72% vs. 58% for placebo but did not achieve statistical significance. Furthermore, patients on 1 mg dosage 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 these did not achieve statistical significance.

Oral 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 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 trials (U.S. and global), KICK 1 and KICK 2. Each trial 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 difelikefalin for the 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 difelikefalin for moderate-to-severe pruritus in 401 adult subjects with AD-aP. KARE enrolled 64% of patients characterized as mild-to-moderate AD (Body Surface Area, or BSA, <10%) and 36% falling into the moderate-to-severe AD category (BSA>10%). Subjects were randomized to three dosage strengths of oral difelikefalin: 0.25 mg, 0.5 mg and 1 mg taken twice daily (BID) vs. placebo for 12 weeks followed by 4 weeks of an open-label 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%) AD patient population (p=0.036, All doses vs. placebo), which was evident at week 1 and sustained through the 12-week 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.

A prespecified analysis by disease severity indicated a statistically significant improvement in the 4-point Responder Analysis in the mild-to-moderate (BSA<10%) AD patient population with 33% of difelikefalin-treated patients achieving a ≥4-point reduction in NRS at Week 12 vs. 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) vs. placebo.

Oral difelikefalin was generally well-tolerated across all doses.

We initiated a Phase 3 program for the treatment of moderate-to-severe pruritus in AD patients in the first quarter of 2022. The pivotal Phase 3 program for difelikefalin in AD will comprise 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 of KIND 1, 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 of KIND 1 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 chronic pruritus has not been adequately controlled by topical therapy alone and who have had chronic pruritus of moderate-to-severe intensity for ≥6 weeks (WI-NRS of ≥ 5). Patients must have an Investigator Global Assessment ≥ 2 and a BSA ≤20%. We will stratify patients to a BSA <10% or ≥ 10% with the aim to enroll 85% of patients with a BSA <10%.

Top-line results for both studies are expected in the first half of 2025.

Oral difelikefalin for the 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 U.S. population. NP falls within the subcategory of chronic neuropathic pruritus which comprises approximately 8% of all cases of chronic pruritus. We estimate that approximately 650,000 adult patients with NP associated pruritus are in the care of a healthcare provider.

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 September 2022, we announced data from our proof-of-concept Phase 2 KOMFORT clinical trial. KOMFORT was a Phase 2 randomized, double-blind, placebo-controlled trial designed to evaluate the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in 125 adult patients with NP and moderate-to-severe pruritus. Patients were randomized to receive oral difelikefalin 2 mg twice daily vs. placebo for eight weeks followed by a 4-week open-label active extension period and follow-up visit approximately 14 days after the last dose of the study drug.

KOMFORT's primary efficacy endpoint was the change from baseline in the weekly mean of the daily 24-hour worst itch NRS score at week 8 of the treatment period. Patients treated with oral difelikefalin achieved the primary endpoint (-4.0 difelikefalin vs. -2.4 placebo, p=0.001) with statistically significant improvement observed as early as Week 1 and sustained through Week 8.

Other endpoints included a ≥4-point improvement in worst itch NRS, complete response in worst itch NRS, and safety assessments. A statistically significantly greater proportion of patients treated with oral difelikefalin achieved a ≥4-point improvement in worst itch NRS score at Week 8 vs. placebo (41% difelikefalin vs. 18% placebo, p=0.007). In addition, oral difelikefalin met the complete response endpoint, defined as a worst itch NRS score of 0 or 1 for 70% of the daily non-missing worst itch NRS scores for the week. At Week 8, a significantly greater proportion of patients receiving oral difelikefalin vs. placebo achieved a complete response (22% difelikefalin vs. 5% placebo, p<0.01).

Oral difelikefalin was generally well tolerated, with all AEs in difelikefalin-treated patients reported as mild or moderate in severity. Nausea, headache, dizziness, constipation, and increased urine output were more commonly reported in patients on difelikefalin.

We are scheduled to meet with the FDA in November 2022 to discuss next steps toward a potential pivotal program for oral difelikefalin in NP.

Oral difelikefalin for the Treatment of Chronic Liver Disease-Associated Pruritus (CLD-aP), including PBC

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 U.S. and approximately 3 million patients received a prescription for an anti-pruritic agent. 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 used off-label, are largely ineffective in treating the disease and/or can produce significant side effects.

We have been evaluating oral difelikefalin in PBC to establish a proof-of-concept in CLD-aP. It has been estimated that 70% of PBC patients experience pruritus.

