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

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 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 August 4, 2022 was: 53,725,925.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2022

PART I –FINANCIAL INFORMATION

PART I
FINANCIAL INFORMATION

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

CARA THERAPEUTICS, INC.

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

	June 30, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 46,718	$ 13,453
Marketable securities	110,794	153,582
Accounts receivable, net - related party	8,003	—
Inventory, net	3,460	2,584
Income tax receivable	697	697
Other receivables	468	455
Prepaid expenses	6,026	2,519
Total current assets	176,166	173,290
Operating lease right-of-use assets	2,278	2,973
Marketable securities, non-current	47,171	69,754
Property and equipment, net	549	631
Restricted cash	408	408
Total assets	$ 226,572	$ 247,056
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 19,332	$ 15,861
Operating lease liabilities, current	1,835	1,755
Total current liabilities	21,167	17,616
Operating lease liabilities, non-current	983	1,918
Commitments and contingencies (Note 16)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at June 30, 2022 and December 31, 2021, zero shares issued and outstanding at June 30, 2022 and December 31, 2021	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at June 30, 2022 and December 31, 2021, 53,710,300 shares and 53,480,812 shares issued and outstanding at June 30, 2022 and December 31, 2021, respectively	53	53
Additional paid-in capital	719,129	708,585
Accumulated deficit	(512,713)	(480,758)
Accumulated other comprehensive loss	(2,047)	(358)
Total stockholders' equity	204,422	227,522
Total liabilities and stockholders' equity	$ 226,572	$ 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		Six Months Ended	
	June 30, 2022	June 30, 2021	June 30, 2022	June 30, 2021
Revenue:				
License and milestone fees	$ 15,000	$ —	$ 15,000	$ 1,192
Collaborative revenue	8,003	—	8,003	706
Commercial supply revenue	—	—	4,790	—
Clinical compound revenue	—	—	—	37
Total revenue	23,003	—	27,793	1,935
Operating expenses:				
Cost of goods sold	—	—	2,081	—
Research and development	19,905	25,225	41,178	44,356
General and administrative	7,570	5,651	16,917	12,016
Total operating expenses	27,475	30,876	60,176	56,372
Operating loss	(4,472)	(30,876)	(32,383)	(54,437)
Other income, net	266	131	428	391
Net loss	$ (4,206)	$ (30,745)	$ (31,955)	$ (54,046)
Net loss per share:				
Basic and Diluted	$ (0.08)	$ (0.61)	$ (0.60)	$ (1.08)
Weighted average shares:				
Basic and Diluted	53,614,668	50,059,984	53,561,161	49,989,379
Other comprehensive loss, net of tax of $0:				
Change in unrealized losses on available-for-sale marketable securities	(324)	(17)	(1,689)	(78)
Total comprehensive loss	$ (4,530)	$ (30,762)	$ (33,644)	$ (54,124)

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

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

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

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Six Months Ended	
	June 30, 2022	**June 30, 2021**
Operating activities		
Net loss	$ (31,955)	$ (54,046)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	10,359	7,608
Depreciation and amortization	126	124
Amortization expense component of lease expense	695	638
Amortization of available-for-sale marketable securities, net	530	384
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	(8,003)	—
Inventory, net	(876)	—
Income tax receivable	—	810
Other receivables	(13)	252
Prepaid expenses	(3,507)	3,781
Accounts payable and accrued expenses	3,471	(3,388)
Operating lease liabilities	(855)	(780)
Net cash used in operating activities	(30,028)	(44,726)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	94,250	80,470
Proceeds from redemptions of available-for-sale marketable securities, at par	—	8,600
Proceeds from sale of available-for-sale marketable securities	—	9,029
Purchases of available-for-sale marketable securities	(31,099)	(63,772)
Purchases of property and equipment	(43)	—
Proceeds from sale of property and equipment	—	70
Net cash provided by investing activities	63,108	34,397
Financing activities		
Proceeds from the exercise of stock options	185	981
Net cash provided by financing activities	185	981
Net increase (decrease) in cash, cash equivalents and restricted cash	33,265	(9,348)
Cash, cash equivalents and restricted cash at beginning of period	13,861	32,091
Cash, cash equivalents and restricted cash at end of period	$ 47,126	$ 22,743

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

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. In 2018, the Company entered into a license agreement with Vifor that provides full commercialization rights of Kapruvia 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, *Collaboration and Licensing Agreements*). In April 2022, Kapruvia was also approved in the UK. The Company expects commercial launch of Kapruvia in certain EU markets in the second half of 2022.

As of June 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 $252,700 under its license and supply agreements for difelikefalin, primarily with Vifor

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International, Vifor, Maruishi Pharmaceutical Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and an earlier product candidate for which development efforts ceased in 2007. In October 2021, the Company received net proceeds of $44,969 from the issuance and sale of 3,282,391 shares of the Company's common stock to Vifor 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 June 30, 2022, the Company had unrestricted cash and cash equivalents and marketable securities of $204,683 and an accumulated deficit of $512,713. 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 $4,206 and $30,745 for the three months ended June 30, 2022 and 2021, respectively, and $31,955 and $54,046 for the six months ended June 30, 2022 and 2021, respectively, and had net cash used in operating activities of $30,028 and $44,726 for the six months ended June 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 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 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-

CARA THERAPEUTICS, INC.

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

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 ongoing 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 June 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

CARA THERAPEUTICS, INC.

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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 June 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.

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

As of June 30, 2022

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 11,033	$ —	$ (32)	$ 11,001
U.S. government agency obligations	9,500	—	(456)	9,044
Corporate bonds	59,053	—	(853)	58,200
Commercial paper	57,846	—	(150)	57,696
Municipal bonds	22,580	—	(556)	22,024
Total available-for-sale marketable securities	$ 160,012	$ —	$ (2,047)	$ 157,965

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

CARA THERAPEUTICS, INC.

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

The following tables summarize the fair value and gross unrealized losses of the Company's available-for-sale marketable securities by investment category and disaggregated by the length of time that individual debt securities have been in a continuous unrealized loss position as of June 30, 2022 and December 31, 2021:

As of June 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	$ 11,001	$ (32)	$ —	$ —	$ 11,001	$ (32)
U.S. government agency obligations	7,123	(377)	1,921	(79)	9,044	(456)
Corporate bonds	53,797	(749)	4,403	(104)	58,200	(853)
Commercial paper	57,696	(150)	—	—	57,696	(150)
Municipal bonds	18,019	(439)	4,005	(117)	22,024	(556)
Total	$ 147,636	$ (1,747)	$ 10,329	$ (300)	$ 157,965	$ (2,047)

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 June 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 June 30, 2022 and December 31, 2021, the Company held a total of 65 out of 65 positions and 58 out of 76 positions, respectively, that were in an unrealized loss position, seven of which had been in an unrealized loss position for 12 months or greater as of June 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

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS
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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 5 out of 5 positions for its U.S. Treasury securities, and 3 out of 3 positions for its U.S. government agency obligations, that were in unrealized loss positions as of June 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 22 out of 22 positions for its corporate bonds, 20 out of 20 positions for its commercial paper, and 15 out of 15 positions for its municipal bonds, that were in unrealized loss positions as of June 30, 2022.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of June 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 June 30, 2022		As of December 31, 2021	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 111,417	$ 110,794	$ 153,631	$ 153,582
One year to three years	48,595	47,171	70,063	69,754
Total	$ 160,012	$ 157,965	$ 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 six months ended June 30, 2022. During the three and six months ended June 30, 2021, the Company sold certain shares of its available-for-sale debt securities with a total fair value of $1,000 and $9,029, respectively, which resulted in no realized gains or losses for the three months ended June 30, 2021, and $39 of realized gains for the six months ended June 30, 2021, respectively.

As of June 30, 2022 and December 31, 2021, accrued interest receivables on our available-for-sale debt securities were $468 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 six months ended June 30, 2022 and 2021, respectively.

	Total Accumulated Other Comprehensive (Loss) Income
Balance, December 31, 2021	$ (358)
Other comprehensive loss before reclassifications	(1,689)
Amount reclassified from accumulated other comprehensive loss	—
Net current period other comprehensive loss	(1,689)
Balance, June 30, 2022	$ (2,047)
Balance, December 31, 2020	$ 73
Other comprehensive loss before reclassifications	(39)
Amount reclassified from accumulated other comprehensive income	(39)
Net current period other comprehensive loss	(78)
Balance, June 30, 2021	$ (5)

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 June 30,		Six Months Ended June 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 June 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 June 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 June 30, 2022 and December 31, 2021.

Fair value measurement as of June 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	$ 46,718	$ 46,718	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	11,001	—	11,001	—
U.S. government agency obligations	9,044	—	9,044	—
Corporate bonds	58,200	—	58,200	—
Commercial paper	57,696	—	57,696	—
Municipal bonds	22,024	—	22,024	—
Restricted cash:				
Commercial money market account	408	408	—	—
Total financial assets	$ 205,091	$ 47,126	$ 157,965	$ —

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 six months ended June 30, 2022 and 2021, respectively. There were no transfers of financial assets into or out of Level 3 classification during the three and six months ended June 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 June 30, 2022, the restricted cash balance for the Stamford Lease was invested in a commercial money market account.

As of June 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.

	June 30, 2022	December 31, 2021
Cash and cash equivalents	$ 46,718	$ 13,453
Restricted cash, long-term assets	408	408
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 47,126	$ 13,861

7. Inventory, net

Inventory, net consists of the following:

	June 30, 2022	December 31, 2021
Raw materials	$ 1,820	$ 927
Work-in-process	639	1,657
Finished goods	1,001	—
Total	$ 3,460	$ 2,584

As of June 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 six months ended June 30, 2022.

8. Prepaid expenses

As of June 30, 2022, prepaid expenses were $6,026, consisting of $3,728 of prepaid R&D clinical costs, $1,467 of prepaid insurance and $831 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:

	June 30, 2022	December 31, 2021
Accounts payable	$ 9,740	$ 5,625
Accrued research projects	4,596	4,648
Accrued compensation and benefits	3,346	4,959
Accrued professional fees and other	1,650	629
Total	$ 19,332	$ 15,861

10. Stockholders' Equity

On June 30, 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 Agreement for a 3% commission on gross proceeds. The common stock will be sold at prevailing market prices at the

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time of the sale, and, as a result, prices may vary. Unless otherwise terminated earlier, the Sales Agreement continues until all shares available under the Sales Agreement have been sold.

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

In 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 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.

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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 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.

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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 three months ended June 30, 2022.

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.

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.

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

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

As of June 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 six months ended June 30, 2022 and 2021:

	Three Months Ended		Six Months Ended	
	June 30, 2022	June 30, 2021	June 30, 2022	June 30, 2021
License and milestone fees				
Vifor	$ 15,000	$ —	$ 15,000	$ —
Maruishi	—	—	—	1,192
Total license and milestone fees	$ 15,000	$ —	$ 15,000	$ 1,192
Collaborative revenue				
Vifor (KORSUVA injection profit sharing)	$ 8,003	$ —	$ 8,003	$ —
Maruishi	—	—	—	706
Total Collaborative revenue	$ 8,003	$ —	$ 8,003	$ 706
Commercial supply revenue				
Vifor (KORSUVA injection)	$ —	$ —	$ 4,790	$ —
Total commercial supply revenue	$ —	$ —	$ 4,790	$ —
Clinical compound revenue				
Maruishi	—	—	—	37
Total clinical compound revenue	$ —	$ —	$ —	$ 37

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

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distinct, and were accounted for as a single performance obligation during the period that the R&D services were rendered (see Note 11, *Collaboration and Licensing Agreements*).

The Company's 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 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*).

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 achieved a $15,000 regulatory milestone payment from Vifor under Vifor Agreement No. 2, which was recorded as license and milestone fees revenue for each of the three and six months ended June 30, 2022. This regulatory milestone payment was considered variable consideration due to the uncertainty of occurrence of this event as specified at inception of the agreement. Therefore, this potential regulatory milestone payment was not included in the transaction price at the inception of the agreement.

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

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 six months ended June 30,

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2022, the Company recorded $8,003 as collaborative revenue for its profit-share from the sales of KORSUVA injection in the U.S.

There was no collaborative revenue recognized under the Maruishi Agreement during the three and six months ended June 30, 2022, or during the three months ended June 30, 2021. During the six months ended June 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 collaboration 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 $4,790 for the six months ended June 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 $2,495 was recognized in March 2022 with associated COGS of $2,081 since these inventory costs were capitalized as inventory subsequent to regulatory approval. There was no commercial supply revenue for the three months ended June 30, 2022.

Clinical compound revenue

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 six months ended June 30, 2022, or during the three months ended June 30, 2021. The Company had clinical compound revenue of $37 during the six months ended June 30, 2021, for the sale of clinical compound to Maruishi.

Contract balances

As of June 30, 2022, the Company recorded accounts receivable, net – related party of $8,003 which related to its profit-sharing revenue from sales of KORSUVA injection in the U.S. by Vifor during the three months ended June 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 June 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 June 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 dilutive. For the three and six months ended June 30, 2022 and 2021, the Company excluded the effects of potentially

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dilutive shares that were outstanding during those respective periods from the denominator as their inclusion would be anti-dilutive due to the Company's net losses during those periods.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Basic:				
Weighted average common shares outstanding	53,614,668	50,059,984	53,561,161	49,989,379
Diluted:				
Weighted average common shares outstanding - Basic	53,614,668	50,059,984	53,561,161	49,989,379
Common stock equivalents*	—	—	—	—
Denominator for diluted net loss per share	53,614,668	50,059,984	53,561,161	49,989,379

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

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Net loss - basic and diluted	$ (4,206)	$ (30,745)	$ (31,955)	$ (54,046)
Weighted-average common shares outstanding:				
Basic and diluted	53,614,668	50,059,984	53,561,161	49,989,379
Net loss per share, Basic and Diluted:	$ (0.08)	$ (0.61)	$ (0.60)	$ (1.08)

As of June 30, 2022, 7,419,027 stock options and 648,450 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 June 30, 2021, 5,995,223 stock options and 409,031 restricted stock units were outstanding, which could potentially dilute basic earnings per share in the future, but were not included in the computation of diluted net loss per share because to do so would have been anti-dilutive as a result of the net loss for the period.

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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 to the Company's interim principal financial officer and principal accounting officer, as a result of his assuming the responsibilities of the Company's former Chief Financial Officer, or CFO, on an interim basis, under the 2014 Plan with a grant date fair value of $7.94

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per share. The restricted stock units vest fully on the earlier of December 31, 2022 or the appointment of the Company's new CFO. As a result, the Company recognizes compensation expense associated with these restricted stock units ratably over the vesting period following the grant date. For the each of the three and six months ended June 30, 2022, the Company recognized $5 of stock compensation expense associated with these awards, all of which was recorded within general and administrative, or G&A, expense. As of June 30, 2022, none of the 7,500 restricted stock units were vested or settled in shares of the Company's common stock.

Pursuant to the Company's non-employee director compensation policy, an aggregate of 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 each of the three and six months ended June 30, 2022, stock compensation expense of $38 was recognized in G&A expense. As of June 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 each of the three and six months ended June 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 six months ended June 30, 2022, no stock compensation expense relating to these restricted stock units was recognized. During the three months ended June 30, 2022, 29,000 of these restricted stock units were forfeited as a result of the resignation of our former CFO in June 2022. As of June 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 six months ended June 30, 2022, the Company recognized $108 and $158, respectively, of stock compensation expense associated with these awards, with $47 recorded in R&D expense and $61 recorded in G&A expense for the three months ended June 30, 2022, and $65 recorded in R&D expense and $93 recorded in G&A expense for the six months ended June 30, 2022. During the three months ended June 30, 2022, 20,000 of these restricted stock units were forfeited as a result of the resignation of our former CFO in June 2022. As of June 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 six months ended June 30, 2022, the Company recognized $82 and $213, respectively, of

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stock compensation expense associated with these awards, with $52 recorded in R&D expense and $30 recorded in G&A expense for the three months ended June 30, 2022, and $104 recorded in R&D expense and $109 recorded in G&A expense for the six months ended June 30, 2022. During the three months ended June 30, 2022, 11,170 of these restricted stock units were forfeited as a result of the resignation of the Company's former CFO in June 2022. As of June 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 six months ended June 30, 2022, stock compensation expense associated with these awards of $149 and $355, respectively, was recognized in G&A expense. As of June 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 three and six months ended June 30, 2022, stock compensation expense associated with these awards of $100 and $239, respectively, was recognized in G&A expense. For each of the three and six months ended June 30, 2021, stock compensation expense of $42 was recognized in G&A expense. As of June 30, 2022, all of the 43,200 restricted stock units vested and were settled in shares of the Company's common stock.

On March 30, 2021, the Compensation Committee approved and granted a total of 176,000 restricted stock units to certain employees under the 2014 Plan with a grant date fair value of $20.59 per share. Vesting of the restricted stock units was contingent on the achievement of certain performance targets related to clinical and regulatory milestones, subject to the recipient's continuous service through each performance target. Recognition of compensation expense associated with these awards begins when, and to the extent, the performance criteria is probable of achievement and the employee has met the service conditions. In February 2022, performance targets relating to 37,999 restricted stock units had been achieved and thus restricted stock units vested and the awards were settled in shares of common stock. For the six months ended June 30, 2022, the Company recognized $729 of stock compensation expense associated with these awards in G&A expense. G&A amounts recorded for the six months ended June 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). As of June 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 June 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 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

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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 six months ended June 30, 2022, the Company recognized $196 and $480, respectively, of stock compensation expense associated with these awards, with $55 recorded in R&D expense and $141 in G&A expense for the three months ended June 30, 2022, and $109 recorded in R&D expense and $371 in G&A expense for the six months ended June 30, 2022. G&A amounts recorded for the three and six months ended June 30, 2022 included $114 and $317, respectively, of stock compensation expense relating to the modification of certain of these restricted stock units on November 1, 2021. For the three and six months ended June 30, 2021, the Company recognized $171 of stock compensation expense, with $55 recorded in R&D expense and $116 in G&A expense. As of June 30, 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 on June 30, 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 has recognized compensation expense associated with these restricted stock units ratably over the one-year vesting period following the grant date. For the three and six months ended June 30, 2021, stock compensation expense of $100 and $239, respectively, was recognized in G&A expense. 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 six months ended June 30, 2021, the Company recognized $1,256 of stock compensation expense relating to the vesting of these restricted stock units, with $524 recorded in R&D expense and $732 in G&A expense. For the three months ended June 30, 2021, no stock compensation expense relating to these restricted stock units were recognized. As of June 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 June 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 the Company's common stock in satisfaction of the first year of vesting. For the three and six months ended June 30, 2022, the Company recognized $175 and $394, respectively, of stock compensation expense associated with these

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awards, with $44 recorded in R&D expense and $131 in G&A expense for the three months ended June 30, 2022, and $87 recorded in R&D expense and $307 in G&A expense for the six months ended June 30, 2022. G&A amounts recorded for the three and six months ended June 30, 2022 included $109 and $264, respectively, of stock compensation expense relating to the modification of certain of these restricted stock units on November 1, 2021. For the three months ended June 30, 2021, the Company recognized $133 of stock compensation expense, with $43 recorded in R&D expense and $90 in G&A expense. For the six months ended June 30, 2021, the Company recognized $265 of stock compensation expense, with $86 recorded in R&D expense and $179 recorded in G&A expense. As of June 30, 2022, 82,001 of the 98,000 restricted stock units vested and were settled in shares of the Company's common stock.