In June 2019, we announced the initiation of a proof-of-concept Phase 2 trial of oral difelikefalin for the treatment of pruritus in patients with hepatic impairment due to PBC. The Phase 2 multicenter, randomized, double-blind, placebo-controlled 16-week trial is designed to evaluate the safety and efficacy of 1 mg of oral difelikefalin taken twice daily vs. 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 itch 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 itch NRS score at week 16.

Based on slow enrollment due primarily to COVID-19, we made a strategic decision to discontinue and unblind the proof-of-concept Phase 2 clinical trial of oral difelikefalin for the treatment of pruritus in patients with PBC. The unblinded data showed no unexpected AEs. However, the low number of patients (N=14) limits the ability to draw a meaningful conclusion regarding the efficacy (worst itch NRS change from baseline at 16 weeks: -3.8 difelikefalin vs. -3.0 placebo) of difelikefalin in this patient population. At this time, we plan to focus our resources on our nephrology and dermatology programs.

Collaboration and License Agreements

Vifor (International) Ltd., or Vifor International

In October 2020, we entered into a license agreement, or Vifor Agreement No. 1, with Vifor International under which we granted Vifor International an exclusive license solely in the U.S. 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 U.S. Under

Vifor Agreement No. 1, we retain all rights with respect to the clinical development of, and activities to gain regulatory approvals of, KORSUVA (difelikefalin) injection in the U.S.

Under the terms of Vifor Agreement No. 1, we received from Vifor International 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. The excess of the stock purchase price over the cost of the purchased shares at the closing price of our common stock on the date of the achievement of the milestone of $5.0 million was included as license and milestone fees revenue for accounting purposes for the three and nine months ended September 30, 2021. In addition, pursuant to Vifor Agreement No. 1, 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, worldwide 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 and for supply of Licensed Product to Vifor International under the terms of a supply agreement, or the Vifor International 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 International Supply Agreement will co-terminate with Vifor Agreement No. 1.

Vifor Agreement No. 1 provides full commercialization rights in dialysis clinics to Vifor International in the U.S. under a profit-sharing arrangement. Pursuant to the profit-sharing arrangement, we are generally entitled to 60% of the net profits (as defined in Vifor Agreement No. 1) from sales of KORSUVA injection in the U.S. and Vifor International is entitled to 40% of such net profits (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by Vifor Agreement No. 2, as defined below), subject to potential temporary adjustment in future years based on certain conditions. Under Vifor Agreement No. 1, 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 as well as Vifor's COGS are deducted from net sales in calculating the net profits that are subject to the profit-sharing arrangement under Vifor Agreement No. 1.

In May 2022, as permitted under Vifor Agreement No. 1 and the Vifor International Supply Agreement, Vifor International assigned its rights and obligations under these agreements to Vifor. Our rights and obligations under these agreements were unaffected by this assignment, and the assignment does not affect our economic rights under these agreements, nor do we expect the assignment to have a material effect on us. Throughout this Quarterly Report, unless the context requires otherwise, references to Vifor's commercialization of KORSUVA injection pursuant to this license agreement, and our provision of KORSUVA injection under the related supply agreement, should be understood to refer to Vifor International prior to the assignment and to Vifor following the assignment, as applicable. Vifor International was acquired by CSL Limited in August 2022. The acquisition of Vifor International by CSL did not affect any of the Company's rights or obligations pursuant to these agreements.

Vifor Fresenius Medical Care Renal Pharma Ltd., or Vifor

In May 2018, we entered into a license agreement, or Vifor Agreement No. 2, with Vifor, a joint venture between Vifor Pharma Group (now CSL Vifor Pharma Group) and Fresenius Medical Care, under which we granted Vifor 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 U.S., 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 Vifor will promote KORSUVA injection under a profit-sharing arrangement. Subsequently, the remaining commercialization rights in the U.S. were assigned to Vifor by Vifor International as permitted by Vifor Agreement No. 1, as discussed above.

Upon entry into Vifor Agreement No. 2, Vifor made a non-refundable, non-creditable $50.0 million upfront payment to us and Vifor International 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.

As a result of the European Commission's regulatory approval of Kapruvia in April 2022, we received a $15.0 million regulatory milestone payment from Vifor under Vifor Agreement No. 2, which was recorded as license and milestone fees revenue for the nine months ended September 30, 2022.

After U.S. regulatory approval of KORSUVA injection in August 2021, we were entitled to receive a $15.0 million regulatory milestone payment which was received in October 2021, and was recorded as license and milestone fees revenue for the three and nine months ended September 30, 2021, as the variable consideration was deemed probable upon the regulatory approval in August 2021 (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).

We are eligible to receive from Vifor commercial milestone payments in the aggregate of up to $440.0 million, 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 U.S., Vifor will promote KORSUVA (difelikefalin) injection in the dialysis clinics of FMCNA under a profit-sharing arrangement (subject to the terms and conditions of Vifor Agreement No. 2) based on net FMCNA clinic sales recorded by us, whereby we are generally entitled to 50% of the annual net profits (as defined in Vifor Agreement No. 2) based on net FMCNA clinic sales (as defined in Vifor Agreement No. 2) and Vifor is entitled to 50% of such net profits, subject to potential adjustments in a calendar year based on certain conditions.

Vifor International was acquired by CSL Limited in August 2022. The acquisition of Vifor International by CSL did not affect any of the Company's rights or obligations pursuant to these agreements.

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 U.S.

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 injection 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 itch scores of Shiratori severity criteria, were significantly improved from baseline compared to the placebo group. Difelikefalin was well-tolerated.

In September 2022, Maruishi submitted an New Drug Application in Japan for approval of difelikefalin injection for the treatment of pruritus in hemodialysis patients. A final decision on the application is expected in the second half of 2023.

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 September 30, 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, a mid-double-digit percentage of all non-royalty payments received by Maruishi from its sublicensees, if any, and 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 U.S.

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 September 30, 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 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. During the three months ended September 30, 2022, Enteris earned a milestone payment of $5.0 million based on the first patient dosing in a Phase 3 trial, which was subsequently paid in October 2022. The milestone payment was recorded in research and development, or R&D, expense for the three and nine months ended September 30, 2022. In June 2021, we paid a $10.0 million milestone payment to Enteris based on a successful End of Phase 2 Meeting with the FDA in April 2021, which was recorded in R&D expense for the nine months ended September 30, 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

The following discussion sets forth certain components of our Condensed Statements of Comprehensive Loss as well as factors that impact those items.

Revenue

To date, we generate revenue primarily from (1) profit-sharing revenue following our commercial launch of KORSUVA injection in April 2022, (2) the receipt of upfront license fees and milestone payments, (3) commercial supply revenue from Vifor, and (4) clinical compound sales from certain license agreements. We expect to receive royalty revenue in the fourth quarter of 2022 in conjunction with the launch of Kapruvia in Europe, and we could receive sales-based milestones in the future in accordance with certain licensing agreements.

To date, we have earned a total of $113.3 million in clinical development or regulatory milestone payments, clinical compound and commercial compound sales from certain license agreements, and profit-sharing revenue from Vifor.

We commenced our commercial launch of KORSUVA injection for the treatment of pruritus in adult patients undergoing hemodialysis in the U.S. in April 2022 following FDA approval of KORSUVA injection in August 2021. The commercial launch of Kapruvia in the EU commenced in September 2022 in Austria and shortly thereafter in Germany. Launches in additional EU countries are planned in the coming months.

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 including the U.S. government, 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 went into effect on April 1, 2022, for a minimum of two years. CMS expressed in its written communication to us and Vifor, 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 during the TDAPA period in the post-TDAPA timeframe, which could significantly impact our revenues in future periods. In June 2022, CMS issued a calendar year 2023 ESRD PPS proposed rule to update Medicare payment policies and rates for renal dialysis services, which included a request for information, or RFI, to seek input on potential methodologies to add additional money through an add-on adjustment methodology for certain TDAPA drugs that enter the PPS in an existing functional category. The options included in the RFI, if proposed and ultimately approved through Notice and Comment Rulemaking, could result in the provision of additional payments for KORSUVA injection post-TDAPA. The rule proposal is subject to a public comment period and formal consideration by CMS. As a result, there can be no guarantee that the proposal will be approved as proposed or at all.

As of September 30, 2022, Vifor International owned 7,396,770, or 13.8%, of our common stock. Both Vifor and Vifor International are considered related parties as of September 30, 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)

Cost of goods sold 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. The related COGS for Vifor associated with the net profit share arrangement as well as the marketing and distribution fee for the applicable period reduces our profit share revenue for the period.

In January 2022, we recorded commercial supply revenue of $2.3 million, with no associated COGS 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. During the three months ended September 30, 2022, we recorded commercial supply revenue of $3.4 million, with associated COGS of $3.1 million. 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 and clinical studies 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, human resources, project management, alliance management, and procurement 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, and accountants. In addition, if oral difelikefalin or any future product candidate obtains regulatory approval for marketing, we may incur expenses associated with building sales and marketing, commercial operations, and market access teams.