A summary of restricted stock unit activity related to employees and non-employee members of the Company's Board of Directors as of and for the six months ended June 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	(199,018)	17.07
Forfeited	(196,002)	17.06
Outstanding, June 30, 2022	648,450	$ 12.45
Restricted stock units exercisable (vested and deferred), June 30, 2022	—	

Stock Options

Under the 2014 Plan, the Company granted 324,981 and 116,050 stock options during the three months ended June 30, 2022 and 2021, respectively, and 1,302,419 and 789,250 stock options during the six months ended June 30, 2022 and 2021, respectively. No stock options were granted under the 2019 Inducement Plan during the three and six months ended June 30, 2022 and 2021. The fair values of stock options granted during the three and six months ended June 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 June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Risk-free interest rate	2.83% - 3.54%	1.07% - 1.23%	1.70% - 3.54%	0.66% - 1.23%
Expected volatility	77.77% - 81.45%	71.78% - 83.48%	77.77% - 81.93%	71.62% - 83.48%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee and Board options (in years)	6.25	6.25	6.25	6.25

The weighted-average grant date fair value per share of options granted to employees and non-employee members of the Company's Board of Directors for their Board service during the three months ended June 30, 2022 and 2021 was $6.30 and $10.88, respectively, and during the six months ended June 30, 2022 and 2021 was $7.23 and $12.25, respectively. No options were granted to non-employee consultants during the three and six months ended June 30, 2022 and 2021.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Research and development	$ 1,744	$ 1,805	$ 3,661	$ 3,395
General and administrative	1,958	1,225	3,988	2,239
Total stock option expense	$ 3,702	$ 3,030	$ 7,649	$ 5,634

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 $198 in R&D expense and $517 in G&A expense for the three months ended June 30, 2022, and $365 in R&D expense and $1,969 in G&A expense for the six months ended June 30, 2022; (ii) the vesting of certain employees' restricted stock units for $98 in R&D expense and $206 in G&A expense for the three months ended June 30, 2021, and $665 in R&D expense and $1,027 in G&A expense for the six months ended June 30, 2021; (iii) compensation expense relating to the Board of Directors' restricted stock units for $238 and $377 in G&A expense for the three and six months ended June 30, 2022, respectively; and (iv) compensation expense relating to the Board of Directors' restricted stock units for $142 and $281 in G&A expense for the three and six months ended June 30, 2021, respectively.

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

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2021	6,512,280	$ 15.58
Granted	1,302,419	10.21
Exercised	(30,470)	6.09
Forfeited	(293,143)	14.85
Expired	(72,059)	19.42
Outstanding, June 30, 2022	7,419,027	$ 14.67
Options exercisable, June 30, 2022	4,694,573	

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 six months ended June 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 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 during the six months ended June 30, 2022.

During the three and six months ended June 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 $999 and $2,563, respectively, which is included in G&A expense for the three and six months ended June 30, 2022, respectively. Of these total amounts, $776 and $1,679 are included in G&A expense in the stock option compensation expense table above for the three and six months ended June 30, 2022, respectively.

15. Income Taxes

The Company has recognized a full tax valuation allowance against its deferred tax assets as of June 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 six months ended June 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 six months ended June 30, 2021. As of June 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 six months ended June 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-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.

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(unaudited)

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

The Company is also obligated, pursuant to the Enteris License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. Until the second anniversary of the entry into the Enteris License Agreement, the Company has the right, but not the obligation, to terminate its obligation to pay any royalties under the Enteris License Agreement in exchange for a lump sum payment in cash, or the Royalty Buyout. The Company did not exercise its Royalty Buyout right and such right expired in August 2021. During each of the three and six months ended June 30, 2022, no milestone payments or royalties were paid to Enteris by the Company in relation to the Enteris License Agreement. In June 2021, the Company paid a $10,000 milestone payment to Enteris based on a successful End of Phase 2 Meeting with the FDA in April 2021, which was recorded in R&D expense for each of the three and six months ended June 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 materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

CARA THERAPEUTICS, INC.

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

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 June 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 six months ended June 30, 2022 and 2021, $812 of operating lease cost, or lease expense, was recognized, consisting of $568 relating to R&D lease expense and $244 relating to G&A lease expense in both periods.

Other information related to the leases was as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Cash paid for amounts included in the measurement of lease liabilities:				
Operating cash outflows relating to operating leases	$ 487	$ 478	$ 972	$ 954
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ —	$ —	$ —
Remaining lease term - operating leases (years)	1.5	2.5	1.5	2.5
Discount rate - operating leases	7.0 %	7.0 %	7.0 %	7.0 %

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

Year Ending December 31,	
2022 (Excluding the six months ended June 30, 2022)	$ 985
2023	1,992
Total future minimum lease payments, undiscounted	2,977
Less imputed interest	(159)
Total	$ 2,818
Operating lease liabilities reported as of June 30, 2022:	
Operating lease liabilities - current	$ 1,835
Operating lease liabilities - non-current	983
Total	$ 2,818

CARA THERAPEUTICS, INC.

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

17. Related Party Transactions

As of June 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 June 30, 2022 and December 31, 2021 (see Note 11, *Collaboration and Licensing Agreements*).

As of June 30, 2022, amounts due from Vifor of $8,003 relating to the Company's profit-share revenue from sales of KORSUVA injection in the U.S. by Vifor were included within Accounts receivable, net – related party on the Company's Condensed Balance Sheet.

Sales of KORSUVA injection to Vifor of $4,790 were included within Commercial supply revenue on the Company's Condensed Statement of Comprehensive Loss for the six months ended June 30, 2022.

Item 2. ***Management's Discussion and Analysis of Financial Condition and Results of Operations.***

Cautionary Note Regarding Forward-Looking Statements

This Quarterly Report on Form 10-Q contains forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that involve substantial risks and uncertainties. In some cases, you can identify forward-looking statements by the words "aim," "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "seek," "should," "will," or "would," and or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Quarterly Report on Form 10-Q, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain.

The forward-looking statements in this Quarterly Report on Form 10-Q include, among other things, statements about:

- our ability to successfully commercialize KORSUVA™ (difelikefalin) injection, or KORSUVA injection, and Kapruvia® (difelikefalin), our difelikefalin injection product which was granted marketing authorization by the European Commission and the UK, or Kapruvia, including the timing of associated revenues and additional regulatory submissions and approvals, and execute on our marketing plans for any other drugs or indications that may be approved in the future;

- our ability to obtain and maintain coverage and adequate reimbursement for KORSUVA injection;

- the 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, Vifor (International) Ltd., or Vifor International, 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, chronic liver disease associated pruritus, or CLD-aP, including primary biliary cholangitis, or PBC, pruritus associated with atopic dermatitis, or AD-aP, and pruritus associated with notalgia paresthetica, or NP, markets;

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

- 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 ongoing 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 the placebo-controlled phase of a Phase 2 proof-of-concept trial of oral difelikefalin for the treatment of moderate-to-severe pruritus in patients with NP. A Phase 2 proof-of-concept trial in PBC patients with moderate-to-severe pruritus is ongoing.

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. As a result of the approval of Kapruvia by the European Commission in April 2022, we expect commercial launch of Kapruvia in certain European Union, or EU, markets in the second half of 2022.

We have partnered with Vifor, a joint venture between 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). Vifor Pharma Group is a leading nephrology commercial organization with a significant presence in nephrology offices and dialysis centers. We are launching KORSUVA injection into a highly concentrated market. The dialysis market in the U.S. is dominated by two key 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.

We have built a pipeline around an oral formulation of difelikefalin, the active compound in KORSUVA injection. 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 pruritus: advanced NDD-CKD, AD, PBC, and NP.

Based on our completed Phase 2 trials and successful End of Phase 2 meetings with the FDA, we initiated two Phase 3 registrational programs of oral difelikefalin for the treatment of 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). This condition currently has no FDA-approved treatments nor robust data to support the use of any single therapy. In addition, we are conducting a proof-of-concept Phase 2 trial of oral difelikefalin for the treatment of PBC for which we currently anticipate a top-line readout in the second half of 2022.

We were incorporated and commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our lead product and product candidates, including conducting preclinical studies

and clinical trials of difelikefalin-based product candidates and raising capital. To date, we have financed our operations primarily through sales of our equity and debt securities and payments from license agreements.

Recent Developments

KORSUVA Injection Launch Progress

In April 2022, we launched the commercialization of KORSUVA injection in the U.S. through the collaboration with Vifor. The commercial launch is in the early stages. To date, the commercial launch has been progressing as expected, with independent and midsize dialysis organizations driving initial product intake. We anticipate volume sales to accelerate in the coming months driven by large dialysis organizations which started purchasing KORSUVA injection early in the third quarter of 2022. In addition, Vifor has 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.

Vifor Milestone Payment

In April 2022, the European Commission granted marketing authorization to Kapruvia for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adult hemodialysis patients. The marketing authorization approved Kapruvia for use in all member states of the EU, as well as Iceland, Liechtenstein, and Norway. Also in April 2022, Kapruvia was approved in the UK. The commercial launch in Europe is anticipated to commence in the second half of this year.

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 (as defined in *Collaboration and Licensing Agreements – Vifor)* during the three months ended June 30, 2022.

Resignation of Chief Financial Officer

In May 2022, Thomas Reilly, our Chief Financial Officer, or CFO, gave notice of his resignation, effective June 15, 2022, to pursue a new opportunity. We have commenced a search for Mr. Reilly's replacement. Mr. Reilly's departure was not due to a dispute or disagreement with us.

Effective immediately following Mr. Reilly's departure, Richard Makara, our Vice President, Head of Accounting & Controller, assumed Mr. Reilly's responsibilities on an interim basis. As of that date, Mr. Makara assumed the position of our principal financial officer and principal accounting officer until such time as his successor is appointed, or until his earlier resignation or removal.

COVID-19 Update

The extent of the impact of the ongoing 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, has affected, and may in the future affect, 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 continuously evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees, partners and other third-parties with

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

Overview of our Product Candidates

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

Program	Product Candidate	Primary Indication	Status	Commercialization Rights
Pruritus	KORSUVA (difelikefalin) injection	Pruritus CKD - Hemodialysis	• FDA approved in August 2021 • TDAPA application granted in December 2021 by CMS, effective April 2022 • EMA MAA granted in April 2022 (Kapruvia) • UK MAA granted in April 2022 (Kapruvia) • 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	Pruritus Primary Biliary Cholangitis (PBC)	• Phase 2 efficacy trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	Oral difelikefalin	Notalgia Paresthetica (NP)	• Phase 2 efficacy trial completed; top-line data reported	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 in multiple clinical trials.

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, neurological, and dermatological 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 NDA received Priority Review by the FDA, which is granted to therapies that, if approved, would offer significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

KORSUVA injection is the first and only FDA-approved product in the U.S. 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 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 in the U.S.

Our U.S. commercial partner, Vifor Pharma Group, submitted the payment reimbursement application for TDAPA and HCPCS to CMS in September 2021. In December 2021, CMS granted TDAPA 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 Pharma, a continuing interest in engaging with the companies regarding potential post-TDAPA support to ensure all beneficiaries with ESRD have access to innovative products such as KORSUVA injection.

Commercialization of KORSUVA injection in the U.S. 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 our 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 itching intensity numeric rating scale, or NRS, score at week 12 (p= 0.02). The study also met the key secondary endpoint with 41% of patients receiving KORSUVA injection achieving a four-point or greater improvement from baseline in the weekly mean of the daily 24-hour worst itching NRS score at week 12 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 efficacy trial of KORSUVA injection for the treatment of CKD-aP in patients undergoing hemodialysis. 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 itching intensity NRS score at week 12 (p= 0.000019). The study also met all secondary endpoints, including assessment of itch-related quality of life changes measured using self-assessment Skindex-10 (patients receiving KORSUVA experienced 43% improvement 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 itching 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. We expect commercial launch of Kapruvia in these markets to commence in the second half of 2022.

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

Vifor has submitted a marketing application for KORSUVA injection via the Access Consortium (which includes applications to Canada, Switzerland, Australia, and Singapore) in the second quarter of 2021. Decision on this application is expected in the third quarter 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 Stage 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 others with varying degrees of success. There is one product, nalfurafine (Remitch®) marketed by Toray Industries, approved to treat CKD-aP in Japan, but not approved in either the U.S. or Europe.

In December 2019, we announced top-line data from our Phase 2 trial of oral 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 itching 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 itching 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 itching NRS scores vs. placebo after the 12-week treatment period (-4.4 difelikefalin vs. -3.3 placebo, p=0.018). The treatment was statistically significant after two weeks of treatment and sustained through the 12-week treatment period. Regarding secondary endpoints, the proportion of patients on 1 mg tablet strength achieving a 3 point or greater improvement from baseline in the weekly mean of the daily worst itching NRS score at week 12 was 72% vs. 58% for placebo but did not achieve statistical significance. Furthermore, patients on 1 mg 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 studies (U.S. and global study), KICK 1 and KICK 2. Each study is expected to enroll approximately 400 patients, who will be randomized 1:1 to either oral difelikefalin 1 mg once daily or matching placebo. The study population will include adult patients suffering from moderate-to-severe pruritus with advanced CKD in Stages 4 or 5, not on dialysis. The primary endpoint will be the proportion of patients with a ≥4-point improvement at Week 12 from baseline in the worst-itch numerical rating scale, or WI-NRS, after which patients will be re-randomized to either oral difelikefalin or placebo for 52-weeks. We expect to report top-line results in the second half of 2024.

Oral 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 of two studies: KIND 1 and KIND 2 and will investigate the use of oral difelikefalin as adjunctive treatment to topical corticosteroids. The KIND 1 study will be composed of two parts: Part A and Part B.

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

The studies will include adult patients with AD whose 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%.

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 June 2022, we announced top-line 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 approximately 120 adult patients with NP. 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 itching 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 improvement in itch-related quality of life assessed by the change from baseline to Week 8, a change from baseline in itch-related sleep disturbance subscale measured by the itch medical outcomes study at

week 8, and safety assessments. A statistically significantly greater proportion of patients treated with oral difelikefalin achieved a ≥4-point improvement in WI-NRS score at Week 8 vs. placebo (41% difelikefalin vs. 18% placebo, p=0.007).

Oral difelikefalin was generally well tolerated with a safety profile consistent with that seen in earlier clinical trials. The most common treatment-emergent AEs reported in ≥5% of patients treated with oral difelikefalin and greater than placebo were nausea, headache, dizziness, constipation, and increased urine output.

We expect to discuss the outcomes of the KOMFORT trial with the FDA in the second half of 2022 to determine appropriate next steps for this development program.

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 tried off-label, are largely ineffective in treating the disease and/or can produce significant side effects.

We are currently 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 itching NRS score at week 16. We continue to screen patients in this ongoing Phase 2 trial and, primarily due to the ongoing effects of the COVID-19 pandemic on patient enrollment, we currently aim to have top-line data in the second half of 2022.

Collaboration and License Agreements

Vifor (International) Ltd., 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. 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 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 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 three and six months ended June 30, 2022.

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.

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

Under the terms of the Maruishi Agreement, we received a non-refundable and non-creditable upfront license fee of $15.0 million and are eligible to receive up to an aggregate of $10.5 million in clinical development and regulatory milestones (before contractual foreign currency exchange adjustments). In January 2021, we met the milestone criteria, as set forth in the Maruishi Agreement, for Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan. As a result, we received the $2.0 million milestone payment ($1.9 million after contractual foreign currency exchange adjustments) in May 2021. As of June 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 June 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 each of the three and six months ended June 30, 2022, no milestone payments or royalties were paid to Enteris by us in relation to the Enteris License Agreement. 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 research and development, or R&D, expense for each of the three and six months ended June 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

We generate revenue primarily from (1) the receipt of upfront license fees and milestone payments, (2) profit-sharing revenue following our commercial launch of KORSUVA injection in April 2022, (3) commercial supply revenue from Vifor, and (4) clinical compound sales from certain license agreements. Although we have not yet received any royalties or sales-based milestones under any of our collaboration agreements through June 30, 2022, we expect to receive royalty revenue in the future and could receive sales-based milestones in the future in accordance with certain licensing agreements.

To date, we have earned a total of $102.4 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. We expect commercial launch of Kapruvia in certain EU markets in the second half of 2022.

Revenue from sales of KORSUVA injection in future periods is subject to uncertainties and will depend on several factors, including the success of our and our commercial partners' commercialization efforts in the U.S., the number of new patients switching to KORSUVA injection, patient retention and demand, the number of physicians prescribing KORSUVA injection, the rate of monthly prescriptions, reimbursement from third-party payors 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 Pharma, a continuing interest in engaging with the companies regarding potential post-TDAPA support to ensure all beneficiaries with ESRD have access to innovative products such as KORSUVA injection. However, there is no assurance that KORSUVA injection will be able to maintain its price established 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, if approved, could result in the provision of additional post-TDAPA funding. 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 June 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 June 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)

COGS includes costs related to sales of our commercial product, KORSUVA injection, to Vifor. Costs related to the sales of KORSUVA injection are generally recognized upon receipt of shipment by Vifor. Our COGS for KORSUVA injection include the cost of producing commercial product that correspond with commercial supply revenue, such as third-party supply and overhead costs, as well as certain period costs related to freight, packaging, stability, and quality testing. 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.

Through February 2022, we had not recorded any COGS related to our commercial supply revenue as all inventory costs were incurred prior to receipt of regulatory approval of KORSUVA injection and, accordingly, were expensed as incurred. In March 2022, we recorded commercial supply revenue of $2.5 million, with associated COGS of $2.1 million as these inventory costs were incurred subsequent to the receipt of regulatory approval of KORSUVA injection and, accordingly, were capitalized as inventory. There was no commercial supply revenue during the three months ended June 30, 2022. We expect our COGS to increase as Vifor generates additional sales of KORSUVA injection in the future.

Research and Development (R&D)

Our R&D expenses relate primarily to the development of difelikefalin. R&D expenses consist of expenses incurred in performing R&D activities, including compensation and benefits for full-time R&D employees, clinical trial and related clinical manufacturing expenses, third-party formulation expenses or milestone payments, fees paid to CROs and other consultants, stock-based compensation for R&D employees and consultants, and other outside expenses. Our R&D expenses also included expenses related to preclinical activities for our earlier stage programs in prior periods and may include such expenses in the future.

R&D costs are expensed as incurred. Non-refundable advance payments for goods or services to be received in the future for use in R&D activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Most of our R&D costs have been external costs, which we track on a program-by program basis. Our internal R&D costs are primarily compensation expenses for our full-time R&D employees. We do not track internal R&D costs on a program-by-program basis.

R&D activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. Based on our current development plans, we presently expect that our R&D expenses for 2022 will be higher than 2021. However, it is difficult to determine with certainty the duration and completion costs of our current or future nonclinical programs and clinical trials of our product candidates, or if, when or to what extent we will generate revenues from the commercialization and sale of any of our product candidates that obtain regulatory approval. We may never succeed in achieving regulatory approval for any of our product candidates.

The duration, costs and timing of clinical trials and development of our product candidates will depend on a variety of factors including, but not limited to:

- per patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trial is conducted;
- the length of time required to enroll eligible patients;

- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;
- the duration of patient follow-up; and
- the efficacy and safety profile of the product candidate.

In addition, the probability of success for each product candidate will depend on numerous factors, including competition, manufacturing capability and commercial viability. We will determine which programs to pursue and how much to fund each program in response to the scientific and clinical success of each product candidate, as well as an assessment of each product candidate's commercial potential.

General and Administrative (G&A)

General and administrative, or G&A, expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, legal, business development, information technology, or IT, and human resources functions. Other costs include facility costs not otherwise included in R&D expenses, legal fees, insurance costs, investor relations costs, patent costs and fees for accounting and consulting services.

We anticipate that our general and administrative expenses for 2022 will be consistent with 2021 to support our continued R&D activities and for our product candidates. These expenses will likely include costs related to the hiring of additional personnel, fees to outside consultants, lawyers, accountants and investor relations firms. In addition, if oral difelikefalin or any future product candidate obtains regulatory approval for marketing, we expect to incur expenses associated with building a sales and marketing team.

Our license 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 Six Months Ended June 30, 2022 and 2021

Revenue

	Three Months Ended June 30,			Six Months Ended June 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
License and milestone fees	$ 15,000	$ —	N/A	$ 15,000	$ 1,192	1159%
Collaborative revenue	8,003	—	N/A	8,003	706	1034%
Commercial supply revenue	—	—	0%	4,790	—	N/A
Clinical compound revenue	—	—	0%	—	37	-100%
Total revenue	$ 23,003	$ —	N/A	$ 27,793	$ 1,935	1336%

License and milestone fees revenue

License and milestone fees revenue of $15.0 million for the three and six months ended June 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 $1.2 million for the six months ended June 30, 2021 was related to the milestone payment we earned in January 2021 from Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan that was allocated to the license fee performance obligation under the Maruishi Agreement. There was no license and milestone fees revenue for the three months ended June 30, 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).

Collaborative Revenue

Collaborative revenue of $8.0 million for the three and six months ended June 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 six months ended June 30, 2021 was related to the milestone payment we earned in January 2021 from Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan that was allocated to the R&D services performance obligation under the Maruishi Agreement. There was no collaborative revenue for the three months ended June 30, 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).

Commercial Supply Revenue

Commercial supply revenue of $4.8 million for the six months ended June 30, 2022 was related to sales of KORSUVA injection to Vifor. There was no commercial supply revenue during the three months ended June 30, 2022, or during the three and six months ended June 30, 2021 as commercial launch began in April 2022.