Our license agreements with Vifor provide full U.S. commercialization rights of KORSUVA injection to Vifor under profit-sharing arrangements. Under these profit-sharing arrangements, 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 as well as Vifor's COGS are 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 and Nine Months Ended September 30, 2022 and 2021

Revenue

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Collaborative revenue	$ 7,443	$ —	N/A	$ 15,446	$ 706	2088%
License and milestone fees	—	20,031	-100%	15,000	21,223	-29%
Commercial supply revenue	3,370	—	N/A	8,160	—	N/A
Clinical compound revenue	—	241	-100%	—	278	-100%
Total revenue	$ 10,813	$ 20,272	-47%	$ 38,606	$ 22,207	74%

Collaborative Revenue

Collaborative revenue of $7.4 million for the three months ended September 30, 2022 related to the profit-sharing revenue from Vifor's sales of KORSUVA injection to third parties. There was no collaborative revenue for the three months ended September 30, 2021.

Collaborative revenue of $15.4 million for the nine months ended September 30, 2022 related to the profit-sharing revenue from Vifor's sales of KORSUVA injection to third parties. Collaborative revenue of $0.7 million for the nine months ended September 30, 2021 was related to the milestone payment we earned in January 2021 from Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan that was allocated to the R&D services performance

obligation under the Maruishi Agreement (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).

License and milestone fees revenue

There was no license and milestone fees revenue for the three months ended September 30, 2022. License and milestone fees revenue of $20.0 million for the three months ended September 30, 2021 was related to milestone payments we earned from Vifor and Vifor International that was allocated to the license and milestone fee performance obligation under Vifor Agreement No. 1 and Vifor Agreement No. 2, as the variable consideration was deemed probable upon the regulatory approval in August 2021. This included $5.0 million of the $50.0 equity milestone investment under the agreement with Vifor International.

License and milestone fees revenue of $15.0 million for the nine months ended September 30, 2022 was related to the regulatory milestone payment earned from Vifor for the approval of Kapruvia by the European Commission in April 2022. License and milestone fees revenue of $21.2 million for the nine months ended September 30, 2021 was related to milestone payments of $20.0 million we earned from Vifor and Vifor International that was allocated to the license and milestone fee performance obligation under Vifor Agreement No. 1 and Vifor Agreement No. 2, as the variable consideration was deemed probable upon the regulatory approval in August 2021, and a milestone payment of $1.2 million that we earned in January 2021 from Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan that was allocated to the license and milestone 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).

Commercial Supply Revenue

Commercial supply revenue of $3.4 and $8.2 million for the three and nine months ended September 30, 2022, respectively, was related to sales of KORSUVA injection to Vifor. There was no commercial supply revenue during the three and nine months ended September 30, 2021 as commercial launch began in April 2022.

Clinical compound revenue

There was no clinical compound revenue for the three and nine months ended September 30, 2022. Clinical compound revenue of $241,000 for the three months ended September 30, 2021 was related to the sale of clinical compound to Vifor. Clinical compound revenue of $278,000 for the nine months ended September 30, 2021 was related to the sale of clinical compound to Vifor for $241,000 and to Maruishi for $37,000.

Cost of Goods Sold (COGS)

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Cost of Goods Sold	$ 3,055	$ —	N/A	$ 5,136	$ —	N/A

Cost of goods sold of $3.1 million and $5.1 million for the three and nine months ended September 30, 2022 was related to commercial supply revenue for KORSUVA injection sales to Vifor. There were no COGS during the three and nine months ended September 30, 2021, as commercialization of KORSUVA injection began in April 2022.

Research and Development Expense

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 10,181	$ 6,264	63%	$ 32,613	$ 22,983	42%
Consultant services in support of clinical trials	1,710	1,296	32%	4,380	3,526	24%
Stock-based compensation	1,919	2,262	-15%	5,945	6,322	-6%
Depreciation and amortization	30	31	-3%	91	93	-2%
Other R&D operating expenses	10,851	5,661	92%	22,840	26,946	-15%
Total R&D expense	$ 24,691	$ 15,514	59%	$ 65,869	$ 59,870	10%

For the three months ended September 30, 2022 compared to the three months ended September 30, 2021, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $5.8 million, mainly from increases in clinical trial spend related to our two oral difelikefalin Phase 3 programs. These increases were partially offset by decreases of $2.0 million, mainly from the Phase 2 efficacy trial for pruritus associated with AD-aP. The increase in other R&D operating expenses primarily resulted from the recognition of a $5.0 million milestone payment due to Enteris during the three months ended September 30, 2022.