Clinical compound revenue

There was no clinical compound revenue for the three and six months ended June 30, 2022, or for the three months ended June 30, 2021. Clinical compound revenue of $37,000 for the six months ended June 30, 2021 was related to the sale of clinical compound to Maruishi.

Cost of Goods Sold (COGS)

	Three Months Ended June 30,			Six Months Ended June 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Cost of Goods Sold	$ —	$ —	0%	$ 2,081	$ —	N/A

COGS of $2.1 million for the six months ended June 30, 2022 was related to commercial supply revenue for KORSUVA injection sales to Vifor. There were no COGS during the three months ended June 30, 2022, or during the three and six months ended June 30, 2021, as commercialization of KORSUVA injection began in April 2022.

Research and Development Expense

	Three Months Ended June 30,			Six Months Ended June 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 10,867	$ 6,718	62%	$ 22,433	$ 16,719	34%
Consultant services in support of clinical trials	1,336	1,059	26%	2,685	2,230	20%
Stock-based compensation	1,942	1,902	2%	4,026	4,060	-1%
Depreciation and amortization	30	31	-3%	61	62	-2%
Other R&D operating expenses	5,730	15,515	-63%	11,973	21,285	-44%
Total R&D expense	$ 19,905	$ 25,225	-21%	$ 41,178	$ 44,356	-7%

For the three months ended June 30, 2022 compared to the three months ended June 30, 2021, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $5.6 million, mainly from increases in startup costs relating to our oral difelikefalin CKD Phase 3 program in non-hemodialysis patients, costs associated with a supportive Phase 1 study, and other general costs associated with our oral programs. These increases were partially offset by decreases of $1.3 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 a $10.0 million milestone earned by Enteris during the three months ended June 30, 2021.

For the six months ended June 30, 2022 compared to the six months ended June 30, 2021, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $8.1 million, mainly from increases in startup costs relating to our oral difelikefalin CKD Phase 3 program in non-hemodialysis patients, costs associated with a supportive Phase 1 study, and other general costs associated with our oral programs. There were also increases of $0.5 million in clinical and manufacturing costs. These increases were partially offset by decreases of $2.4 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 a $10.0 million milestone earned by Enteris during the six months ended June 30, 2021, partially offset by increases in payroll related costs.

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

	Three Months Ended June 30,			Six Months Ended June 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
KORSUVA (difelikefalin) injection - Pruritus	$ 1,700	$ 2,381	-29%	$ 4,803	$ 5,376	-11%
Oral difelikefalin - Pruritus	10,488	5,384	95%	20,499	13,454	52%
Other	—	1	-100%	—	17	-100%
Internal research and development expenses/milestone payments[1]	7,717	17,459	-56%	15,876	25,509	-38%
Total research and development expenses	$ 19,905	$ 25,225	-21%	$ 41,178	$ 44,356	-7%

[1] Includes a milestone payment of $10.0 million to Enteris for each of the three and six months ended June 30, 2021, based on a successful End of Phase 2 Meeting with the FDA in April 2021.

General and Administrative Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 1,469	$ 1,358	8%	$ 3,404	$ 2,235	52%
Stock-based compensation	2,713	1,574	72%	6,333	3,548	79%
Depreciation and amortization	32	31	4%	64	62	2%
Other G&A operating expenses	3,356	2,688	25%	7,116	6,171	15%
Total G&A expense	$ 7,570	$ 5,651	34%	$ 16,917	$ 12,016	41%

For the three months ended June 30, 2022 compared to the three months ended June 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 increase in stock-based compensation expense was primarily related to the modification of our former CEO's equity awards in November 2021 resulting in additional compensation expense of approximately $1.0 million during the three months ended June 30, 2022 for the continuation of the consulting period through June 30, 2022, and additional stock option and time-based restricted stock unit grants to existing employees. The increase in other G&A operating expenses was primarily the result of increases in payroll related costs.

For the six months ended June 30, 2022 compared to the six months ended June 30, 2021, the increase in professional fees and public/investor relations expenses was primarily the result of an increase in consultants' costs, legal fees, 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 six months ended June 30, 2022 for the continuation of the consulting period through June 30, 2022, and additional stock option and time-based restricted stock unit grants to existing employees. The increase in other G&A operating expenses was primarily the result of increases in payroll related costs.

Other Income, Net

	Three Months Ended June 30,			Six Months Ended June 30,		
	2022	2021	% change	2022	2021	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other income, net	$ 266	$ 131	103%	$ 428	$ 391	9%

For the three months ended June 30, 2022 compared to the three months ended June 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 June 30, 2022, partially offset by an increase in net amortization expense of available-for-sale marketable securities during the three months ended June 30, 2022.

For the six months ended June 30, 2022 compared to the six months ended June 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 six months ended June 30, 2022, partially offset by an increase in net amortization expense of available-for-sale marketable securities during the six months ended June 30, 2022 and realized gains on sales of available-for-sale securities and property and equipment during the six months ended June 30, 2021.

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 six months ended June 30, 2021. As of June 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 six months ended June 30, 2022.

We recognized a full valuation allowance against deferred tax assets at June 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 six months ended June 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 June 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 June 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]	$ 2,977	$ 1,974	$ 1,003
Manufacturing purchase obligations[2]	9,893	7,298	2,595
Other obligations[3]	408	—	408
Total	$ 13,278	$ 9,272	$ 4,006

(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, there were no future payments that were considered cash requirements in the table above as of June 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 $4.2 million and $30.7 million for the three months ended June 30, 2022 and 2021, respectively, and $32.0 million and $54.0 million for the six months ended June 30, 2022 and 2021, respectively. As of June 30, 2022, we had an accumulated deficit of $512.7 million. Although we generated net income for the year ended December 31, 2020 as a result of a commercial license transaction, we expect to continue to incur significant expenses and operating and net losses in the foreseeable future, as we and our partner Vifor Pharma 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, PBC, and NP;
- seek regulatory approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any other products for which we may obtain regulatory approval;
- maintain, expand and protect our global intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development and potential future commercialization efforts.

The successful commercialization of KORSUVA injection and 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 ongoing COVID-19 pandemic, introducing additional uncertainty.

Although commercial launch of KORSUVA injection began in the U.S. in April 2022, commercialization of Kapruvia in certain EU markets is expected in the second half of 2022, and our other product candidates are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the commercialization of KORSUVA injection and 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 financial markets in the U.S. and worldwide resulting from the ongoing 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 $870.3 million to fund our operations, including (1) net proceeds of $446.3 million from the sale of shares of our common stock in five public offerings, including our initial public offering; (2) proceeds of $73.3 million from the sale of shares of our convertible preferred stock and from debt financings prior to our initial public offering; (3) payments of $244.7 million under our license and supply agreements, primarily with Vifor, Vifor International, Maruishi, CKDP, and an earlier product candidate for which development efforts ceased in 2007; (4) net profit-sharing revenue of $8.0 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.

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 June 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 June 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 June 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 June 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 Pharma, a continuing interest in engaging with the companies regarding potential post-TDAPA support to ensure all beneficiaries with ESRD have access to innovative products such as KORSUVA injection. Commercial launch of KORSUVA injection 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, we also expect commercial launch of Kapruvia in certain EU markets in the second half of 2022.

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

Outlook

Based on timing expectations and projected costs for our current clinical development plans, which include conducting supportive Phase 1 trials, Phase 2 trials in PBC and NP, and Phase 3 trials in CKD and AD, we expect that our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient for us to fund our currently anticipated operating expenses and capital requirements into the first half of 2024, without giving effect to product revenue we receive from the commercialization of KORSUVA injection or Kapruvia or any potential milestone payments or potential additional product revenue we may receive under our collaboration agreements. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs. Because the process of testing product candidates in clinical trials is costly and the timing of progress in these trials is uncertain, it is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we presently expect.

Cash Flows

The following is a summary of the net cash flows provided by (used in) our operating, investing and financing activities for the six months ended June 30, 2022 and 2021:

	Six Months Ended June 30,	
	2022	2021
	Dollar amounts in thousands	
Net cash used in operating activities	$ (30,028)	$ (44,726)
Net cash provided by investing activities	63,108	34,397
Net cash provided by financing activities	185	981
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 33,265	$ (9,348)

Net cash used in operating activities

Net cash used in operating activities for the six months ended June 30, 2022 consisted primarily of a net loss of $32.0 million and a $9.8 million cash outflow from net changes in operating assets and liabilities, partially offset by a $11.7 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of an increase of $8.0 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., an increase in prepaid expenses of $3.5 million, primarily related to an increase in prepaid clinical costs, an increase of $0.9 million of inventory, net for our commercial supply of KORSUVA injection to Vifor, and a cash outflow of $0.9 million relating to operating lease liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, partially offset by a cash inflow of $3.5 million from an increase in accounts payable and accrued expenses. Net non-cash charges primarily consisted of stock-based compensation expense of $10.4 million, which includes incremental expense related to the modification of our former CEO's equity awards in 2021 of $2.6 million, the amortization expense component of lease expense of $0.7 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 six months ended June 30, 2021 consisted primarily of a net loss of $54.0 million, partially offset by an $8.6 million cash inflow from net non-cash charges and a $0.7 million cash inflow from net changes in operating assets and liabilities. Net non-cash charges primarily consisted of stock-based compensation expense of $7.6 million and the amortization expense component of lease expense of $0.6 million relating to our Stamford operating leases. The change in operating assets and liabilities primarily consisted of a cash inflow of $3.8 million from a decrease in prepaid expenses, primarily related to an decrease in prepaid clinical costs and a cash inflow of $0.8 million due to a decrease in income tax receivable, partially offset by a cash outflow of $3.4 million from a decrease in accounts payable and accrued expenses and a cash outflow of $0.8 million relating to operating lease

liabilities associated with our lease agreements for our operating facility in Stamford, Connecticut, or the Stamford operating leases.

Net cash provided by investing activities

Net cash provided by investing activities was $63.1 million for the six months ended June 30, 2022, which primarily included cash inflows of $94.3 million from maturities of available-for-sale marketable securities, partially offset by cash outflows of $31.1 million for the purchases of available-for-sale marketable securities.

Net cash provided by investing activities was $34.4 million for the six months ended June 30, 2021, which primarily included cash inflows of $89.1 million from maturities and redemptions of available-for-sale marketable securities and proceeds of $9.0 million from the sales of available-for-sale marketable securities, partially offset by cash outflows of $63.8 million for the purchases of available-for-sale marketable securities.

Net cash provided by financing activities

Net cash provided by financing activities for the six months ended June 30, 2022 and 2021 consisted of proceeds of $185,000 and $981,000, respectively, received from the exercise of stock options.

Recent Accounting Pronouncements

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

Critical Accounting Estimates

The preparation of our condensed financial statements and related disclosures in conformity with GAAP and our discussion and analysis of financial condition and results of operations require us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the condensed financial statements and the reported amounts of revenues and expenses during the reporting period. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments, and assumptions. We periodically review our estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates are reflected in the condensed financial statements prospectively from the date of the change in estimate. Note 2 of Notes to Financial Statements, *Summary of Significant Accounting Policies*, in our Annual Report on Form 10-K for the year ended December 31, 2021 describes the significant accounting policies and methods used in the preparation of our condensed financial statements.

We define our critical accounting estimates as those subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply GAAP.

During the three months ended June 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 June 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 June 30, 2022, we had invested $158.0 million of our cash reserves in such marketable securities. Those marketable securities included $158.0 million of investment grade debt instruments with a yield of approximately 0.70% 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 June 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 six months ended June 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 June 30, 2022, we had $8.0 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 during the three months ended June 30, 2022. We did not identify any credit risks associated with our licensing partner Vifor during the three months ended June 30, 2022. As a result, we had an insignificant allowance for credit losses as of June 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 Principal Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of June 30, 2022. Based on such evaluation, our Chief Executive Officer and Principal Financial Officer have concluded that, as of June 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

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. As a result, we revised our internal controls and procedures to review qualitative and quantitative information provided by Vifor to determine whether our profit-sharing revenue for the three months ended June 30, 2022, and future periods, is materially accurate.

There were no changes in our internal control over financial reporting that occurred during the quarter ended June 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 Principal Financial Officer, recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost benefit relationship of possible controls and procedures. Because of the inherent limitations in all control systems, no evaluation of controls and procedures can provide absolute assurance that all control issues and instances of fraud, if any, within Cara Therapeutics, Inc. have been detected.

PART II

OTHER INFORMATION

Item 1. ***Legal Proceedings***

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

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

In addition to 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 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 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, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. KORSUVA 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 United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the 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 are also required to have our independent registered public accounting firm issue an opinion on the effectiveness of our internal control over financial reporting on an annual basis as a large accelerated filer. However, based on our public float as of June 30, 2022, we have qualified as a smaller reporting company as of the last business day of our second fiscal quarter and we expect to qualify as a non-accelerated filer at the end of our fiscal year. We are currently evaluating whether 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 new 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
10.1+	Amended and Restated Non-Employee Director Compensation Policy	10-Q	001-36279	10.1	May 9, 2022
10.2#†	License Agreement by and between Cara Therapeutics, Inc. and Vifor Fresenius Medical Care Renal Pharma Ltd.				
31.1†	Certification of Chief Executive Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
31.2†	Certification of Principal Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
32.1†*	Certifications of Chief Executive Officer and Principal Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.CAL†	Inline XBRL Taxonomy Extension Calculation Linkbase.				
101.INS†	Inline XBRL Instance Document.				
101.LAB†	Inline XBRL Taxonomy Extension Label Linkbase.				
101.PRE†	Inline XBRL Taxonomy Extension Presentation Linkbase.				
101.SCH†	Inline XBRL Taxonomy Extension Schema Linkbase.				
101.DEF†	Inline XBRL Taxonomy Extension Definition Linkbase Document.				
104†	Cover page interactive data file (formatted as Inline XBRL and contained in Exhibit 101).				

+ Indicates management contract or compensatory plan.

Portions of this exhibit (indicated by asterisks) have been omitted because the Registrant has determined they are not material and

are the type that the Registrant treats as private and confidential.

† Filed herewith.

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

SIGNATURES

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

CARA THERAPEUTICS, INC.

Date: August 8, 2022

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

Date: August 8, 2022

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

EXHIBIT 10.2

Certain portions of this exhibit (indicated by "[***]") have been excluded pursuant to Item 601(b)(10) of Regulation S-K because they are both not material and are the type that the registrant treats as private or confidential.

LICENSE AGREEMENT

BY AND BETWEEN

CARA THERAPEUTICS, INC.

AND

VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA LTD.

MAY 17, 2018

LICENSE AGREEMENT

This LICENSE AGREEMENT (the "**Agreement**") is entered into as of May 17, 2018 (the "**Effective Date**"), by and between Cara Therapeutics, Inc., a corporation organized and existing under the laws of Delaware and having an office located at offices at 4 Stamford Plaza,107 Elm Street, 9th Floor Stamford, CT 06902 ("**Cara**"), and Vifor Fresenius Medical Care Renal Pharma Ltd., a corporation organized and existing under the laws of Switzerland and having an office located at Rechenstrasse 37, CH-9014 St. Gallen, Switzerland ("**VFMCRP**").

INTRODUCTION

1. Cara is a biopharmaceutical company focused on, among other things, the discovery, research and development of novel drugs to address unmet medical needs.

2. VFMCRP is a pharmaceutical company focused on renal care that has expertise and resources relating to, among other things, promotion, marketing, sale and distribution of pharmaceutical products useful in treating patients with renal diseases.

3. Cara has developed expertise, technology and intellectual property relating to its drug candidate referred to as CR-845, in intravenous (or I.V.) form, and wishes to license such drug candidate (solely in I.V. form, except as otherwise provided per Section 2.7 below) on an exclusive basis in a specified territory to a company for conducting certain further development, seeking regulatory approval and commercializing such candidate in such territory (with certain limitations on such license rights in the United States, as specified below).

5. VFMCRP desires to obtain such license rights in accordance with the terms of this Agreement.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, and other good and valuable consideration, the receipt of which is hereby acknowledged, Cara and VFMCRP agree as follows:

ARTICLE I

DEFINITIONS

Unless specifically set forth to the contrary herein, the following capitalized terms, when used in this Agreement and whether used in the singular or plural, shall have the respective meanings set forth below:

1.1 "**Accounting Standards**" means, (a) with respect to Cara or its Affiliates, United States generally accepted accounting principles (GAAP), consistently applied, (b) with respect to VFMCRP or its Affiliates, International Financial Reporting Standards (IFRS), and (c) with respect to either Party's Sublicensees/(sub)licensees, GAAP or IFRS, in each case, as such standards exist from time to time, consistently applied throughout the applicable entity or organization.

1.2 "**Affiliate**" means, with respect to an entity, any corporation or other business entity controlled by, controlling, or under common control with the first entity, with term "controlling" (with correlative meanings for the terms "controlled by" and "under common control with") meaning that the applicable entity has direct or indirect beneficial ownership of more than 50% of the voting stock of, or the actual ability (direct or indirect) to direct and control the management and business policies of, the applicable other entity. Notwithstanding the foregoing, the "**Affiliates**" of VFMCRP will not include, FMC or any member of the FMC Group.

1.3 "**Alliance Manager**" means a Party's employee appointed as provided in Section 3.5 to be the primary contact of such Party with respect to Development activities under this Agreement.

1.4 "**API**" means active pharmaceutical ingredient, which is also commonly referred to as drug substance.

1.5 "**Applicable Law**" means all laws, statutes, rules, codes, regulations, orders, judgments or ordinances applicable to a Party in connection with the applicable activities of such Party as contemplated under this Agreement.

1.6 "**Business Day**" means a day that is not a Saturday, Sunday or a day on which national banking institutions in Stamford, Connecticut and in Zurich, Switzerland are authorized by Law to remain closed.

1.7 "**Bundle**" means a treatment protocol for which CMS has either (a) issued a final ruling to include a Licensed Product in the bundled payment under the End-Stage Renal Disease Prospective Payment System for renal dialysis services, or (b) provided written confirmation that CMS considers the Licensed Product to be included as part of the bundled payment under such End-Stage Renal Disease Prospective Payment System.

1.8 "**Bundled Product**" means one or more Licensed Products together with one or more other products that are either (a) packaged together for sale or shipment as a single unit or sold at a single price or (b) marketed or sold collectively as a single product.

1.9 "**Calendar Quarter**" means any of the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 or December 31.

1.10 "**Calendar Year**" means any successive period of twelve (12) consecutive months commencing on a January 1 and ending on the following December 31.

1.11 "**Cara Product Technology**" means all Licensed Patent Rights and Licensed Know-How.

1.12 "**Clinical Trial**" means a human study designed to measure the safety, efficacy, tolerability and appropriate dosage of a Licensed Product or Compound in support of achieving Regulatory Approval of such Licensed Product or Compound, as the context requires, including a phase 1 clinical study, a phase 2 clinical study, a pivotal clinical study or a Phase 3 Study, as applicable, and including, where applicable, post-Regulatory Approval clinical studies, such as "phase 4" trials.

1.13 "**CMS**" means Center for Medicaid & Medicare Services.

1.14 "**Combination Product**" means any Licensed Product that is comprised of two or more APIs, at least one of which is the Licensed Compound.

1.15 "**Commercially Reasonable Efforts**" means, with respect to particular efforts to be expended by a Party with respect to any objective, including, without limitation, Development, seeking Regulatory Approval or Reimbursement Approval, Commercialization and manufacturing of the Licensed Products under the Agreement, those efforts and resources commonly used and applied by a similarly situated pharmaceutical company to conduct similar tasks or obligations for compounds or pharmaceutical products at a similar stage of research, development, commercialization and which are of similar market potential as the Licensed Product and (if applicable) at a similar stage of product life, in each case taking into account the Relevant Factors in effect at the time such efforts are expended.

1.16 "**Commercialization**" or "**Commercialize**" means any activity directed to obtaining pricing or reimbursement approvals, manufacturing, marketing, promoting, distributing, importing, offering to sell or selling a Licensed Product.

1.17 "**Completion**" means, with respect to a Clinical Trial, that all activities that are to be conducted under the complete protocol for such Clinical Trial (including dosing, data collection and study subject follow-up) have been completed for all study subjects to be enrolled in such Clinical Trial, that all data and results of such Clinical Trial have been appropriately recorded and analyzed as provided in the protocol, and the final clinical study report for such Clinical Trial has been prepared in final form and provided to Cara and VFMCRP.

1.18 "**Compound**" means the kappa opioid receptor agonist compound of Cara known as "**CR-845**", having the chemical structure set forth in Exhibit 1.18 of this Agreement, including any salt, known pro-drug (i.e., a chemically modified form of such agonist compound that is designed and intended to be metabolized in a human to become such agonist compound), freebase, partially protonated or deprotonated form, or crystal form of such compound or a stereoisomer thereof.