For the nine months ended September 30, 2022 compared to the nine months ended September 30, 2021, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $13.1 million, mainly from increases in clinical trial spend related to our two oral difelikefalin Phase 3 programs, and other general costs associated with our oral programs. These increases were partially offset by decreases of $3.6 million, mainly from the Phase 2 efficacy trial for pruritus associated with AD-aP. The decrease in other R&D operating expenses primarily resulted from the recognition of a $5.0 million milestone payment due to Enteris during the 2022 period as compared to the recognition of a $10.0 million milestone payment due to Enteris during the 2021 period, partially offset by increases in payroll related costs.

The following table summarizes our R&D expenses by programs for the three and nine months ended September 30, 2022 and 2021:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
KORSUVA (difelikefalin) injection - Pruritus	$ 1,254	$ 1,296	-3%	$ 6,057	$ 6,672	-9%
Oral difelikefalin - Pruritus	10,611	6,217	71%	31,110	19,671	58%
Other	—	1	-100%	—	18	-100%
Internal research and development expenses/milestone payments[1]	12,826	8,000	60%	28,702	33,509	-14%
Total research and development expenses	$ 24,691	$ 15,514	59%	$ 65,869	$ 59,870	10%

[1] Includes a milestone payment of $5.0 million earned by Enteris for the three and nine months ended September 30, 2012, based on the first patient dosing in a Phase 3 trial, and a milestone payment of $10.0 million earned by Enteris for the nine months ended September 30, 2021, based on a successful End of Phase 2 Meeting with the FDA in April 2021.

General and Administrative Expenses

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 1,364	$ 1,042	31%	$ 4,768	$ 3,277	46%
Stock-based compensation	1,656	2,131	-22%	7,988	5,679	41%
Depreciation and amortization	32	31	4%	96	93	4%
Other G&A operating expenses	3,860	2,678	44%	10,977	8,849	24%
Total G&A expense	$ 6,912	$ 5,882	18%	$ 23,829	$ 17,898	33%

For the three months ended September 30, 2022 compared to the three months ended September 30, 2021, the increase in professional fees and public/investor relations expenses was primarily the result of an increase in accounting and auditing fees for the period. The decrease in stock-based compensation expense was primarily related to the ending of the consulting period of our former CEO on June 30, 2022 which resulted in the full vesting of his modified awards during the second quarter of 2022. The increase in other G&A operating expenses was primarily the result of increases in payroll related costs.

For the nine months ended September 30, 2022 compared to the nine months ended September 30, 2021, the increase in professional fees and public/investor relations expenses was primarily the result of an increase in consultants' costs, and accounting and auditing fees for the period. 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 $2.6 million during the nine months ended September 30, 2022 for the continuation of the consulting period through June 30, 2022. The increase in other G&A operating expenses was primarily the result of increases in payroll related costs.

Other Income, Net

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other income, net	$ 665	$ 111	500%	$ 1,093	$ 502	118%

For the three months ended September 30, 2022 compared to the three months ended September 30, 2021, the increase in other income, net was primarily due to an increase in interest income resulting from a higher yield on our portfolio of investments during the three months ended September 30, 2022 and a decrease in net amortization of available-for-sale marketable securities during the three months ended September 30, 2022.

For the nine months ended September 30, 2022 compared to the nine months ended September 30, 2021, the increase in other income, net was primarily due to an increase in interest income resulting from a higher yield on our portfolio of investments during the nine months ended September 30, 2022.

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 and nine months ended September 30, 2021. As of September 30, 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 during the three and nine months ended September 30, 2022.

We recognized a full valuation allowance against deferred tax assets at September 30, 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 each of the three and nine months ended September 30, 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 difelikefalin program.

As of September 30, 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 September 30, 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
	Dollar amounts in thousands		
Operating lease obligations[1]	$ 2,486	$ 1,983	$ 503
Manufacturing purchase obligations[2]	14,154	14,154	—
Other obligations[3]	408	—	408
Total	$ 17,048	$ 16,137	$ 911

(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 2023. 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 and Kapruvia, 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. During the three months ended September 30, 2022, Enteris earned a $5.0 million milestone payment, which was subsequently paid in October 2022, and was included within accounts payable and accrued expenses on our condensed balance sheet as of September 30, 2022. As a result, there were no future payments that were considered cash requirements in the table above as of September 30, 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 $23.2 million and $1.0 million for the three months ended September 30, 2022 and 2021, respectively, and $55.1 million for each of the nine months ended September 30, 2022 and 2021. As of September 30, 2022, we had an accumulated deficit of $535.9 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 expand the commercial launch of KORSUVA injection and to develop and seek marketing approval for oral 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, 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 difelikefalin for pruritus associated with AD, NDD-CKD, 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 Kapruvia 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 and Kapruvia, 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 COVID-19 pandemic, introducing additional uncertainty.

Although commercial launch of KORSUVA injection began in the U.S. in April 2022, and commercial launch of Kapruvia in the EU commenced in September 2022 in Austria and shortly thereafter in Germany, launches in additional EU countries are planned in the coming months. Our other product candidates are still in clinical development and since the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the commercialization of KORSUVA injection and Kapruvia 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, 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 equity markets in the U.S. and worldwide resulting from the COVID-19 pandemic and its variants and geopolitical tensions, such as Russia's incursion into Ukraine, which resulted in a global slowdown of economic activity, decades-high inflation, rising interest rates and a potential recession. 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 $881.1 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 $248.1 million under our license and supply agreements, primarily with Vifor, Vifor International, Maruishi, CKDP, and an earlier product candidate for which development efforts ceased in 2007; (4) net profit-sharing revenue of $15.4 million from sales of KORSUVA injection to third parties by Vifor; and (5) net proceeds of $98.0 million from the purchase of our common stock in relation to the license agreements with Vifor and Vifor International (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 was declared effective by the Securities and Exchange Commission on May 11, 2022. 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 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 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, 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. No shares were sold under the Sales Agreement during the nine months ended September 30, 2022.

Under Vifor Agreement No. 1, 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 International in exchange for the issuance of 3,282,391 shares of our common stock to Vifor International as a result of the regulatory approval of KORSUVA injection in August 2021. As of September 30, 2022, we have received $50.0 million of regulatory milestones from Vifor International.

Under Vifor Agreement No. 2, we are eligible to receive commercial milestone payments in the aggregate of up to $440.0 million, 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 Vifor Agreement No. 2, of difelikefalin injection in the licensed territories. In June 2022, we received a $15.0 million milestone payment from Vifor as a result of the regulatory approval of Kapruvia by the European Commission in April 2022. In October 2021, we received a $15.0 million milestone payment from Vifor as a result of the regulatory approval of KORSUVA injection in August 2021. As of September 30, 2022, we have received $30.0 million of regulatory milestones from Vifor.

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 September 30, 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 September 30, 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 designation to KORSUVA injection in the anti-pruritic functional category. TDAPA went into effect on April 1, 2022, for a minimum of two years. CMS expressed in its written communication to us and Vifor, 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 commenced in April 2022 and we began recording associated profit-sharing revenues in the second quarter of 2022. As a result of the European Commission's approval of Kapruvia in April 2022, the commercial launch of Kapruvia in the EU commenced in September 2022 in Austria and shortly thereafter in Germany and launches in additional EU countries are planned in the coming months.

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

We expect that our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient to fund our currently anticipated operating plan into the first half of 2024. This guidance assumes KORSUVA injection revenue profit share contribution consistent with what we have reported for the quarter ended September 30, 2022. 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 nine months ended September 30, 2022 and 2021:

	Nine Months Ended September 30,	
	2022	2021
	Dollar amounts in thousands	
Net cash used in operating activities	$ (55,220)	$ (58,842)
Net cash provided by investing activities	84,284	48,830
Net cash provided by financing activities	289	1,320
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 29,353	$ (8,692)

Net cash used in operating activities

Net cash used in operating activities for the nine months ended September 30, 2022 consisted primarily of a net loss of $55.1 million and a $15.8 million cash outflow from net changes in operating assets and liabilities, partially offset by a $15.7 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of an increase in prepaid expenses of $16.0 million, primarily related to an increase in prepaid clinical costs, an increase of $9.6 million in accounts receivable, net – related party relating to amounts due from Vifor from our profit sharing arrangements governing KORSUVA injection sales in the U.S. and for commercial supply of KORSUVA injection to Vifor, and a cash outflow of $1.3 million relating to operating lease liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, partially offset by cash inflows of $10.5 million from an increase in accounts payable and accrued expenses and a decrease of $0.7 million of inventory, net. Net non-cash charges primarily consisted of stock-based compensation expense of $13.9 million, which includes incremental expense of $2.6 million related to the modification of our former CEO’s equity awards in 2021 through the end of the consulting period on June 30, 2022, the amortization expense component of lease expense of $1.1 million relating to our Stamford operating leases, and the amortization of available-for-sale marketable securities, net of $0.5 million.

Net cash used in operating activities for the nine months ended September 30, 2021 consisted primarily of a net loss of $55.1 million and a $17.4 million cash outflow from net changes in operating assets and liabilities, partially offset by a $13.6 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of a $19.8 million increase in other receivables related to the milestone payments due from Vifor and Vifor International, a cash outflow of $3.1 million from a decrease in accounts payable and accrued expenses, and a cash outflow of $1.2 million relating to operating lease liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, partially offset by a decrease in prepaid expenses of $5.8 million, primarily related to an decrease in prepaid clinical costs, and a cash inflow of $0.8 million due to a decrease in income tax receivable. Net non-cash charges primarily consisted of stock-based compensation expense of $12.0 million, the amortization expense component of lease expense of $1.0 million relating to our Stamford operating leases, and the amortization of available-for-sale marketable securities, net of $0.6 million.