1.19 "**Competing Product**" means any pharmaceutical product, other than the Licensed Product, that is an agonist of the kappa-opioid receptor and is directed to the inhibition, prevention or treatment of uremic pruritus.

1.20 "**Confidential Information**" means, with respect to a Party, any and all data, results and other Know- How, which may include scientific, pre-clinical, clinical, regulatory, manufacturing, marketing, financial and commercial results, data and other information, that is or was provided or disclosed by such Party (or its Affiliate) to the other Party (or its Affiliate), whether communicated in writing or orally or by any other method, in connection with this Agreement including all such information that was disclosed under the Prior Agreement. Notwithstanding the foregoing, the term "**Confidential Information**" excludes particular information that, in each case as demonstrated by competent written documentation:

(a) is publicly disclosed and made generally available to the public, either before or after it becomes known to the receiving Party, and other than through any act or omission of the receiving Party or its Affiliates in breach of this Agreement;

(b) was known to the receiving Party or its Affiliate, without obligation to a Third Party to keep it confidential, prior to the date of first disclosure by the disclosing Party to the receiving Party;

(c) is subsequently disclosed to the receiving Party or its Affiliate by a Third Party lawfully in possession thereof without obligation to keep it confidential and without a breach of such Third Party's obligations of confidentiality; or

(d) has been independently developed by the receiving Party or its Affiliate without the aid, application or use of the disclosing Party's Confidential Information (the competent written proof of which must be contemporaneous with such independent development).

1.21 "**Control**" means, with respect to any item of or right under Patent Rights or Know-How, that the applicable Party owns or has a license (or sublicense, as applicable) under (other than a license granted by the other Party pursuant to this Agreement) such items or right, and has the actual rights to grant the other Party access to and/or a license or sublicense (as applicable) under such item or right, as provided for in this Agreement, without violating the terms of any agreement or other arrangement with any Third Party existing at the time such Party would be required hereunder to grant the other Party such access or license or sublicense.

1.22 "**Cover**" means (with correlative meanings for the terms "**Covering**" or "**Covered**"), with respect to a compound, composition of matter, formulation, apparatus, article of manufacture, product, technology, process or method (collectively, "**Compositions or Technology**") that, in the absence of ownership of or a license granted under a particular Valid Claim, the manufacture, use, offer for sale, sale or importation of such Compositions or Technology would infringe such Valid Claim, or, in the case of a Valid Claim that has not yet issued, would infringe such Valid Claim if it were to issue.

1.23 "**Default**" means, with respect to a Party, that (a) any material representation and warranty of such Party set forth in this Agreement shall have been untrue in any material respect when made, or (b) such Party shall have failed to perform fully any material obligation of such Party set forth in this Agreement.

1.24 "**Development**" or "**Develop**" means all internal and external research, development prior to receipt of Regulatory Approval in the applicable country, including (as applicable): research, preclinical testing, test method development and stability testing, toxicology, formulation, process development, manufacturing scale-up, development-stage manufacturing, quality assurance/quality control procedure development and performance with respect to clinical materials, statistical analysis and report writing and clinical studies, regulatory affairs, and all other

pre-Regulatory Approval activities. "**Development**" will also include development and regulatory activities for additional forms, formulations or indications for a Licensed Product after Regulatory Approval of such Licensed Product, and clinical trials initiated following receipt of Regulatory Approval, or to be conducted after a Regulatory Approval, that was mandated by the applicable Regulatory Authority as a condition of such Regulatory Approval with respect to an approved indication. When used as a verb, "**Develop**" means to engage in Development.

1.25 "**Development Plan**" means the plan developed by JDC and approved by the JSC, as set forth in Section 4.3, that sets forth the Development activities to be undertaken by Cara and (if applicable) VFMCRP with respect to Licensed Product, and as such plan may be amended or modified in writing by the Parties.

1.26 "**Dollars**" or "$" means the legal tender of the U.S.

1.27 "**EEA**" means, collectively, the countries that are members of the European Union (as redefined from time to time) (the "**EU**"), and member states of the EFTA (European Free Trade Association) such as Iceland, Liechtenstein, Norway and any other country in the European Economic Area European Free Trade Association (EEA-EFTA) in which a centralized marketing authorization issued by the EMA is valid.

1.28 "**EMA**" means the European Medicines Agency, or any successor agency.

1.29 "**FDA**" or "**Food and Drug Administration**" means the United States Food and Drug Administration, or any successor agency thereto.

1.30 "**Field**" means all therapeutic uses relating to the inhibition, prevention or treatment of itch associated with pruritus in hemodialysis and peritoneal-dialysis patients in the Licensed Territory using the Licensed Product.

1.31 "**First Commercial Sale**" means, as to a particular Licensed Product in a country in the Licensed Territory, on a country-by-country and Licensed Product-by-Licensed Product basis, the first sale of such Licensed Product in a bona fide arms-length transaction by or on behalf of VFMCRP or its Affiliate or Sublicensee to a Third Party in such country in exchange for cash or some equivalent to which value can be assigned after such Licensed Product has been granted all necessary Regulatory Approvals by a Regulatory Authority having jurisdiction for such country. First Commercial Sale excludes any sale or other distribution for use in a clinical trial or other Development activity, or for compassionate or named-patient use sold at or below seller's costs.

1.32 "**FMC Group**" means FMC and FMC's Affiliates and FMC US Dialysis Clinics, which for purposes of this Agreement are not considered to be Affiliates of VFMCRP.

1.33 "**FMC**" means Fresenius Medical Care, which for purposes of this Agreement is not considered to be an Affiliate of VFMCRP.

1.34 "**FMC US Dialysis Clinics**" means mean Majority Owned Clinics and Formulary Clinics (in each case, as defined below), and home hemodialysis and peritoneal-dialysis programs administered through Majority Owned Clinics or Formulary Clinics.

For the purposes of this Agreement: (i) "**Majority Owned Clinics**" shall mean all dialysis clinics and home dialysis programs in the U.S. that are Affiliates of FMC; and (ii) "**Formulary Clinics**" shall mean, except as otherwise provided below, all dialysis clinics (including home dialysis programs) in the U.S. that purchase pharmaceutical products under FMC's or FMC's Affiliates' formulary guidelines and all dialysis clinics (including home dialysis programs) for which FMC or its Affiliates provide management or administrative services that include the purchase of pharmaceutical products. For clarity, the Majority Owned Clinics and Formulary Clinics existing on the Effective Date are all listed by name and address on the "**List of FMC US Dialysis Clinics**" document provided to Cara as of just prior to the Effective Date. Notwithstanding the foregoing, the term "**Formulary Clinics**" expressly excludes (except as otherwise agreed by the Parties in writing) all dialysis clinics and home dialysis programs owned or operated by any of the five dialysis providers listed on Exhibit 1.34 of this Agreement or any affiliate of any such provider (and, for clarity, any

sales of Licensed Product by Cara (or its Affiliate) to any such clinics or programs shall not be included in FMC Clinic Sales or in the calculation of "**Net Profit**" hereunder).

1.35 "**Generic Product**" means, with respect to a Licensed Product, any other product sold by a Third Party that (a) contains the same active ingredient (and no other active ingredient(s)) and has regulatory approval for the same use as the Licensed Product, (b) has received marketing approval in the Licensed Territory by reference to any Regulatory Approval for the Licensed Product (or any data therein) and (c) is sold in such country by a Third Party that is not a sublicensee of Licensee or its Affiliates and did not purchase such product in a chain of distribution that included Licensee, its Affiliates or sublicensees.

1.36 "**Good Clinical Practices**" or "**GCP**" means the then-current good clinical practice standards, practices, and procedures promulgated or endorsed by the applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

1.37 "**Good Laboratory Practices**" or "**GLP**" means the then-current good laboratory practice standards, practices, and procedures promulgated or endorsed by the applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

1.38 "**Good Manufacturing Practices**" or "**GMP**" means the then-current good manufacturing practice standards, practices and procedures promulgated or endorsed by the applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

1.39 "**Governmental Authority**" means any United States federal, state or local government agency or authority, or any governmental agency or authority of a country or jurisdiction in the Licensed Territory outside the United States, or political subdivision thereof, or any multinational organization or authority in the Licensed Territory, or any authority, agency or commission entitled to exercise any administrative, executive, judicial, legislative, police, regulatory or taxing authority or power, any court or tribunal (or any department, bureau or division thereof), or any governmental arbitrator or arbitral body.

1.40 "**Improvement**" means any data, results and other Know-How, including any improvements, enhancements or modifications to Compound, Licensed Product, and/or Cara Product Technology, patented or not, that are conceived, reduced to practice or otherwise discovered, generated, invented or developed during the Term by or on behalf of VFMCRP or its Affiliate or Sublicensee, alone or in collaboration with a Third Party (which includes, for clarity, all clinical and study data and results of research or Development conducted by any such party on Compound or Licensed Product), *provided*, *however*, that an Improvement will not include any Invention directed towards any compound (*excluding*, for clarity, the Compound) that is proprietary to Licensee or any Affiliate of Licensee or that is developed by or on behalf of Licensee or any Affiliate of Licensee outside of the scope of this Agreement.

1.41 "**Invention**" means any new and useful method, process, article of manufacture, compound, composition of matter, formulation, apparatus, discovery or finding, or any improvement thereof, that is or may be patentable in at least one country in the Licensed Territory.

1.42 "**Investigator-Sponsored Studies**" (ISS) shall mean research efforts in which the investigator designs and implements the study and the investigator or his/her institution acts as the study sponsor. As the sponsor, the investigator assumes all responsibilities for complying with applicable regulatory requirements. ISS may be supported by Cara or VFMCRP in the form of investigational product, funding, and/or technical input.

1.43 "**Joint Development Committee**" or "**JDC**" means the committee formed by the Parties as provided in Section 3.3, to supervise certain Development of the Licensed Parties by the Parties under this Agreement.

1.44 "**Joint Know-How**" means any Know-How that is jointly made, identified, discovered or created during the Term by at least one employee of Cara or its Affiliate or person contractually required to assign or license such Know-How to Cara and at least one employee of VFMCRP or its Affiliate or person contractually required to assign such Know-How to VFMCRP, but excluding any Improvements.

1.45 "**Joint Patents**" mean all Patent Rights claiming Inventions in Joint Know-How.

1.46 "**Joint Technology**" means Joint Know-How and Joint Patents

1.47 "**Joint Steering Committee**" or "**JSC**" means the committee formed by the Parties as provided in Section 3.1, to oversee the activities of the Parties under this Agreement.

1.48 "**Know-How**" means (a) any scientific or technical results, data and other information of any type whatsoever, in any tangible or intangible form whatsoever, that is not in the public domain, which may include databases, practices, methods, techniques, specifications, formulations, formulae, protein sequences, DNA sequences, knowledge, know-how, skill, experience, test data including pharmacological, medicinal chemistry, biological, chemical, biochemical, toxicological and clinical test data, analytical and quality control data, stability data, studies and procedures, and manufacturing process and development information, results and data, (b) any biological, chemical, or physical material that is not in the public domain or otherwise generally available to the public and (c) any dosage regimens, control assays, product specifications, analytical and quality control data, marketing, pricing, distribution cost and sales data or descriptions that are not in the public domain or otherwise generally available to the public, and including, for clarity, all Inventions.

1.49 "**Licensed Know-How**" means all Know-How that (a) is Controlled by Cara as of the Effective Date or during the Term and (b) is related to the development or use of Licensed Product in the Field.

1.50 "**Licensed Patent Rights**" means all Patent Rights in the Licensed Territory or the U.S. that (a) are Controlled by Cara as of the Effective Date or during the Term, and (b) Cover Licensed Product or its manufacture or method of use in the Field (which includes Cara's rights in applicable Joint Patents).

1.51 "**Licensed Product**" means any intravenous (I.V.) pharmaceutical drug product, including any appropriate IV preparation, formulation, or dosage form thereof, that includes the Compound as at least one API therein.

1.52 "**Licensed Territory**" means all countries in the world excluding the U.S., Japan and South Korea (and subject to Section 10.2(e).

1.53 "**Major Market**" means any of the following territories: (a) the United Kingdom; (b) Germany; (c) Spain; (d) Italy, or (e) France.

1.54 "**NDA**" means (a) a New Drug Application filed with the FDA, or (b) any similar application required for the purpose of marketing or selling or commercially using a drug product filed with a Regulatory Authority in a non-U.S. country or group of countries in the Licensed Territory, including a Product License Application or Marketing Authorization Application ("**MAA**") in the EEA, but excluding Reimbursement Approval applications.

1.55 "**Net Sales**" means the gross amount invoiced for sales (during the applicable period) of Licensed Product in the Licensed Territory by VFMCRP or its Affiliates or Sublicensees to unaffiliated Third Parties, or (as applicable) for sales of Licensed Product by Cara to FMC US Dialysis Clinics based on orders taken by VFMCRP (or its Sublicensee, if applicable) from such FMC US Dialysis Clinics for such Licensed Products, less the following deductions from such amount to the extent actually allowed or incurred with respect to such sales:

(1) [***]

such deductions, in each case, to the extent allowable in calculating net sales in accordance with the Accounting Standards, consistently applied through the selling party's corporate organization.

Net Sales will be determined from books and records of sellers, maintained in accordance with the Accounting Standards, as consistently applied, with respect to sales of any Licensed Product.

[***].

Net Sales will not include [***].

Each of the foregoing deductions shall be permitted if incurred in the ordinary course of business in type and amount consistent with good industry practice and in accordance with the Accounting Standards on a basis consistent with VFMCRP's audited consolidated financial statements.

If Licensed Product is sold other than for cash, the Net Sales on such sale shall be calculated by [***].

In the event that a Licensed Product is sold as part of a Combination Product (which Combination Product has been approved by the Parties, as required in Section 2.1), the Net Sales from such sale of the Combination Product, for the purposes of determining royalty payments, will be determined (a) [***]. In such event, Licensee will in good faith make a determination of the respective fair market values of the Licensed Product and all other API(s) included in the Combination Product, or (b) as otherwise agreed in writing by the Parties.

If a Licensed Product is sold as part of a Bundled Product, then the Seller will [***].

1.56 "**Recognized Agent**" or "**Third Party Distributor**" for the purpose of this Agreement shall mean, with respect to a particular country, any Third Party that is engaged by VFMCRP to distribute Products directly to customers in such country (as permitted under the terms of this Agreement).

1.57 "**Party**" means VFMCRP or Cara individually, and "**Parties**" means VFMCRP and Cara collectively.

1.58 "**Patent Rights**" means patents, patent applications or provisional patent applications, utility models and utility model applications, petty patents, innovation patents, patents of addition, divisionals, continuations, continuation-in-part applications, continued prosecution applications, requests for continued examinations, reissues, renewals, reexaminations and extensions and supplementary protection certificates granted in relation thereto, in any country of the world.

1.59 "**Phase 3 Study**" means a human Clinical Trial conducted in any country in the Licensed Territory on Licensed Product that meets the requirements of 21 CFR §312.21(c), and that, when the results of such trial are combined with the clinical data from other Clinical Trials on Licensed Product completed as of the Completion of such trial, are intended (by sponsor thereof) to be sufficient to be able to prepare and file an NDA with the FDA covering Licensed Product. A Phase 3 Study typically is a large scale clinical study (usually several hundreds of patients) performed after preliminary evidence suggesting effectiveness of the drug has been obtained in phase 2 clinical studies, and it is intended to gather the pivotal information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and, along with other Clinical Trials, to provide an adequate basis for Regulatory Approval.

1.60 "**Phase IV Clinical Trial**" means clinical study of a pharmaceutical product on human subjects commenced after receipt of Regulatory Approval of such pharmaceutical product for the purpose of satisfying a condition imposed by a Regulatory Authority to obtain Regulatory Approval, or to support the marketing of such pharmaceutical product, and not for the purpose of obtaining initial Regulatory Approval of a pharmaceutical product. The term "**Phase IV Clinical Trials**" shall not include Investigator-Sponsored Studies.

1.61 "**Prior Agreement**" means the Confidentiality Agreement between Cara and VFMCRP effective as of September 16, 2016.

1.62 "**Product Trademark**" means the trademark of Cara set forth in Exhibit 1.62 of this Agreement.

1.63 "**Prosecution**" means, with respect to a Patent Right, the preparation, filing, prosecution and maintenance of such Patent Right (and all directly related activities), as well as all activities relating to post grant review proceedings, reexaminations, reissues and the like with respect to such Patent Right, together with the conduct

of interferences, the defense of oppositions and other similar proceedings with respect to the particular Patent Right; the term "**Prosecute**" shall have the correlative meaning.

1.64 "**Regulatory Approval**" means, with respect to a particular Licensed Product in a specific country or regulatory jurisdiction, obtaining the technical, medical and scientific licenses, registrations, authorizations and approvals (including approvals of NDAs and labeling approvals), in each case as necessary under Applicable Law for the promotion or sale of such Licensed Product in such country or regulatory jurisdiction.

1.65 "**Regulatory Authority**" means any applicable Government Authority involved in granting approvals, registrations or licenses for the manufacturing, marketing, selling, reimbursement or pricing of a Licensed Product in the Licensed Territory or any portion thereof, including but not limited to the FDA, EMA and PMDA (in each case as applicable), and any successor governmental authority having substantially the same function.

1.66 "**Reimbursement Approval**" means an approval, agreement, determination or other decision by the applicable Governmental Authority and/or Regulatory Authority that establishes prices charged to end-users for biopharmaceutical products that a Licensed Product will be reimbursed by the Governmental Authorities and/or Regulatory Authorities in the Territory.

1.67 "**Relevant Factors**" means, with respect to a particular activity or obligation of a Party under this Agreement relating to the Development, Regulatory Approval, Reimbursement Approval, Commercialization or manufacturing of a Licensed Product, the applicable of the following factors that likely apply to or affect such activity or obligation (without taking into account any other product or products that such Party may be developing, manufacturing or commercializing): actual issues of safety, efficacy or stability; product profile (including product modality, category and mechanism of action); stage of development or life cycle status; actual projected costs of the applicable development, Regulatory Approval, manufacturing or Commercialization activities (without taking into account any payments under this Agreement); issues regarding the ability to manufacture or have manufactured any Licensed Product; the likelihood of obtaining Regulatory Approvals and the timing of such Regulatory Approvals; the labeling and anticipated labeling of such Licensed Product; present and future market potential of such Licensed Product; existing or projected pricing, sales, reimbursement and profitability of such Licensed Product; pricing or reimbursement changes in the relevant country in the Licensed Territory; and proprietary position, strength and duration of patent protection and anticipated exclusivity of such Licensed Product.

1.68 "**Royalty Term**" means, with respect to a Licensed Product being sold in a particular country or territory in the Licensed Territory, on a Licensed Product-by-Licensed Product and a country-by-country basis, the period commencing on First Commercial Sale of the Licensed Product in such country or territory, and ending on the latest to occur of: (a) the expiration of the last Valid Claim within the Licensed Patent Rights that Covers (i) the composition of matter of the Compound or Licensed Product in such country, or (ii) a method of use of the Compound for which Licensed Product has obtained a Regulatory Approval in such country, (b) expiration of marketing or regulatory exclusivity in such country in the Territory, or (c) the tenth (10th) anniversary of the date of the First Commercial Sale by VFMCRP or any of its Affiliates or Sublicensees of such Licensed Product in such country.

1.69 "**Senior Executive**" means (a) in the case of Cara, the Chief Executive Officer of Cara (or a senior executive officer designated by the Chief Executive Officer of Cara), and (b) in the case of VFMCRP, the Chief Executive Officer of VFMCRP, or such individual's nominated designee who is a member of the applicable Party's senior management with appropriate decision making authority.

1.70 "**Sublicensee**" means any Third Party or other entity that is granted a sublicense under the license rights granted in Section 2.1, 2.2 or 2.3 of this Agreement in compliance with Section 2.4.

1.71 "**Supply Agreement**" means a supply agreement covering manufacture and supply of Licensed Product to VFMCRP, to be negotiated and entered into by the Parties as provided in Section 5.4.

1.72 "**Term**" means the term of this Agreement, as defined in Section 10.1 of this Agreement.

1.73 "**Third Party**" means an entity or person other than Cara, VFMCRP and their respective Affiliates.

1.74 "**U.S.**" means the United States of America, including all its territories.

1.75 "**Valid Claim**" means: (a) a claim of an issued patent that has not expired or been abandoned, and has not been revoked, held invalid or unenforceable by a patent office, court or other governmental agency of competent jurisdiction in a final judgment from which no further appeal can be taken, or (b) a claim within a pending patent application which application has not been pending for more than seven (7) years from the date of its priority filing date and which claim has not been irretrievably revoked, irretrievably cancelled, irretrievably withdrawn, held invalid or abandoned by a patent office, court or other governmental agency of competent jurisdiction in a final judgment from which no further appeal can be taken, or finally determined to be unallowable in a decision from which an appeal cannot or can no longer be taken. For clarity, a claim of an issued patent that ceased to be a Valid Claim before it issued because it had been pending too long, but subsequently issues and is otherwise described by clause (a), shall again be considered to be a Valid Claim once it issues. The same principle shall apply in similar circumstances such as if, for example (but without limitation), a final rejection of a claim is overcome. "**Valid Claim**" does not include any claim in any issued and unexpired Cara Patent in the Territory Covering (i) an alternative manufacturing process to produce the Compound or the Licensed Product, including its components (i.e., a manufacturing process other than the manufacturing process used by or on behalf of Cara or its Affiliate to produce the Compound or the Licensed Product as of the applicable time) or (ii) an Improvement made solely by one or more employees of Licensee or its Affiliates or persons contractually required to assign or license such Improvement (or Patent Covering such Improvement) to Licensee or an Affiliate of Licensee.

1.76 "**VFMCRP Product Technology**" means all Improvements and all Patent Rights and other intellectual property rights that claim or cover or otherwise relate to any Improvements.

1.77 **Additional Definitions.** Each of the following definitions is set forth in the section of this Agreement indicated below:

Defined Term	**Section**
Additional Clinics	1.29
Additional I.V. Indications	2.9
Bankruptcy Code	2.8
Breach Notice	10.2(a)
Cara Indemnitees	9.5
Defaulting Party	10.2(a)
Dispute	11.1
EU	1.22
Europe Diligence Requirement	5.1(b)
Field Infringement	7.4(b)
FKC	2.2(c)
Defined Term	Section
FMC Clinic Sales	6.6
Global Development Program	4.2(a)
Initiating Party	7.4(d)
Jointly-Owned Patent Rights	7.2
Knowledge	9.2
Local Trademark	5.5
Local Trade Dress	7.6
Losses	9.5
MAA	1.42
Mark Infringement	7.5
Non-Defaulting Party	10.2(a)
Non-Europe Diligence Requirement	5.1(b)
Net Profit	6.6
Patent Challenge	10.2(d)
Recognized Agent	1.43

Defined Term	Section
Records	4.5
Royalty Term	6.4(b)
SEC Filing	8.3(c)
Supply Agreement	5.4
Supply Price	5.4
Taxes	6.9
Third Party Claim	9.5
Third Party Distributor	1.43
VAT	6.9(b)
VFMCRP Indemnitees	9.6

1.78 Interpretation. (a) Whenever any provision of this Agreement uses the term "including" (or "includes"), such term will be deemed to mean "including without limitation" and "including but not limited to" (or "includes without limitations" and "includes but is not limited to") regardless of whether the words "without limitation" or "but not limited to" actually follow the term "including" (or "includes"); (b) "herein," "hereby," "hereunder," "hereof" and other equivalent words will refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word is used; (c) all definitions set forth herein will be deemed applicable whether the words defined are used herein in the singular or the plural; (d) wherever used herein, any pronoun or pronouns will be deemed to include both the singular and plural and to cover all genders; (e) the recitals set forth at the start of this Agreement, along with the schedules and exhibits to this Agreement, and the terms and conditions incorporated in such recitals and schedules and exhibits will be deemed integral parts of this Agreement and all references in this Agreement to this Agreement will encompass such recitals and schedules and exhibits and the terms and conditions incorporated in such recitals and schedules and exhibits; *provided that* in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions set forth in the recitals, schedules or exhibits, the terms of this Agreement will control; (f) in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement or otherwise, the terms and conditions of this Agreement will govern; (g) this Agreement will be construed as if both Parties drafted it jointly, and will not be construed against either Party as principal drafter; (h) unless otherwise provided, all references to Sections, Articles and Schedules in this Agreement are to Sections, Articles and Schedules of and to this Agreement; (i) any reference to any federal, national, state, local or foreign statute or law will be deemed to also refer to all rules and regulations promulgated thereunder, unless the context requires otherwise; (j) wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another; (k) the word "or" will not be exclusive; (l) references to a particular person include such person's successors and assigns to the extent not prohibited by this Agreement and (m) the section headings and captions used herein are inserted for convenience of reference only and will not be construed to create obligations, benefits or limitations.

ARTICLE II

GRANTS OF RIGHTS; LIMITATIONS

2.1 Development and Commercialization Licenses to VFMCRP in Territory. Subject to the terms and conditions of this Agreement, Cara hereby grants to VFMCRP an exclusive (even as to Cara), royalty-bearing license in the Licensed Territory, with the right to grant sublicenses as provided in Section 2.5 below, under the Cara Product Technology and its interest in the Joint Technology solely to:

(a) conduct those Development activities allocated to VFMCRP in the Development Plan;

(b) seek Regulatory Approvals for the Commercialization of the Licensed Product in the Field in the Licensed Territory; and

(c) import and export solely into the Licensed Territory, use, distribute, offer for sale, promote, sell and otherwise Commercialize the Licensed Product solely for use in the Field in the Licensed Territory.

Notwithstanding the above license, VFMCRP covenants and agrees that it and its Affiliates and Sublicensees shall not Develop or Commercialize any Combination Product except as agreed by the Parties in writing.

2.2 Manufacture License. Subject to the terms and conditions of this Agreement, Cara hereby grants to VFMCRP a non-exclusive, royalty-free (but subject to payment of all consideration owed by VFMCRP with respect to Development or Commercialization of Licensed Products hereunder) license, with the right to grant sublicenses as provided in Section 2.5 below, under the Cara Product Technology and its interest in the Joint Technology to manufacture and have manufactured the Licensed Products in and outside the Licensed Territory subject to and solely in accordance with Section 5.6 and solely for use in exercising the licenses in Section 2.1.

2.3 Promotion License Rights to VFMCRP in the U.S.

(a) Subject to the terms and conditions of this Agreement, Cara hereby grants to VFMCRP an exclusive (but subject to subsection (b) below) license under the Cara Product Technology and its interest in the Joint Technology in the U.S. solely to promote the Licensed Product to FMC US Dialysis Clinics and to take orders for the Licensed Products solely for sale by Cara to FMC US Dialysis Clinics for use in treating their customers in the Field.

(b) Notwithstanding the license grant in Section 2.3(a) above, Cara retains and shall retain the rights to promote Licensed Product in FMC US Dialysis Clinics, in compliance with the relevant commercialization plan(s) as approved by the JSC.

(c) Nothing in this Agreement will prohibit Fresenius Kidney Care ("**FKC**") or any entity in the FMC Group from including references to Licensed Product or otherwise engaging in customary and routine clinical communications with their respective patient care staff regarding License Product or dosing regimens that include Licensed Product.

2.4 License to Product Trademark. Subject to the other terms and conditions of this Agreement, Cara hereby grants to VFMCRP an exclusive (even as to Cara), royalty-free license in the Licensed Territory, with the right to grant sublicenses as provided in Section 2.5 below, under the Product Trademark solely to promote and otherwise Commercialize the Licensed Product in the Licensed Territory. In exercising the foregoing license, VFMCRP shall comply with all reasonable and typical restrictions and obligations (as provided in writing by Cara) regarding use of the Product Trademark, and quality of the finished Licensed Product (or related promotional or advertising materials) that bear the Product Trademark. Cara shall have the right to inspect samples of Finished Licensed Product (and related promotional or advertising materials) that bear the Product Trademark, to ensure compliance with such restrictions, and VFMCRP agrees to provide such samples on reasonable request, for such purposes.

2.5 Sublicenses.

(a) Subject to the terms of this Agreement, VFMCRP shall have the right to grant sublicenses through multiple tiers, under the rights granted in Section 2.1, 2.2, 2.3 and 2.4 to its Affiliates and to Third Party sub-licensees, with Cara's prior written consent, which shall not be unreasonably withheld, delayed or conditioned, provided that Cara's prior consent shall not be required for VFMCRP to grant such sublicenses to the following entities:

(i) VFMCRP's Affiliates in existence on the Effective Date, as listed in Exhibit 2.5(a) of the Agreement;

(ii) Vifor Pharma's Affiliates in existence on the Effective Date, as listed in Exhibit 2.5(a) of the Agreement;

(iii) FMC and its Affiliates solely to the extent operating as distributors of VFMCRP; and

(iv) The specific Third Parties that are listed in subpart (c) of Exhibit 2.5(a) of the Agreement.

(b) With respect to any such sublicenses granted, the sublicense agreement must be expressly subject to and comply with all terms of this Agreement, and VFMCRP is and shall remain fully responsible for the compliance by all Sublicensees with all terms of the Agreement and for any breach of such terms by any Sublicensee.

2.6 Grantback License to Cara. VFMCRP hereby grants to Cara a worldwide, royalty-free, perpetual, irrevocable, non-exclusive license, with full rights to grant sublicenses through multiple tiers, under the VFMCRP Product Technology and its interest in the Joint Technology: (a) to research, Develop, use, import, offer for sale, sell and have sold and export Compound and Licensed Products outside the Licensed Territory, and (b) to make and have made Licensed Products worldwide, and (c) to conduct Development of Licensed Product in the Licensed Territory as provided in the Development Plan.

2.7 [***]

2.8 Rights Retained by the Parties; License Limitations.

(a) Except as expressly set forth in this Agreement, neither Party shall be granted, acquire or retain any license or other intellectual property interest, by implication or otherwise, in any Confidential Information of the other Party or under any Patent Right or proprietary Know-How in which such other Party or its Affiliates has rights. Without limiting the generality of the foregoing, any of Cara's rights to Cara Product Technology that is not specifically licensed to VFMCRP shall be retained by Cara.

(b) Without limiting the generality of Section 2.8(a) above, Cara retains and shall retain the rights under the Cara Product Technology (i) to make and have made Licensed Product, on a non-exclusive basis (but subject to Section 5.6), in the Licensed Territory for commercial sale of the Licensed Product for use in the Field in or outside the Licensed Territory (in compliance with the terms of this Agreement), (ii) to supply Licensed Products to VFMCRP under the terms of the Supply Agreement (in compliance with the terms of the Supply Agreement) and (iii) to import, distribute promote, sell and otherwise Commercialize the Licensed Product on an exclusive basis outside of the Field either in or outside of the Licensed Territory.

(c) VFMCRP covenants and agrees that, unless otherwise agreed by Cara in writing, VFMCRP shall not assign or otherwise sell or transfer to any Third Party any of the Cara Product Technology and shall not practice or use the Cara Product Technology (including to use, offer for sale or sell Licensed Product for use outside the Field) except as permitted in the license rights (including the rights to sublicense, subject to Section 2.5) expressly granted in Sections 2.1, 2.2, 2.3 and 2.4.

(d) Cara covenants and agrees that, unless otherwise agreed by VFMCRP in writing, Cara shall not assign or otherwise sell or transfer to any Third Party any of the VFMCRP Product Technology and shall not practice or use the VFMCRP Product Technology (including to use, offer for sale or sell Licensed Product for use in the Field in the Licensed Territory) except as permitted in the license rights (including the rights to sublicense) expressly granted in Section 2.6.

2.9 Section 365(n) of the Bankruptcy Code. All rights and licenses granted under or pursuant to any section of this Agreement are and will otherwise be deemed to be for purposes of Section 365(n) of the United States Bankruptcy Code (Title 11, U.S. Code), as amended (the "**Bankruptcy Code**") or any comparable Law outside the United States, licenses of rights to "intellectual property" as defined in Section 101(35A) of the Bankruptcy Code. Each of the Parties will retain and may fully exercise all of its respective rights and elections under the Bankruptcy Code and any comparable Law outside the United States. Each Party agrees that the other Party, as licensee of such rights under this Agreement, will retain and may fully exercise all of its rights and elections under the Bankruptcy Code or any other provisions of Applicable Law outside the United States that provide similar protection for "intellectual property." The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against a Party under the Bankruptcy Code or analogous provisions of Applicable Law outside the United States, the other Party will be entitled to a complete copy of (or complete access to, as appropriate) such intellectual property and all embodiments of such intellectual property, which, if not already in such other Party's possession, will be promptly delivered to it upon such other Party's written request thereof.

2.10 Right of Negotiation. Cara grants to VFMCRP a first right of negotiation to obtain an exclusive license to develop and commercialize Licensed Product in the Licensed Territory in therapeutic uses relating to the prevention or treatment of acute pain in hospital settings (the "**Additional I.V. Indications**"). To exercise such right, VFMCRP shall give Cara written notice of its desire to obtain such license, and such notice shall include its proposed main terms for such license. Upon such exercise of such right by VFMCRP, the Parties shall negotiate exclusively and in good faith the terms of an agreement under which Cara would grant VFMCRP an exclusive license to develop, manufacture and commercialize the Licensed Product in the Additional I.V. Indications in the Licensed Territory, such negotiation for up to [***].

If, after VFMCRP exercises such right, the Parties cannot agree within [***] after such exercise on a term sheet setting forth the main terms of an agreement covering the desired license, then thereafter Cara shall be free to negotiate and enter into any such license agreement(s) with one or more third parties. If the Parties agreed on such term sheet during such [***] period, then the Parties shall negotiate in good faith a license agreement based on such term sheet during a further [***] period, during which Cara shall not be free to negotiate and enter into any such license agreement(s) with one or more third parties, and provided that if the Parties have not entered into such license agreement by the end of such [*** period, then thereafter Cara shall be free to negotiate and enter into any such license agreement(s) with one or more third parties and shall not have any further obligations to VFMCRP with respect to any Additional I.V. Indications.

If Cara or its Affiliates Commercialize, or grant a license to Third Party to Commercialize, a Licensed Product for an Additional I.V. Indication and/or an oral formulation of the Compound in the Licensed Territory, in compliance with the above obligations of this Section 2.10, then the Parties shall agree in good faith on an effective mechanism to (i) seek to prevent off-label sales in each other's respective field (for VFMCRP, in the Field, and for Cara (and its Affiliates and Third Party licensees), outside the Field) in the Licensed Territory of such Licensed Product and (ii) provide adequate compensation to the other Party for off- label sales in its respective field in the Licensed Territory of such Licensed Product. If such an agreement is not reached, the matter will be resolved as provided under Section 11.4.

2.11 Exclusivity.

(a) Exclusive Efforts in the Field. During the Term, and for [***] thereafter, neither Party nor any of its Affiliates will directly, or indirectly through the grant of rights to any Third Party, promote, sell, offer for sale or otherwise commercialize any Competing Product in the Field in the Licensed Territory, without the prior written consent of the other Party, *provided that* the foregoing provisions of this Section 2.11(a) shall have no force or effect (a) in any country of the Licensed Territory where, and to the extent, such provisions contravene any applicable antitrust or antimonopoly law, and (b) with respect to any future Affiliate of either Party that becomes an Affiliate through acquisition (or similar change of control transaction) of such Party, as to any compound or product that is in a development or commercialization program of such Affiliate that exists prior to such acquisition or similar transaction closes.

ARTICLE III

GOVERNANCE - JSC AND JDC

3.1 Formation of Joint Steering Committee. As of the Effective Date, the Parties establish a Joint Steering Committee, which shall have the responsibilities for overall coordination and oversight of the activities of the Parties under this Agreement and (as applicable) the Supply Agreement, including (i) discussing and agreeing on indications in the Field to be pursued in Development; (ii) reviewing, commenting on, and (when acceptable) approving the Development Plan (including any proposed amendments or modifications thereto)); (iii) exchanging appropriate information about the Development and Commercialization of the Licensed Products in the Field outside the Licensed Territory; (iv) reviewing and commenting on commercialization plans for the Licensed Product in the Licensed Territory in the Field; and (v) otherwise reviewing and discussing each Party's activities under this Agreement as needed to ensure efficient and effective progress towards achieving the goals and intention of the Agreement. The JSC can establish additional committees as it deems necessary to manage the business under the Agreement, which committees shall have the responsibilities and authority as designated in writing by the JSC and

shall be subject to the direct oversight and control of the JSC. The JSC may also have such other authority or make such other decisions as may be delegated to the JSC by written agreement of the Parties.

3.2 JSC Membership and Decisions. Promptly after the Effective Date, each Party shall designate, in its sole discretion, at least three(3) employees to serve as members of the JSC, each with the requisite experience and seniority to make decisions on behalf of the Parties with respect to issues falling within the responsibility of the JSC. The JSC shall meet at least once per Calendar Quarter (in person, or by teleconference, if requested by a Party), or as otherwise agreed by the Parties. Promptly following formation of the JSC, each Party shall nominate one of its JSC members as a co-chair of the JSC. The co-chairpersons shall be responsible for agreeing on and circulating to all members of the JSC (a) an agenda for each meeting, at least [***] before each meeting, which agenda shall include all agenda items requested by any member. The co-chairpersons shall also be responsible, on an alternating basis, for preparing reasonably detailed accurate written minutes of each meeting of the JSC, setting forth in reasonable detail all matters discussed and all decisions made and actions taken by the JSC at the meeting, within [***] after the meeting. Each Party may invite a reasonable number of non-voting representatives to attend JSC meetings; provided that such Party provides advance notice to the other Party of such attendance, and such representatives are bound by the confidentiality provisions of this Agreement. The JSC shall make decisions or take actions only with the unanimous consent of the Parties with each Party having collectively one (1) vote. The members of the JSC shall use reasonable efforts to reach agreement on all matters requiring a decision or action by the JSC. If, despite such efforts, agreement on a particular matter cannot be reached by the JSC within [***] after the JSC first considers such matter (or such shorter time as may be reasonable in the circumstances), then either Party shall have the right to refer such issue to the Senior Executives of each Party for discussion and resolution by good faith negotiations during a period of [***]. Any final decision mutually agreed to by the Senior Executives shall be conclusive and binding on the Parties. If such issue has not been resolved by the Senior Officers within such [***] period, then:

(a) Cara shall have the final decision making authority to the extent that such particular matter relates to (i) the Development of the Compound or the Licensed Product anywhere in the world (to the extent that the Development matter may affect the safety profile of the Licensed Product or the Commercialization of the Licensed Product outside of the Licensed Territory, such as potentially negatively affecting the risk/benefit relationship or assessment for the Licensed Product), or (ii) obtaining or maintaining Regulatory Approvals for the Compound or the Licensed Product outside of the Licensed Territory or communicating with Regulatory Authorities outside of the Licensed Territory in regards to the Compound or Licensed Product (subject to such decision will not materially negatively impact the rights granted to VFMCRP under this Agreement), and/or (iii) Commercialization of the Compound or the Licensed Product outside of the Licensed Territory, including reimbursement by governmental and non-governmental payers;

(b) VFMCRP shall have final decision making authority to the extent that such particular matter relates to (i) obtaining or maintaining Regulatory Approvals for the Licensed Product in the Licensed Territory or communicating with Regulatory Authorities in the Licensed Territory in regards to the Compound or Licensed Product, and/or (ii) Commercialization of the Licensed Product in the Licensed Territory, including reimbursement by governmental and non-governmental payers. and

(c) any other matter that is not described in subsection (a) or (b) above shall be deadlocked and neither Party shall have final decision-making authority with respect thereto and such dispute shall be resolved in accordance with the procedures set forth in Article 11. Without limiting the foregoing, the Parties hereby agree that matters explicitly reserved to the consent, approval or other decision-making authority of one or both Parties, as expressly provided in this Agreement, are outside the jurisdiction and authority of the JSC or any subcommittee thereof (including the JDC), including amendment, modification or waiver of compliance with this Agreement.

For clarity, the JSC shall not have any authority to amend, modify or waive the provisions of this Agreement.