Net cash provided by investing activities

Net cash provided by investing activities was $84.3 million for the nine months ended September 30, 2022, which primarily included cash inflows of $162.2 million from maturities of available-for-sale marketable securities, partially offset by cash outflows of $77.9 million for the purchases of available-for-sale marketable securities.

Net cash provided by investing activities was $48.8 million for the nine months ended September 30, 2021, which primarily included cash inflows of $147.7 million from maturities and redemptions of available-for-sale marketable securities and proceeds of $10.0 million from the sales of available-for-sale marketable securities, partially offset by cash outflows of $109.0 million for the purchases of available-for-sale marketable securities.

Net cash provided by financing activities

Net cash provided by financing activities for the nine months ended September 30, 2022 and 2021 consisted of proceeds of $0.3 million and $1.3 million, 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 September 30, 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, other than our net profit-sharing revenue from the sale of KORSUVA injection to third parties in the U.S. by Vifor. This estimate is

subject to uncertainty because we are dependent on Vifor for timely and accurate information regarding the net revenues from sales of KORSUVA injection in the U.S. in accordance with Accounting Standards Update, or ASU, 2014-09, *Revenue from Contracts with Customers (Topic 606)*, as amended by ASU 2016-08, 2016-10, 2016-12 and 2016-20, or ASC 606, to accurately report our results of operations. If we do not receive timely and accurate information or incorrectly estimate activity levels associated with the profit share arrangement at a given point in time, we could be required to record adjustments in future periods (see Note 2 of Notes to Condensed Financial Statements, *Basis of Presentation*, in this Quarterly Report on Form 10-Q).

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

Interest Rate Risk

As of September 30, 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 September 30, 2022, we had invested $136.7 million of our cash reserves in such marketable securities. Those marketable securities included $136.7 million of investment grade debt instruments with a yield of approximately 1.86% 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 September 30, 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 and nine months ended September 30, 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 September 30, 2022, we had $9.6 million in Accounts receivable, net - related party relating to our profit-sharing revenue earned from sales of KORSUVA injection in the U.S. by Vifor and commercial supply of KORSUVA injection to Vifor during the three months ended September 30, 2022. We did not identify any credit risks associated with our licensing partner Vifor during the three months ended September 30, 2022. As a result, we had an insignificant allowance for credit losses as of September 30, 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 September 30, 2022. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of September 30, 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 September 30, 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***

In addition to the risk factors set forth below and the information set forth in this Quarterly Report on Form 10-Q, you should carefully consider our material risk factors disclosed in "Risk Factors" in Part I, Item 1A. *Risk Factors* of our Annual Report on Form 10-K for the year ended December 31, 2021. There have been no material changes to our risk factors as presented in our Annual Report on Form 10-K, other than the risk factors set forth below:

Risks Related to Legal and Compliance Matters

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

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

On October 31, 2019, CMS issued a final rule that revises payment policies and rates under the ESRD PPS for renal dialysis services furnished to beneficiaries on or after January 1, 2020. The final rule also updates the TDAPA. In the final rule, CMS revised ESRD PPS eligibility to focus on innovative drugs and excluded certain drugs from being eligible for the TDAPA. CMS will pay the revised TDAPA adjustment, which is called the Transitional Add-on Payment Adjustment for New and Innovative Equipment and Supplies , or TPNIES, for equipment and supplies that: (1) have been designated by CMS as a renal dialysis service, (2) are new, meaning granted marketing authorization by FDA on or after January 1, 2020, (3) are commercially available by January 1 of the particular calendar year, meaning the year in which the payment adjustment would take effect, (4) have a HCPCS application submitted in accordance with the official Level II HCPCS coding procedures by September 1 of the particular calendar year, (5) are innovative, meaning they meet the substantial clinical improvement criteria specified in the Inpatient Prospective Payment System regulations and related guidance, and (6) are not capital-related assets. TDAPA went into effect on April 1, 2022, for a minimum of two years, for 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.

On November 2, 2020, CMS issued a final rule outlining its payment policies and rates under the ESRD PPS for the 2021 calendar year. In addition to the annual technical updates to the ESRD PPS, the final rule, among other things, expands eligibility under the TPNIES. In particular, the final rule provided for biannual coding cycles for new HCPCS Level II code applications, revised the definition of "new" to be three (3) years beginning on the date of FDA marketing authorization, and expanded eligibility under the TPNIES to include certain home dialysis capital-related assets.

Additionally, in October 2021, CMS issued a final rule that updates the ESRD PPS for calendar year 2022. Further, on June 28, 2022, CMS published a Calendar Year 2023 ESRD PPS proposed rule that would, among others, update Medicare payment policies and rates for renal dialysis services. This proposed rule would rebase and revise ESRD bundled market basket to a 2020 base year, update the labor-related share, change the ESRD PPS methodology for calculating the outlier threshold for adult patients, apply a permanent 5% cap on decreases in the ESRD PPS wage index, and increase the wage index floor. In the proposed rule, CMS also issued a request for information, or RFI, to seek input on potential methodologies to add additional money through an add-on adjustment methodology for certain TDAPA drugs that enter the prospective payment system in an existing functional category. The options included in the RFI, if proposed and ultimately approved through Notice and Comment Rulemaking, could result in the provision of additional payments for KORSUVA injection post-TDAPA. As this is a proposed rule, these provisions have not been implemented and there is no guarantee that CMS will implement this rule as currently drafted or will formally propose a change in policy in the form presented in the RFI. Our failure to maintain coverage and adequate reimbursement for KORSUVA injection in the post-TDAPA timeframe could affect our ability to commercialize KORSUVA injection successfully and could impact our profitability, results of operations, financial condition, and prospects.

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

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

Risks Related to Employee Matters and Managing Growth

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

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act of 2002 and the rules and regulations of The Nasdaq Global Market. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting and we have also been required to have our independent registered public accounting firm issue an opinion on the effectiveness of our internal control over financial reporting on an annual basis as a large accelerated filer. However, based on our public float as of June 30, 2022, we expect to qualify as a non-accelerated filer at the end of this year, which would allow us to forgo the auditor attestation requirement for the fiscal year ending December 31, 2022. However, we have determined to voluntarily comply with the auditor attestation requirement for the fiscal year ended December 31, 2022.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. Further,

we may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. For example, beginning in April 2022, we began recognizing profit-sharing revenue from the sale of KORSUVA injection in the U.S. by Vifor under ASC 606. We are dependent on Vifor for timely and accurate information regarding the net revenues from sales of KORSUVA injection in the U.S. in accordance with ASC 606 to accurately report our results of operations. If we do not receive timely and accurate information or incorrectly estimate activity levels associated with the profit share arrangement at a given point in time, we could be required to record adjustments in future periods. Moreover, our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Moreover, we are aware that the remote working arrangements implemented in connection with the COVID-19 pandemic potentially present additional areas of risk, including cyber, privacy and productivity risks, and we are carefully monitoring any impact to our internal controls and procedures.

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

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

None.

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

None.

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

Not applicable.

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

None.

Item 6. ***Exhibits.***

Exhibit No.	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit No.	Date Filed
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-36279	3.1	February 7, 2014
3.2	Amended and Restated Bylaws.	8-K	001-36279	3.2	February 7, 2014
31.1†	Certification of Chief Executive Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
31.2†	Certification of Chief Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
32.1†*	Certifications of Chief Executive Officer and Chief Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.CAL†	Inline XBRL Taxonomy Extension Calculation Linkbase.				
101.INS†	Inline XBRL Instance Document.				
101.LAB†	Inline XBRL Taxonomy Extension Label Linkbase.				
101.PRE†	Inline XBRL Taxonomy Extension Presentation Linkbase.				
101.SCH†	Inline XBRL Taxonomy Extension Schema Linkbase.				
101.DEF†	Inline XBRL Taxonomy Extension Definition Linkbase Document.				
104†	Cover page interactive data file (formatted as Inline XBRL and contained in Exhibit 101).				

† Filed herewith.

* This certification is 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: November 7, 2022

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

Date: November 7, 2022

By /s/ RYAN MAYNARD
Ryan Maynard
Chief Financial Officer
(Principal Financial and Accounting Officer)

EXHIBIT 31.1

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

I, 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: November 7, 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, Ryan Maynard, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: November 7, 2022

By: /s/ Ryan Maynard
RYAN MAYNARD
CHIEF FINANCIAL OFFICER
(PRINCIPAL FINANCIAL OFFICER)

EXHIBIT 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended September 30, 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 Ryan Maynard, 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: November 7, 2022

/s/ RYAN MAYNARD
Name: Ryan Maynard
Title: Chief Financial Officer
(Principal Financial Officer)
Date: November 7, 2022