3.3 Formation of Joint Development Committee. As of the Effective Date, the Parties establish a Joint Development Committee, which shall have the responsibilities for overall coordination and oversight of the Development activities of the Parties under this Agreement, including (i) coordinating communication and operations regarding the development of, and the making of regulatory filings for the Licensed Products in the Licensed Territory in the Field in order to obtain Regulatory Approvals of Licensed Products in the Licensed Territory in the Field; (ii) preparing the Development Plan (including regulatory filing plans), and any amendments or modifications of the

approved Development Plan for review and approval by the JSC; (iii) discussing and establishing a regulatory strategy (and updates thereto) for Licensed Product, for review and comment and, when acceptable, approval by the JSC; (iv) exchanging appropriate information about the Development of the Licensed Products in the Field in the countries outside the Licensed Territory; (v) reviewing and discussing any regulatory, scientific and medical aspects of Clinical Trials (including, but not limited to Phase IV Clinical Trials) in the Licensed Territory, including but not limited to protocols and synopsis for such Clinical Trials; (vi) reviewing progress reports on Development results and providing direction and comments to the Alliance Managers regarding Development tasks and strategy; and (vii) facilitating the flow of information between the Parties with respect to Development activities being conducted for the Licensed Product, in or outside the Field, that are relevant to the Licensed Territory and facilitating exchange of data and results arising in Clinical Trials of Licensed Products relevant to the Licensed Territory, whether conducted in or outside the Licensed Territory and in the Field. The JDC shall be subject to the direct oversight and control of the JSC. The JDC may also have such other authority or make such other decisions as may be delegated to the JDC by written agreement of the Parties.

3.4 JDC Membership, Meetings and Decisions. Promptly after the Effective Date, each Party shall designate, in its sole discretion, at least three (3) employees to serve as members of the JDC, each with the requisite experience and seniority to make decisions on behalf of the Parties with respect to the Development matters and issues falling within the responsibility of the JDC. The JDC shall meet at least once per Calendar Quarter (in person, or by teleconference, if requested by a Party), or as otherwise agreed by the Parties. Each Party may invite a reasonable number of non-voting representatives to attend JDC meetings; provided that such Party provides advance notice to the other Party of such attendance, and such representatives are bound by the confidentiality provisions of this Agreement. The JDC shall elect a Chair, who shall be responsible for circulating to all members of the JDC (a) an agenda for each meeting, at least [***] before each meeting, which agenda shall include all agenda items requested by any member, and (b) the accurate minutes of each meeting of the JDC, setting forth in reasonable detail all matters discussed and all decisions made and actions taken by the JDC at the meeting, within [***] after the meeting. The JDC shall make decisions or take actions only with the unanimous consent of its members. The members of the JDC shall use reasonable efforts to reach agreement on all matters requiring a decision or action by the JDC. If, despite such efforts, agreement on a particular matter cannot be reached by the JDC within [***] after the JDC first considers such matter (or such shorter time as may be reasonable in the circumstances), then the matter shall be referred to the JSC for discussion and resolution in accordance with Section 3.2.

3.5 Formation of Supply Chain Committee. Within 120 days of the Effective Date, the Parties shall establish a Supply Chain Committee (the "**SCC**"), which shall have the responsibilities for overall coordination and oversight of the manufacturing and supply of Licensed Product under this Agreement, including (i) coordinating communication and operations regarding manufacturing of Licensed Products, and resolving supply chain issues; and (ii) exchanging appropriate information about manufacture and supply chain, both in and outside the Licensed Territory. The SCC shall be subject to the direct oversight and control of the JSC. The SCC may also have such other authority relating to manufacturing and supply chain matters, or make such other related decisions, as may be delegated to the SCC by written agreement of the Parties.

3.6 SCC Membership, Meetings and Decisions. Within 120 days of the Effective Date, each Party shall designate, in its sole discretion, at least three (3) employees to serve as members of the SCC, each with the requisite experience and seniority to make decisions on behalf of the Parties with respect to the manufacturing, supply chain and quality matters and issues falling within the responsibility of the SCC. The SCC shall meet at least once per Calendar Quarter (in person, or by teleconference, if requested by a Party), or as otherwise agreed by the Parties. Each Party may invite a reasonable number of non- voting representatives to attend SCC meetings; provided that such Party provides advance notice to the other Party of such attendance, and such representatives are bound by the confidentiality provisions of this Agreement. The SCC shall elect a Chair, who shall be responsible for circulating to all members of the SCC (a) an agenda for each meeting, at least [***] before each meeting, which agenda shall include all agenda items requested by any member, and (b) the accurate minutes of each meeting of the SCC, setting forth in reasonable detail all matters discussed and all decisions made and actions taken by the JDC at the meeting, within [***] after the meeting. The SCC shall make decisions or take actions only with the unanimous consent of its members. The members of the SCC shall use reasonable efforts to reach agreement on all matters requiring a decision or action by the SCC. If, despite such efforts, agreement on a particular matter cannot be reached by the SCC within [***] after the SCC first considers such matter (or such shorter time as may be reasonable in the circumstances), then the matter shall be referred to the JSC for discussion and resolution in accordance with Section 3.2.

3.7 Alliance Managers. Promptly after the Effective Date, each Party shall appoint one of its employees, who is significantly involved on a managerial level for Development and/or Commercialisation of Licensed Product, as such Party's Alliance Manager with respect to the Development and/or Commercialisation project under this Agreement. The Alliance Managers shall serve coordinate and facilitate day-to-day communication between the Parties about and exchange relevant information and progress on each Party's Development and/or Commercialisation activities hereunder. Each Party shall ensure that its Alliance Manager is reasonably available for meeting or discussions with the other Alliance Manager and cooperates reasonably in all such communications and information exchange.

3.8 Discontinuation of Participation on a Committee. For clarity, Cara's membership in the JSC, JDC or SCC shall be at its sole discretion, as a matter of right and not obligation, for the sole purpose of participation in governance, decision-making, and information exchange with respect to activities within the jurisdiction of the Committee. Cara shall have the right to withdraw, at any time, from membership on any of the JSC, JDC or SCC upon [***] prior written notice to VFMCRP, which notice shall be effective upon the expiration of such [***] period. Following the issuance of such notice: (a) Cara's membership in such committee shall be terminated and (b) each Party shall have the obligation to provide and the right to continue to receive the information it would otherwise be required to provide and entitled to receive under the Agreement and to participate directly with the other Party in discussions, reviews and approvals currently allocated to such committee pursuant to this Article 3. If, at any time following issuance of such a withdrawal notice, Cara wishes to resume participation in the committee, Cara shall notify VFMCRP in writing and, thereafter, Cara's representatives to the committee shall be entitled to attend any subsequent meeting of the committee and to participate in the activities of, and decision-making by, the committee as provided in this Article 3 as if such withdrawal notice had not been issued by Cara pursuant to this Section 3.8. If the JSC, JDC or SCC is disbanded, then any data and information of the nature intended to be shared within such committee hereunder shall thereafter be provided by each Party directly to the other Party.

ARTICLE IV

DEVELOPMENT PROGRAM; REGULATORY MATTERS

4.1 General. The Parties intend to collaborate with respect to clinical development to gain Regulatory Approvals of the Licensed Product by the applicable Regulatory Authorities in the U.S., EU, Switzerland, United Kingdom as well as outside the EU in the Licensed Territory, as provided herein.

4.2 Development Program.

(a) The Parties will collaborate (through the JDC) in defining and agreeing on the details of the development program for the Licensed Product in the Field with the applicable Regulatory Authorities in the U.S. (FDA) as well as in the EU (EMA) (and in applicable other countries in the Licensed Territory), which program (the "**Global Development Program**") will be described in a comprehensive and detailed Development Plan prepared by the JDC and approved by the JSC. Cara shall be responsible, at its own cost, to undertake any clinical and non-clinical development agreed with FDA and EMA and set forth in the Development Plan to gain such Regulatory Approvals of Licensed Product in the U.S. and in the EU for the indications in the Field the JSC determined to pursue. VFMCRP shall on a regular basis be informed about the progress on such Development activities performed by Cara. VFMCRP shall contribute and provide, at its own cost, to Cara VFMCRP's clinical development expertise as reasonably useful for such Development activities. Notwithstanding the foregoing, should Third Party costs associated with Cara's clinical EMA Development exceed $20,000,000, Cara and VFMCRP shall split the Third Party costs in excess of $20,000,000 on a 50%/50% basis (with VFMCRP reimbursing Cara for such excess costs based on invoices for such costs as submitted by Cara, within [***] of each invoice), provided that the Parties shall agree reasonably and in good faith on a reasonable budget for such excess costs, such budget to reflect the actual efforts needed to achieve the goals of such clinical EMA Development, given the circumstances then prevailing. Any and all clinical studies on the Licensed Product to be undertaken in the Field in the Licensed Territory by or on behalf of either Party (or its Affiliate or Sublicensee) shall be jointly developed and discussed between the Parties (through the JDC) and ultimately approved by the JSC, acting reasonably and in good faith, and shall be set forth in detail in the Development Plan.

(b) In the event that a Party desires to conduct local clinical studies in or outside the Licensed Territory to obtain a Regulatory Approval and/or in support of reimbursement for the Licensed Product (that is, studies

that are in addition to those set forth in the Development Plan), then such local clinical study shall be performed (as applicable) by VFMCRP (if needed for the Licensed Territory excluding the US) or by Cara, if needed for outside the Licensed Territory, in each case at such Party's own cost in accordance with an amended Development Plan covering the details of such studies prepared by the JDC and as approved by the JSC. Should the other Party wish to get access to the data resulting from such local clinical studies, then it shall participate by reimbursing [***] of the cost for such local clinical study (provided that it shall in any event have access to and rights to use any safety data or other non-efficacy data required to be reported by such Party to a Regulatory Authority).

(c) If any Clinical Trial proposed to be conducted by VFMCRP is determined by the JSC to be likely to generate efficacy data that will be useful for the Regulatory Approval applications in countries outside the Licensed Territory, other than trials or studies that are part of the Global Development Program, then: (i) if Cara desires to use the resulting data (other than safety data), both Parties shall equally bear the cost for such study. The Parties also shall discuss reasonably and in good faith other Development activities that may be conducted jointly by the Parties together (and co-founded by both Parties), or by VFMCRP alone (funded by VFMCRP) in the Licensed Territory. All such Development activities need prior approval by the JSC, which shall not unreasonably be withheld with the JSC acting in good faith, and which shall be included in the Development Plan.

(d) VFMCRP - through its joint venture partner FMC - shall use Commercially Reasonable Efforts to accelerate the clinical Development process in the U.S.to the largest extent possible, as requested by Cara and consistent with the Development Plan. This includes engaging with Frenova (or the applicable other Affiliate of FMC, as appropriate) to facilitate CRO services. For the avoidance of doubt, Cara shall be liable for any cost and/or expenses charged by Frenova for its CRO services performed for Cara hereunder.

(e) A separate Safety Data Exchange Agreement, on reasonable and typical terms, shall be negotiated and entered into between the Parties, to specify each Party's respective responsibilities for exchanging safety data and information and maintaining safety databases and safety and adverse event reporting obligations.

(f) Upon reasonable request by VFMCRP, with sufficient notice of no less than [***], VFMCRP may conduct an audit of the Clinical Trials systems and data supporting the filing and initial application for Regulatory Approval in the Licensed Territory, such audit to be conducted in compliance with Cara's reasonable confidentiality and regulatory requirements. VFMCRP will bear the cost of the audit. In the event that such audit reveals significant issues and concerns related to non- compliance of processes and validity of data with Applicable Law, then on written notice of such issues and concerns, Cara will use Commercially Reasonable Efforts to solve the noncompliance issues and to inform VFMCRP of the corrective and preventative actions taken.

4.3 Development Plan. The JDC shall be responsible for preparing, and submitting to the JSC for review and comment and, when acceptable, approval, the initial Development Plan, which sets forth in reasonable detail the tasks, timeline and budget for Development activities of Licensed Product under the Global Development Program (including regulatory approvals filing plans), and for preparing, and submitting to the JSC for review and comment and, when acceptable, approval, all subsequent amendments or modifications to the Development Plan, as reasonably needed or appropriate for the Development of Licensed Product consistent with this Agreement. Each Party shall conduct its respective Development activities on Licensed Product in strict accordance with the approved Development Plan, including using Commercially Reasonable Efforts to achieve the timelines set forth therein. The Development Plan shall set forth the tasks to be undertaken by each Party (including relevant technology to be used and materials to be provided) under the Global Development Program, or otherwise as provided in Section 4.2. From time to time, either Party may propose amendments or modifications to the Development Plan as needed based on the progress or results of the Development of Licensed Products, and in such case the JDC shall review in good faith and comment on the proposed amendments or modifications, and if the JDC agrees, shall subject the agreed amendments or modifications to the JSC for review and comment and, if acceptable, approval.

4.4 Conduct of Development.

(a) Each Party shall use diligent Commercially Reasonable Efforts to conduct the Development tasks assigned to it under the Development Plan, with the goal of obtaining Regulatory Approvals in the Licensed Territory (in such countries where it is commercially reasonable to seek such approvals) and in the U.S. as

soon as reasonably possible, with all such efforts in accordance with the Development Plan. Each Party shall comply with Applicable Law (including GLP and/or GCP) in all such efforts.

(b) Each Party shall have the right to engage and utilize the services of appropriate Third Party contractors to perform particular tasks or services under the Development Plan on its behalf with the selection of any such Third Party contractor to be specifically discussed and consulted with the JDC. Any such engagement shall be pursuant to contracts that are fully consistent with this Agreement and protect all rights and interests under this Agreement of each Party. Cara and VFMCRP shall remain at all times fully responsible and liable for its responsibilities and commitments under this Agreement.

(c) Each Party shall keep the other Party reasonably informed of its progress and all data and results of its Development activities under the Agreement.

4.5 Records. Each Party shall maintain, and shall ensure that its Affiliates or Sublicensees involved in any Development activities hereunder maintains, records, in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes, which shall fully and accurately reflect all work done and results achieved in the performance of the Development program hereunder by or on behalf of such party (the "**Records**"), including the procedures, techniques and methodologies used, the progress made, all data, results and any Invention conceived or reduced to practice or otherwise created, made or obtained within the scope of or in connection with such Development program. As part of keeping the Records, each such party shall ensure that all of its personnel, and all of its agents that are involved in the Development program, will keep accurate laboratory notebooks (which may be in electronic form), which laboratory notebooks: (A) shall be duly signed, dated and witnessed; and (B) shall be created and maintained in accordance with its standard operating procedures that the Party reasonably believes will be sufficient to allow for said laboratory notebooks to be used in any proceeding before the United States Patent and Trademark Office or United States courts, in order to establish the date of Invention for any Invention and to defend against a charge of derivation in accordance with the United States patent laws. During the Term, each Party shall, upon reasonable written request by the other, provide to such other Party copies of the Records or (if applicable) a requested part or summary thereof.

4.6 Regulatory Matters.

(a) The JDC shall discuss and establish (and update as needed) a reasonable regulatory strategy for the Licensed Product in the Licensed Territory, consistent with this Agreement, that ultimately shall be submitted to the JSC for review and comment and, when acceptable, approval by the JSC.

(b) VFMCRP shall have primary responsibility and obligation, at its cost, for preparing the EMA dossier for registration in the EU with Cara having the obligation to provide all the content and subject matter expertise required for such registration process at its own cost, consistent with the Global Development Program. Upon completion of the dossier, VFMCRP shall file the dossier with the competent authorities in the EU and be responsible for adaptation of the dossier for other countries of the Licensed Territory.

(c) Subject to any requirements of local legislation to the contrary, the holder of Regulatory Approvals for the Licensed Products in the Licensed Territory (excluding, for clarity, the U.S.) shall be VFMCRP, or its Affiliates or Sublicensees, as applicable. As such, VFMCRP, or its applicable Affiliate or Sublicensee, shall be responsible for the maintenance of all such Regulatory Approvals in the Licensed Territory at its own cost. VFMCRP shall keep Cara fully informed of the progress and results of all regulatory activities for Licensed Products in the Licensed Territory and shall provide to Cara copies of all relevant regulatory filings and material correspondence relating to Licensed Product, including copies of all Regulatory Approval applications (and approvals thereof), in the United Kingdom, France, Italy, Spain, Switzerland, Germany, Canada, Mexico, Australia, Brazil and China. In addition, if requested by Cara based on reasonable needed, VFMCRP shall provide to Cara copies of all relevant regulatory filings and material correspondence relating to Licensed Product, including copies of all Regulatory Approval applications (and approvals thereof), in the other applicable countries in the Licensed Territory. Cara shall use Commercially Reasonable Efforts to support VFMCRP by sharing its Licensed Product related expertise as reasonably needed by VFMCRP for its regulatory activities, and shall participate in regulatory meetings in the Licensed Territory as needed, provided such competent authorities allow for such participation. Cara shall use

Commercially Reasonable Efforts to support, at is own cost, VFMCRP in the maintenance of the Regulatory Approvals obtained in the Licensed Territory.

(d) Cara shall retain full rights for all regulatory activities and interactions outside the Licensed Territory, including preparing, filing, pursuing and maintaining Regulatory Approval applications outside the Licensed Territory and shall own all such Regulatory Approvals for Licensed Product outside the Licensed Territory (including for clarity in the U.S.).

(e) Information Rights Granted to Licensee. Cara will provide access to a complete electronic copy of all relevant filings with Regulatory Authorities covering Licensed Product for use in the Field outside the Licensed Territory that are Controlled by Cara and are necessary or reasonably useful to VFMCRP in support of VFMCRP's preparation and filing of any applications for Regulatory Approvals with respect to Licensed Product for use in the Field in the Licensed Territory in accordance with this Agreement. To the extent not already provided by Cara to VFMCRP, Cara will make available to VFMCRP copies of material documentation related directly to the Compound or Licensed Product, including relevant material research data and reports, material regulatory materials and correspondence (including INDs and MAA(s) in the U.S.), material clinical and nonclinical data, and chemistry, manufacturing and controls ("**CMC**") data (collectively, the "**Clinical Data**") to the extent the applicable such Clinical Data is necessary to conduct clinical studies and/or obtain Regulatory Approvals for Licensed Product in the Licensed Territory for use in the Field, in each case, in accordance with a Development Plan approved or reviewed, as the case may be, by the JSC. VFMCRP and its Affiliates and permitted Sublicensees will be entitled at no cost to access, use and reference the filings made to Regulatory Authorities by Cara, and the applicable Clinical Data, that is provided to VFMCRP by Cara under the above for all uses in the Development and Commercialization of the Compound or Licensed Product in the Licensed Territory, subject to and in accordance with the terms of this Agreement. In furtherance of the foregoing, subject to the rules of the relevant Regulatory Authority and the terms and conditions of this Agreement, Cara hereby grants to VFMCRP a right of reference to any Regulatory Approval that covers Licensed Product for use in the Field outside the Licensed Territory and is Controlled by Cara during the Term (including the right to rely upon and otherwise use all information and data included in the application for such Regulatory Approval and used to support such Regulatory Approval), solely for VFMCRP's or its Affiliates' or its permitted Sublicensees' use in Development and Commercialization of Licensed Product in the Licensed Territory in the Field during the Term in accordance with this Agreement. All such filings with Regulatory Authorities and Clinical Data will be considered Confidential Information of Cara for all purposes of this Agreement including the rights and obligations under Article VIII hereof.

4.7 Changes to Applicable Laws. In the event that following the Effective Date there is a change in the Applicable Laws existing as of the Effective Date with respect to any import or export of pharmaceutical products from Canada into the US, the Parties shall promptly meet and discuss in good faith the consequences of such new Applicable Laws or changes to current Applicable Laws as they relate to the Parties' respective rights and obligations under the License Agreement and endeavor to find a mutual agreement on how to address these consequences (by amendment to this agreement or otherwise) in a manner designed to preserve each Party's respective rights and obligations as such rights and obligations existed prior to the relevant change in Applicable Laws.

4.8 Investigator-Sponsored Studies. The JDC shall establish and implement a policy regarding publications of investigator-sponsored trials of the Licensed Product in the Field in the Licensed Territory, which shall include the ability of the Parties to comment thereon, including without limitation with respect to study design and endpoints, and to request delays to allow the filing of patent applications on any patentable inventions disclosed therein in a manner consistent with Section 7.

4.9 Adverse Drug Events. The Parties will, within 90 days after the Effective Date, finalize and enter into a reasonable and customary Safety Data Exchange Agreement. Such Safety Data Exchange Agreement will provide for the exchange by the Parties of any information that a Party becomes aware of in the Licensed Territory concerning any adverse event in or involving a research patient or subject or, in the case of non-clinical studies, an animal in a toxicology study, and the seriousness thereof, whether or not determined to be attributable to the Compound or any Licensed Product, including any such safety information received by either Party from a Third Party (subject to receipt of any required consents from such Third Party) (such information, the "**Safety Data**"). Cara will own all of the Safety Data, and the Safety Data Exchange Agreement will include provisions requiring the establishment of a global safety database owned and maintained by Cara. It is understood that each Party and its

Affiliates or licensees/sublicensees will have the right to disclose such information if such disclosure is reasonably necessary to comply with applicable laws and regulations and requirements of Regulatory Authorities within its respective territory with respect to its filings and activities related to the Compound and the Licensed Products.

ARTICLE V

COMMERCIALIZATION OF LICENSED PRODUCTS

5.1 Responsibility for Commercialization in the Licensed Territory.

(a) VFMCRP shall have the responsibility and obligation, at its sole expense and using Commercially Reasonable Efforts (subject to subsection (b) below), for the Commercialization (other than manufacturing, to the extent Cara is supplying Licensed Product under the Supply Agreement) of Licensed Products throughout the Licensed Territory, subject to the payment and other relevant obligations under this Agreement. VFMCRP shall conduct, and is responsible for ensuring that its applicable Affiliates and Sublicensees conduct, all such responsibilities and activities subject to and in compliance with the other terms of this Agreement and all Applicable Law. In particular, but without limiting the foregoing, VFMCRP is solely responsible, at its sole cost, for the following activities on Licensed Products in the Licensed Territory: (i) developing and executing a commercial launch and pre-launch plan for Licensed Product Commercialization in the Licensed Territory, which would be reviewed and commented on by the JSC, (ii) marketing and promotion activities; (iii) booking sales and distributing Product and performing related activities; (iv) handling all aspects of order processing, invoicing and collection, inventory and receivables; and (v) providing customer support to all customers and end users in the Licensed Territory.

(b) VFMCRP shall use Commercially Reasonable Efforts to Commercialize the Licensed Product in at least the following countries: (i) within Europe in the United Kingdom, France, Italy, Spain, Switzerland and Germany after receiving required Regulatory Approvals and Reimbursement Approval therefor ("**Europe Diligence Requirement**"), and (ii) outside of Europe in Canada, Mexico, Australia, Brazil and China after receiving required Regulatory Approvals and Reimbursement Approval in these countries ("**Non-Europe Diligence Requirement**"). If VFMCRP determines that it will not seek Regulatory Approval and/or Reimbursement Approval of any Licensed Product in any of the countries set forth in this Section 5.1(b), then VFMCRP will promptly notify Cara of such determination.

5.2 VFMCRP Promotion in U.S. Pursuant to the rights granted in Section 2.2, VFMCRP shall use Commercially Reasonable Efforts to promote sales of Licensed Product to the FMC US Dialysis Clinics and to obtain orders for purchase of the Licensed Product from the FMC US Dialysis Clinics. All such promotion and order-taking efforts shall be consistent with Applicable Law and reasonable promotion and detailing guidelines of Cara. Cara shall be responsible and have sole rights for booking and fulfilling sales of Licensed Product based on orders received by VFMCRP (or its Affiliate or its Sublicensee) from FMC US Dialysis Clinics. Cara shall use Commercially Reasonable Efforts to fulfil all orders for Licensed Product that VFMCRP (or its Affiliate or its Sublicensee) receives from FMC US Dialysis Clinics and submits to Cara. The Parties acknowledge and agree to use commercially reasonable efforts to work together in good faith to establish appropriate market access for Licensed Product in the U.S., including Medicare reimbursement (as a part of the Bundle or otherwise) and reimbursement by other federal or state government payor programs. Cara shall be responsible for leading discussions with federal or state government payors, including but not limited to CMS, regarding reimbursement for Licensed Product sold in the U.S.

5.3 Progress Reports and Reporting. Until the First Commercial Sale of a Product in each Major Market country, VFMCRP shall provide to Cara, within [***] after the end of each Calendar Quarter, a reasonably detailed report that provides reasonably detailed summaries of the activities undertaken in the prior twelve (12) calendar months to Develop the Licensed Products and the results and progress of all such activities and efforts. In addition, VFMCRP shall promptly disclose fully to Cara the discovery, development, invention or creation of any Improvements and other VFMCRP Product Technology and shall transfer copies of such Improvements and other VFCRP Product Technology. VFMCRP agrees to make reasonably available to Cara the VFMCRP project managers with responsibility for managing or overseeing the Development of Licensed Product, no more than [***] each Calendar Year, to discuss the reports and the Development efforts hereunder. After the date that the First Commercial Sale of a Product has occurred in each Major Market country, VFMCRP shall provide to Cara, within [***] after end of each Calendar Year, a reasonably detailed report that provides reasonably detailed summaries of the activities

undertaken in the prior twelve (12) calendar months to Commercialize the Licensed Products in the countries in the Licensed Territory where Regulatory Approval has been obtained) and the results and progress of such activities and efforts. In addition, VFMCRP agrees to make reasonably available to Cara the VFMCRP project managers with responsibility for managing or overseeing the Commercialization of Licensed Product, no more than [***] each Calendar Year, to discuss the reports and the Commercialization efforts hereunder.

5.4 Global Brand Plan; Promotional Materials. Within [***] after the Effective Date, Cara will submit to the JSC, for its review and discussion, a global brand plan, including the key positioning and messaging strategy, for commercialization of the Licensed Product in the Field (the "**Global Brand Plan**"), and Cara shall update such plan annually. VFMCRP will provide Cara with copies of all its material promotional materials for the Licensed Product for use in the United Kingdom, France, Italy, Spain, Switzerland, Germany, Canada, Mexico, Australia, Brazil and China in the Field (and including English translations of such materials (if the original is not in English)), and for use in promoting Licensed Product to FMC Clinics in the United States as permitted herein, for Cara's prior review and approval. VFMCRP will obtain Cara's prior written consent before using any particular promotional materials or information for Licensed Product that have content or messaging that is inconsistent with the approved Global Brand Plan or that is not already included in other VFMCRP promotional materials that have been prior approved by Cara for use by VFMCRP. All promotional, advertising or other marketing materials used by VFMCRP or its Affiliate or Sublicensee shall comply with all Applicable Law.

5.5 Trademark. VFMCRP will Commercialize Licensed Product under the Product Trademarks using the global brand name for such Licensed Product selected by Cara in the Global Brand Plan and under the trade dress set forth in the Global Brand Plan, except to the extent that VFMCRP reasonably believes that the use or registration of any particular Product Trademark in a particular country in the Licensed Territory (i) would be commercially inappropriate due to such country's linguistic or cultural particularities or would violate the Applicable Laws of such country, (ii) is rejected by local Regulatory Authorities or (iii) is in conflict with any Third Party's intellectual property rights in such country. If VFMCRP is unable to use any Product Trademark for the foregoing reasons, then VFMCRP will use one of two alternative trademarks and trade dresses selected by Cara in the Global Brand Plan, or if such alternative trademarks are unacceptable for the reasons set forth in the preceding sentence, then VFMCRP will use another trademark and trade dress to be agreed upon by VFMCRP and Cara acting reasonably (the "**Local Trademarks**"). Cara will own all such Local Trademarks, including all trademark registrations and applications therefor and all goodwill associated therewith. Cara agrees to grant and hereby grants to VFMCRP an exclusive (even as to Cara), royalty-free license in the Licensed Territory, with the right to grant sublicenses as provided in Section 2.5 above, under the Local Trademarks to promote and otherwise Commercialize Licensed Product in the Licensed Territory. Once the brand name for a Licensed Product has been selected for a country pursuant to this Section 5.5, the Party that submits and files the MAA(s) for such Licensed Product in such country will be responsible for obtaining Regulatory Approval of such brand name for use in the Commercialization of such Licensed Product in such country.

5.6 Manufacture and Supply of Licensed Product to VFMCRP. No later than 120 days after the Effective Date of this Agreement, the Parties will discuss and use good faith efforts to agree on the material terms to be included in the Supply Agreement. No later than 120 days before the filing of the NDA for Licensed Product in a country in the Licensed Territory, the Parties will enter into a supply agreement for the commercial supply to VFMCRP of the Licensed Products that contains standard and customary terms for commercial supply arrangements (the "**Supply Agreement**"), which Supply Agreement will include those material terms on which the Parties have agreed pursuant to this Section. The supply price for the Licensed Products supplied by Cara to VFMCRP pursuant to the Supply Agreement will be equal to Cara's COGS (calculated according to U.S. GAAP) plus [***] (but without allocation of idle costs)) (the "**Supply Price**") and the term of the Supply Agreement will be coterminous with the Term of the Agreement. The Parties acknowledge and agree that they shall discuss in good faith the best solution for the supply chain, taking into account the interests of both Parties (which may include the supply of bulk products and the right for VFMCRP to package and label the Licensed Products for the Licensed Territory (excluding for clarity the U.S.)). The Supply Agreement shall provide that, after the end of the Term (other than due to early termination of the Agreement), Cara shall continue to supply VFMCRP with Product (on a non-exclusive basis) under the terms of the Supply Agreement to ensure supply continuity until VFMCRP has either set up its own manufacturing capacity or the Parties have agreed on terms for continued supply by Cara after the Term. For clarity, VFMCRP shall not exercise the manufacturing license under Section 2.2, unless the Parties fail to enter into the Supply Agreement, or as otherwise provided in the Supply Agreement with respect to failure of Cara to supply on a timely basis material amounts of Compound or Licensed Product ordered under the Supply Agreement. The Parties will also enter into a reasonable

and customary Quality Agreement. Such Quality Agreement will establish each Party's manufacturing activities as well as responsibilities relating to recalls and withdrawals of Licensed Products.

ARTICLE VI

PAYMENTS; ROYALTIES AND REPORTS

6.1 Initial License Payment. Upon execution of this Agreement, VFMCRP shall make a non-refundable, non- creditable cash payment of fifty million U.S. dollars (USD $50,000,000) to Cara.

6.2 Purchase of Cara Equity. As part consideration for the rights granted hereunder, an Affiliate of VFMCRP (Vifor (International) Ltd.) is purchasing shares of Cara common stock pursuant to the Stock Purchase Agreement entered into by the Cara and such Affiliate concurrently with this Agreement. The Parties agree that the rights granted by Cara to VFMCRP under this Agreement are contingent upon closing of such equity purchase by Vifor (International) Ltd.) under such Stock Purchase Agreement.

6.3 Milestone Payments. Subject to Section 6.5, VFMCRP shall pay to Cara the milestone payment amounts set forth in the tables below within [***] after the achievement of the corresponding milestone event. Each such payment shall be made by wire transfer of immediately available funds into an account designated by Cara. Except as set forth in Section 6.5, each such payment is nonrefundable and non-creditable against any other payments due hereunder. For the avoidance of doubt, each such payment will only be payable one time upon the occurrence of the indicated event in the Licensed Territory unless otherwise indicated, and VFMCRP will not be obligated to pay any milestone payment more than once unless otherwise indicated.

(a) Approval Milestones.

Milestone Event	**Milestone Payment**
[***]	[***]
[***]	[***]

(b) Sales Milestones in the Licensed Territory.

Milestone Event	**Milestone Payment**
(i) Annual Net Sales exceed [***] in the Licensed Territory	[***]
(ii) Annual Net Sales exceed [***] in the Licensed Territory	[***]
(iii) Annual Net Sales exceed [***] in the Licensed Territory	[***]
(iv) Annual Net Sales exceed [***] in the Licensed Territory	[***]
(v) Annual Net Sales exceed [***] in the Licensed Territory	[***]
(vi) Annual Net Sales exceed [***] in the Licensed Territory	[***]
(vii) Annual Net Sales exceed [***] in the Licensed Territory	[***]

For the avoidance of doubt, any sales made by Cara to FMC US Dialysis Clinics shall not be included in the calculation of Annual Net Sales.

6.4 Royalties. In part consideration of rights granted to VFMCRP and obligations undertaken by Cara hereunder, VFMCRP shall pay to Cara royalties on Net Sales of Licensed Products sold in the Licensed Territory as provided in this Section 6.4:

(a) Royalty Rate. VFMCRP shall pay to Cara royalties on the Net Sales of all Licensed Products sold in the Licensed Territory at the applicable of following incremental royalty rates, depending on the amount of such Net Sales in the applicable Calendar Year:

Amount of Net Sales in Licensed Territory During Calendar Year	**Royalty Rate Applicable to Net Sales Tier**
Amount of Net Sales less than $[***] during the Calendar Year	[***]%
Amount of Net Sales greater than $[***] but less than $[***] during the Calendar Year	[***]%
Amount of Net Sales greater than $[***] but less than $[***] during the Calendar Year	[***]%
Amount of Net Sales greater than $[***] but less than $[***] during the Calendar Year	[***]%
Amount of Net Sales greater than $[***] during the Calendar Year	[***]%

For example, if there is $[***] in aggregate annual Net Sales during the Royalty Term in the Licensed Territory in a given calendar year, after conversion to Dollars of the Net Sales in each country in the Licensed Territory, VFMCRP will owe a royalty of [***].

(b) Royalty Terms. VFMCRP's royalty obligations to Cara under this Section 6.4 shall be in effect during the Royalty Terms. Upon expiration of the Royalty Term for a Licensed Product in a country, the license under Section 2.1 shall thereafter be fully paid-up, non-exclusive, perpetual, and irrevocable under the relevant Cara Product Technology and its interests in the Joint Technology solely for such Licensed Product in such country in the Field; and provided that, for clarity, sales of such Licensed Product in other countries where the applicable Royalty Term(s) has not expired shall continue to be royalty- bearing, notwithstanding the foregoing limited license. For the sake of clarity, no multiple royalties shall be payable because more than one Valid Claim or more than one Patent Right in the Cara Product Technology is applicable to the Licensed Product (or its use) during the applicable Royalty Term.

(c) Third Party Royalties. If VFMCRP, or its Affiliate or Sublicensee, is required to pay third party royalty payments (directly to a Third Party) based directly on the sale of Licensed Product in a country in the Licensed Territory in consideration for a license from such Third Party under relevant patents owned or controlled by such Third Party that claim the composition of matter of the License Product, or method of use of the Licensed Product in the Field, or the Compound as a "product by process" using the manufacturing method that is used (as of the applicable time) by Cara to manufacture Compound, and that in the absence of a license thereunder would be infringed by the sale, offer for sale, use, or import of the Licensed Product in the Field in the applicable country in the Licensed Territory, then VFMCRP shall be entitled to credit [***] of such portion of such third party royalty payments against any Royalty payments due under this Section 6.4 with respect to the Net Sales of the applicable Licensed Product in such country to which such royalty payment to such Third Party pertains; provided, however, in no event shall the Royalty payment to Cara under this Section 6.4 for sales of such applicable Licensed Product be reduced by more than [***] of the royalty amount otherwise owed under Section 6.3(a) for such Licensed Product sales. For the purposes of determining if a royalty is required, reference shall be to the Licensed Product as supplied by Cara, and not to the Licensed Product as it may finally be labeled or packaged.

(d) Generic Sales. If, in any country or region (e.g., EU) in the Licensed Territory, (a) one or more Generic Products being sold in such country or region achieves during [***] Calendar Quarters a market share (calculated on a units basis) for use in the Field in the aggregate equal to or higher than [***] of the total unit sales of Licensed Products sold in such country or region, then the Royalty payments with respect to the relevant Licensed Product in such country or region shall thereafter be reduced by [***].

(e) Joint Patent/Joint Improvement Valid Claim Reduction. On a country by country basis, in the event that the last to expire Valid Claim in a particular country in the Licensed Territory that would, but for the licenses granted hereunder, be infringed by the making, using, selling or importing of a Licensed Product in such country is a claim of a Joint Patent or a Patent claim Covering an Improvement made jointly by at least one employee of Cara or its Affiliate or person contractually required to assign or license such Invention to Cara, and at least one employee of Licensee or its Affiliate or person contractually required to assign or such Invention to Licensee, then in each subsequent calendar quarter royalty payments on Net Sales attributable to such Licensed Product in such country (based on the royalty rate applicable under Section6.4(a) before taking into any reduction) will be reduced by [***].

(f) Blended Rates. The Parties acknowledge and agree that the Licensed Patent Rights and the Licensed Know-How licensed under this Agreement may justify royalty rates and/or Royalty Terms of differing amounts for sales of Products, which rates could be applied separately to Licensed Products involving the exercise of Licensed Patent Rights and/or the incorporation of Licensed Know-How, and that if such royalties were calculated separately, royalties relating to the Licensed Patent Rights and royalties relating to the Licensed Know-How would last for different terms. The Parties have determined in light of such considerations and for reasons of mutual convenience that blended royalty rates for the Licensed Patent Rights and the Licensed Know-How licensed hereunder will apply during a single Royalty Term (which blended royalty rates would be advantageous for both Parties) for sales of Licensed Products in a country. Consequently, the Parties have agreed to adopt the royalty rates set forth in this Section 6.4 with respect to the sales of Licensed Products as blended royalty rates.

6.5 [***]

6.6 Cara Payment of Share of Certain Profits in U.S. Except as provided in the following sentence, for Cara's sales of Licensed Products to FMC Dialysis Clinics during a Calendar Year that are fulfilling orders taken by VFMCRP and submitted to Cara for fulfillment (such sales, the "**FMC Clinic Sales**"), Cara will pay to VFMCRP (on an annual basis) 50% of the annual Net Profit (as defined below) resulting from such FMC Clinic Sales during such Calendar Year using the below calculation for Net Profit. If, for a particular Calendar Year, the Annual FMC HD Patients (as defined below) number is more than [***] for such Calendar Year, then the payment by Cara to VFMCRP of a share of Net Profits resulting from FMC Clinic Sales shall be as follows: Cara shall pay to VFMCRP, for such Calendar Year a share of the Net Profit for such Calendar Year, in an amount equal to (a) [***].

As used in this Section, the following defined terms have the following meanings:

"**Net Profit**" means, for a particular Calendar Year and the FMC Clinic Sales during such Calendar Year, the Net Sales of Cara resulting from such FMC Clinic Sales in such Calendar Year, minus Cara's COGS (as such term is defined in the Supply Agreement, calculated according to U.S. GAAP) for the Licensed Product sold in such FMC Clinic Sales.

"**Total HD Patients**" means, as of the particular time, the total number of kidney disease patients in the United States receiving hemodialysis treatments.

"**Annual Total HD Patients**" means, for a particular Calendar Year, the simple arithmetic average of the Total HD Patients number existing at the beginning of each month during such year.

"**FMC HD Patients**" means, as of a particular time, the number kidney disease patients in the United States receiving hemodialysis treatments at FMC US Dialysis Clinics. \

"**Annual FMC HD Patients**" means, for a particular Calendar Year, the simple arithmetic average of the FMC HD Patients number existing at the beginning of each month during such year.

"**Baseline**" means [***], which is the number of FMC HD Patients as of the Effective Date.

[***].

"**50% Profit Share Ratio**" means, for a particular Calendar Year where the Annual FMC HD Patients number is more than [***] for such Calendar Year, the fraction equal to: (a) [***] for such Calendar Year, divided by (b) such Annual FMC HD Patients number.

For example, if for a particular Calendar Year, the following numbers are assumed: [***]. Based on the foregoing assumptions, in such example, the amount payable by Cara to VFMCRP as its share of such Net Profit for such Calendar Year under this Section 6.6, would be calculated as follows:

[***]

VFMCRP covenants that it shall obtain from the applicable member of the FMC Group, on a quarterly basis, the actual total number for FMC HD Patients as of the beginning of each Calendar Quarter during the Term and shall provide such information to Cara for use under this Section 6.6. VFMCRP warrants that all such numbers shall be accurate, and that if it determines that any such number provided to Cara underreported the actual number of FMC HD Patients for the applicable period, then it shall immediately provide such actual number, and Cara then will be able to recalculate the applicable split of Net Profit and will be entitled to reimbursement by VFMCRP for any overpayment by Cara to VFMCRP of a share in Net Profit, due to such inaccuracy in the number as reported by VFMCRP. Cara shall use the numbers reported in the United States Renal Data System Annual Data Report ("**USRDS Report**") as published on the website at https://www.usrds.org/reference.aspx for determining the Total HD Patients and the Annual Total HD Patients for each particular time point or period, under the above. In the event the Total HD Patients and Annual Total HD Patients must be derived from multiple data sources in the report, Cara shall use the average of the Total HD Patients and Annual Total HD Patients from such data sources. If the USRDS Report is no longer made, or if changes are made to the USRDS Report so that such data is no longer available, then such number shall be determined by the equivalent listing of Total HD Patients in the U.S. as determined by the appropriate U.S. government agency, as reasonably agreed by the Parties at such time.

6.7 Reports; Payments. Within [***] after the end of each Calendar Quarter during which there are sales of Licensed Product in the Licensed Territory giving rise to a payment obligation under Section 6.4, (a) VFMCRP shall submit to Cara a report listing the total Net Sales for Licensed Product for each country in the Licensed Territory for such Calendar Quarter, the calculation of royalties owed (including listing the deductions taken from gross sales to arrive at Net Sales), and the royalties payable to Cara under Section 6.3, including the basis for any adjustments taken under Sections 6.3(c) or (d), and (b) VFMCRP shall pay to Cara the royalties owed under Section 6.3 on the date such report is due. Within [***] after the end of each Calendar Year during which there are sales by Cara of Licensed Product in the U.S. that are FMC Clinic Sales (as defined in Section 6.5 above) giving rise to a payment obligation under Section 6.5, (a) Cara shall submit to VFMCRP a report listing the total Net Sales for such FMC Clinic Sales for such Calendar Year, the calculation of COGS for the Licensed Product sold, and the share of the resulting Net Profit that is payable to VFMCRP under Section 6.5, and (b) Cara shall pay to VFMCRP the share of such Net Profit owed under Section 6.5 on the date such report is due.

6.8 Books and Records; Audit Rights.

(a) VFMCRP shall keep and shall cause its applicable Affiliates and Sublicensees to keep complete, true and accurate books and records in accordance with Accounting Standards in sufficient detail to determine the royalties due to Cara under Section 6.4. Cara shall keep complete, true and accurate books and records in accordance with Accounting Standards in sufficient detail to determine the amounts due to VFMCRP under Section 6.6.

(b) Cara shall have the right, once annually at its own expense, to have an independent, certified public accounting firm of nationally recognized standing, selected by Cara and reasonably acceptable to VFMCRP, review (i) the applicable records of VFMCRP and such Affiliates and Sublicensees, in the location(s) where such records are maintained by the audited party, upon reasonable notice (which shall be no less than [***]

prior notice) and during regular business hours and under obligations of confidence, for the sole purpose of verifying the accuracy of, and determine any discrepancies in, the royalty amounts paid and payable under this Agreement, and (ii) to the extent that such numbers are not in the public domain (e.g., through public reporting obligations of the FMC Group), the applicable records of the applicable member(s) of the FMC Group relating to the numbers of FMC HD Patients existing during the applicable times, in each case within a [***] Calendar Year period preceding the date of the request for review. VFMCRP also shall ensure that FMC shall provide Cara the right to perform the review set forth in subclause (ii) above. The report of such accounting firm shall be limited to: (x) for a review under subclause (i) above, a certificate stating whether any report made or invoice or payment submitted by VFMCRP during such period is accurate or inaccurate, the actual amounts of royalty payments owed under Section 6.3, and the amount of any Net Sales, royalty or other payment discrepancy, and a reasonable summary of the factual basis for any such discrepancy, and (y) for a review under subclause (ii) above, a certificate stating whether the reports of VFMCRP submitted under Section 6.6 reporting the number of FMC HD Patients as of the applicable time(s) during the inspected period were accurate or inaccurate, and if inaccurate, the amount of the discrepancies and a reasonable summary of the factual basis for such discrepancies. VFMCRP shall receive a copy of each such report concurrently with receipt by Cara. Should such inspection lead to the discovery of a discrepancy to Cara's detriment, VFMCRP shall pay the amount of the discrepancy (including, if applicable, a discrepancy in the reported FMC HD Patients which results in overpayment to VFMCRP of Net Profits under Section 6.6) within [***] after its receipt from the accounting firm of the certificate showing the amount of the discrepancy. Cara shall pay the full cost of the review unless the audit determined an underpayment of royalties and/or an overpayment of VFMCRP's share of Net Profits under Section 6.6 that is greater than [***] of the amount actually due for the period audited, in which case VFMCRP shall pay the costs charged by such accounting firm for such review. Any overpayment of royalties by VFMCRP revealed by an inspection shall be creditable against future royalty payments under Section 6.3.

(c) VFMCRP shall have the right, once annually at its own expense, to have an independent, certified public accounting firm of nationally recognized standing, selected by VFMCRP and reasonably acceptable to Cara, review the applicable records of Cara, in the location(s) where such records are maintained by Cara, upon reasonable notice (which shall be no less than [***] prior notice) and during regular business hours and under obligations of confidence, for the sole purpose of verifying the accuracy of, and determine any discrepancies in, the amounts paid and payable under Section 6.6 within a three (3) Calendar Year period preceding the date of the request for review. The report of such accounting firm shall be limited to a certificate stating whether any report made or invoice or payment submitted by Cara during such period is accurate or inaccurate, the actual amounts of payments owed by Cara under Section 6.5, and the amount of any Net Profits for the applicable Calendar Year(s), share of Net discrepancy, and a reasonable summary of the factual basis for any such discrepancy. Cara shall receive a copy of each such report concurrently with receipt by VFMCRP. Should such inspection lead to the discovery of a discrepancy in Cara payment of shares of Net Profits to VFMCRP's detriment, Cara shall pay the amount of the discrepancy within [***] after its receipt from the accounting firm of the certificate showing the amount of the discrepancy. VFMCRP shall pay the full cost of the review unless the audit determined an underpayment of owed the share of Net Profit that is greater than [***] of the amount actually due for the period audited, in which case Cara shall pay the costs charged by such accounting firm for such review. Any overpayment by Cara of a shares of Net Profit revealed by an inspection shall be refunded by VFMCRP within [***] of the report.

6.9 Taxes. All payments under or in connection with this Agreement shall be inclusive of any taxes, and each Party shall be responsible for its own taxes assessed by a tax or other authority except as otherwise set forth in this Agreement. "**Taxes**" mean all present and future taxes, import deposits assessments, and other governmental charges and any related penalties and interest not attributable to the fault or delay of a Party.

(a) Withholding Taxes: If Applicable Law require withholding of any Taxes by VFMCRP and imposed upon Cara on account of any royalties payable to Cara under Section 6.4, and paid by VFMCRP under this Agreement, such Taxes shall be deducted by VFMCRP as required by law from such remittable royalty payment and shall be paid by VFMCRP to the proper Tax authorities. Official receipts of payment of any withholding Tax shall be secured and sent, upon request, to Cara as evidence of such payment. The Parties shall exercise their good faith reasonable efforts to ensure that any withholding Taxes imposed are reduced as far as possible under the provisions of any relevant tax treaty, including filing any needed certificates or documents with applicable tax authorities and seeking to obtain the benefits of any such treaty. Withholding Taxes have to be paid in applicable local currency. Any possible refund of withholding tax previously withheld will also be paid in local currency to the Party on which such withholding was imposed. Any currency conversion will be based on the exchange rate applicable on the day of the

withholding Tax payment. Resulting currency exchange losses shall be borne by Cara and not be refunded by VFMCRP.

(b) VAT or similar Taxes: All payments due to the terms of this Agreement are expressed to be exclusive of value added tax ("**VAT**") or similar indirect Taxes (e.g., goods and service tax), which shall be and remain the obligations of the paying party.

6.10 Payment Method and Currency Conversion. Except as otherwise provided herein, all payments due to a Party hereunder shall be due and payable on the date specified to be owed, and shall be paid via a bank wire transfer to such bank account as such Party shall designate. For the purposes of determining the amount of royalties due for the relevant Calendar Quarter under Section 6.3, the amount of Net Sales in any foreign currency shall be converted into U.S. dollars in accordance with the normal business practice of VFMCRP consistently applied. In accordance with VFMCRP's normal business practice, when Licensed Products are sold for monies other than U.S. dollars, earned royalties in such countries will be determined by (a) converting the Net Sales in each country in the Licensed Territory into U.S. dollars, using the monthly exchange rates as customarily used by VFMCRP in its regular accounting system and (b) calculating the respective royalty payments per country based on the respective into U.S. dollars values.

6.11 Blocked Payments. If, by reason of Applicable Law in any country in the Licensed Territory, it becomes impossible or illegal for VFMCRP or any of its Affiliates or Sublicensees to transfer, or have transferred on its behalf, royalties or other payments to Cara, VFMCRP shall promptly notify Cara of the conditions preventing such transfer and such royalties or other payments shall be deposited in local currency in the relevant country to the credit of Cara in a recognized banking institution with a good creditworthiness, such banking institution to be designated by Cara or, if none is designated by Cara within [***], in a recognized banking institution selected by VFMCRP, and identified in a written notice given to Cara. If so deposited in a foreign country, VFMCRP shall provide reasonable cooperation to Cara so as to allow Cara to assume control over such deposit as promptly as practicable.

6.12 Late Payments. Any payment not made within [***] after the due date for such payment pursuant to the terms of this Agreement shall bear interest at a rate of the thirty-day U.S. dollar LIBOR rate effective for the date that payment was due (as published in The Wall Street Journal, Eastern Edition) plus [***] per annum. Calculation of interest will be made for the exact number of days the payment was past due based on a year of 360 days (actual days/360).

ARTICLE VII

PATENT MATTERS

7.1 Ownership.

(a) As between the Parties, each Party shall exclusively own all Know-How (including Inventions), Patent Rights, and other intellectual property rights conceived, created, made, discovered, generated or invented solely by employees, agents and consultants of such Party or its Affiliates either prior to the Effective Date, or thereafter either pursuant activities conducted independent of, or under and in connection with this Agreement, but in each case subject to the licenses granted to the other Party under Article 2, as applicable.

(b) The Parties will jointly own (i.e., each Party shall own an undivided one-half interest in and to) the entire rights, title and interests in and to all Joint Technology (except as may otherwise be agreed by the Parties under Section 7.2). The Parties will promptly disclose to each other any Joint Technology conceived or reduced to practice no later than [***] after the Intellectual Property or Legal Department of the Party receives a written disclosure of such conception or reduction to practice. Except to the extent either Party is restricted by the licenses granted to the other Party under this Agreement, each Party shall be entitled to practice, license, assign, and otherwise exploit its interests in the Joint Technology without a duty of accounting to or seeking consent from the other Party.

(c) The Parties intend that this Agreement is a joint research agreement under the provisions of pre- AIA 35 U.S.C. 103(c) and AIA 35 U.S.C. 102(c). The Parties further agree to cooperate and to take reasonable

actions to maximize the protections available under the safe harbor provisions of 35 U.S.C. 100 et seq. for U.S. Patent Rights.

7.2 Prosecution and Maintenance of Joint Patents. With respect to any Inventions in the Joint Know-How, Cara and VFMCRP shall discuss reasonably and endeavor to agree on the Prosecution of any Joint Patents claiming potentially patentable Inventions within the Joint Know-How. All such Joint Patents shall be jointly-owned by the Parties (i.e., each Party shall own an undivided one-half interest in and to the entire rights, title and interests in and to the Joint Patents), absent a written agreement of the Parties otherwise, in appropriate countries throughout the world. Absent agreement of the Parties otherwise, VFMCRP shall be responsible for the Prosecution of any such Joint Patents in countries and jurisdictions in the Licensed Territory, at its sole expense, and Cara shall be responsible for the Prosecution of any such Joint Patents in countries and jurisdictions outside the Licensed Territory, at its sole expense, *provided that* Cara and VFMCRP shall discuss reasonably and endeavor to agree on all filings and responses in the Licensed Territory. Each Party shall keep the other fully informed regarding the filing, prosecution, defense and maintenance of the Joint Patents being prosecuted by such Party (including in any case, a detailed update at least once per Calendar Quarter). If reasonably requested by either Party, the other Party shall provide reasonable assistance and support to such Party in the above Prosecution and Maintenance, provided that any reasonable out-of-pocket costs of such assistance (including appearances at any compelled hearings or preparation or attendance at discovery responses) shall be paid for by the Party providing assistance.

7.3 Prosecution and Maintenance of Licensed Patent Rights. Cara shall have the sole right (except as otherwise provided below and be responsible for the Prosecution of the Licensed Patent Rights throughout the Licensed Territory, at its own expense (except as provided below) and at its reasonable discretion. VFMCRP shall reimburse Cara for [***] of annual maintenance fee costs for Licensed Patents in the Licensed Territory, based on invoices submitted. Cara shall keep VFMCRP fully informed regarding the filing, prosecution, defense and maintenance of such Licensed Patent Rights (including in any case, a detailed update at least once per Calendar Year). If reasonably requested by Cara, VFMCRP shall provide reasonable assistance and support to Cara in the above Prosecution and Maintenance, provided that any reasonable out-of-pocket costs of such assistance (including appearances at any compelled hearings or preparation or attendance at discovery responses) shall be paid for by Cara.

7.4 VFMCRP's rights. If Cara decides that it shall no longer continue the Prosecution of a particular Licensed Patent Right in the Licensed Territory during the Term, then it will promptly advise VFMCRP of this decision at least [***] in advance of any Prosecution filing or response deadline that would result in the loss of such Licensed Patent Right. Thereafter VFMCRP may, upon written notice to Cara, assume the Prosecution of such Licensed Patent Right in the Licensed Territory at its sole expense and discretion. Upon such written notice, Cara will grant to VFMCRP the right to conduct the Prosecution, on Cara's behalf, of such Licensed Patent Right, and shall transfer copies of all documents relating directly to Cara's prior Prosecution of same, at VFMCRP's cost. Following such grant, such Licensed Patent Right will remained licensed to VFMCRP under the license grants hereunder, but will no longer be considered a Licensed Patent Right for the purpose of determining applicable Royalty Terms. Cara will reasonably cooperate, upon VFMCRP's reasonable request and at its expense, in connection with the prosecution of all patent applications included within such Licensed Patent Right, including providing (at VFMCRP's expense) reasonable and related technical expertise, technical data, prosecution history and other relevant expertise, to the extent required for VFMCRP to conduct such Prosecution.

7.5 European Unified Patent System. With regard to any Licensed Patents Rights or jointly-owned Patent Rights that fall under the new European Unified Patent System, the Party prosecuting such Licensed Patent Right or jointly-owned Patent Right will elect the opt-out option unless the Parties mutually agree otherwise.

7.6 Patent Term Extensions. The Party prosecuting a Licensed Patent Right or Joint Patent will be solely responsible for making all decisions regarding patent term extensions, including supplementary protection certificates and any other extensions, that are now available or become available in the future, that are applicable to such Licensed Patent Right or jointly- owned Patent Right and that become available directly as a result of the Regulatory Approval of a Licensed Product by VFMCRP or any of its Affiliates or sublicensees; *provided that* the prosecuting Party will consult the other Party with respect to such decisions and will consider the comments and concerns of the other Party in good faith, and *further provided that*, Cara will consult with VFMCRP with respect to such decisions (including selection of the patent(s) for patent term extension, supplementary protection certificates or any other extensions) as a result of the first Regulatory Approval in territory of any product containing the Compound,

even if outside the Field and even if not by VFMCRP or any of its Affiliates or sublicensees and that the patent(s) selected for patent term extension, supplementary protection certificates or any other extensions in a territory within the Licensed Territory shall Cover the Licensed Product.

7.7 Third Party Infringement.

(a) Notice. Each Party shall promptly report in writing to the other Party any known or reasonably suspected (i) infringement of any Licensed Patent Right or Joint Patent, or (ii) unauthorized use or misappropriation of any of the Licensed Know-How or Joint Know-How, of which such Party becomes aware and shall provide the other Party with all material evidence in its possession regarding such known or suspected infringement or unauthorized or use misappopriation (to the extent able to be disclosed).

(b) Initial Right to Enforce. Cara shall have the first right, but not the obligation, to initiate a lawsuit or take other reasonable action to enforce the applicable Licensed Patent Rights or Joint Patent with respect to an infringement by a Third Party by making, using, importing or selling in the Licensed Territory a product that contains a Compound or otherwise competes or likely would compete with Licensed Product or a misappropriation or other violation of the Licensed Know-How (in each case, a "**Field Infringement**"). Cara shall consult with VFMCRP and give good faith consideration to any reasonable objection from VFMCRP regarding Cara's proposed course of action prior to initiating any such lawsuit or other enforcement action asserting any such Licensed Patent Rights or Joint Patent against a Field Infringement in the Licensed Territory. VFMCRP shall reasonably cooperate in the prosecution of any such suit or other action against a Field Infringement as may be reasonably requested by Cara, including joining any action as party-plaintiff at Cara's request if needed for Cara to have standing to bring such suit; *provided, that* Cara shall promptly reimburse all out-of-pocket expenses (including reasonable counsel fees and expenses) incurred at Cara's request and actually incurred by VFMCRP in connection with such cooperation. Cara shall keep VFMCRP reasonably informed regarding the prosecution and results of any such enforcement suit or action (including in any case, a detailed update at least once per Calendar Quarter).

(c) Step-In Right. If Cara does not initiate a lawsuit or take other reasonable action intended to cause a Field Infringement of Licensed Patent Rights or jointly-owned Patent Rights against a Field Infringement in the Licensed Territory to cease and obtain remedies for the harm resulting therefrom, pursuant to Section 7.4(b), within one hundred [***] of actual notice provided under Section 7.4(a) with respect to any such Field Infringement, then VFMCRP shall have the right, but not the obligation, to initiate such lawsuit or take such other action, after providing [***] notice to Cara and giving good faith consideration to the Cara's reason(s) for not initiating a lawsuit or taking other action. For this purpose, Cara shall cooperate in the prosecution of such suit as may be reasonably requested by VFMCRP, including joining any action as party-plaintiff at VFMCRP's request if required for VFMCRP to have standing to bring such suit; *provided, that* VFMCRP shall promptly reimburse all out-of-pocket expenses (including reasonable counsel fees and expenses) of Cara incurred in connection with such cooperation.

(d) Conduct of Certain Actions; Costs. The Party initiating legal action against a Field Infringement shall have the sole and exclusive right to select counsel for any suit initiated by it pursuant to Section 7.4(b) or 7.4(c) (the "**Initiating Party**"). The Initiating Party shall bear its own internal and out-of-pocket costs incurred in any such legal action, including the fees and expenses of the counsel selected by it. The other Party shall have the right to participate and be represented in any such legal action (in cases where such other Party has standing) by its own counsel at its own expense, *provided that* the Initiating Party shall in any event have the final say about the strategy and decisions in the suit and any settlement.

(e) Recoveries. Any amount recovered in any action or settlement of any such action against a Field Infringement in the Licensed Territory shall be allocated first to reimburse on a pro-rata basis each Party's actual out-of-pocket costs (including reasonable attorneys' fees and expenses) incurred in such action and any amount remaining shall be allocated as follows: (i) if Cara is the Initiating Party, then Cara shall provide to VFMCRP [***] of the net amount remaining, and (ii) if VFMCRP is the Initiating Party, with respect to any remaining portion of such recovery, such net amounts remaining shall be considered as Net Sales and shall be subject to payment of the applicable royalty thereon in accordance to Section 6.4. For clarity, Cara shall retain any amounts it recovers from enforcing all Cara Patent Rights, the Joint Patents or its rights in any Cara Know-How outside the Licensed Territory. For clarity, Cara retains the sole and exclusive rights to enforce Cara Patent Rights, the Joint Patents or its rights in any Cara Know-How outside the Licensed Territory.

(f) Responsibility for Third Party Licenses. At any time during the Term, if Cara believes it is necessary or advisable to seek to acquire or obtain a license from any Third Party in order to avoid infringement of Patents owned or controlled by such Third Party during the exercise of the rights herein granted, whether or not there has been the institution of any infringement claim, Cara will have the sole right, but not the obligation, to negotiate and acquire or obtain a license under such Patents from such Third Party. Cara will be responsible for the amounts payable to such Third Party assignor, licensor or grantor of rights pursuant to such agreement to the extent such payments arise out of or relate to the research, Development, use, import, offer for sale or sale of the Licensed Products (including Combination Products and Bundled Products) in the Licensed Territory by VFMCRP or its Affiliates or Sublicensee. This section will not be interpreted as placing on either Party a duty of inquiry regarding Third Party intellectual property rights. Each Party will keep the other Party informed of the status of any Third Party claim of infringement.

7.8 Enforcement of Product Trademark. Cara shall have the sole initial rights to initiate lawsuits and/or take any other action to enforce the Product Trademark or Local Trademark, against any infringement, dilution or other violation (a "**Mark Infringement**") anywhere in the world. VFMCRP shall reasonably cooperate in the prosecution of any such suit or other action brought by Cara against such Mark Infringement as may be reasonably requested by Cara, including joining any action as party-plaintiff at Cara's request if needed for Cara to have standing to bring such suit; *provided*, *that* Cara shall promptly reimburse all out-of-pocket expenses (including reasonable counsel fees and expenses) incurred at Cara's request and actually incurred by VFMCRP in connection with such cooperation. Cara shall keep VFMCRP reasonably informed regarding the prosecution and results of any such enforcement suit. If Cara does not initiate a lawsuit or take other reasonable action intended to cause a Mark Infringement in the Licensed Territory to cease and obtain remedies for the harm resulting therefrom, pursuant to this Section 7.5, within one hundred [***] of actual notice with respect to any such Mark Infringement, then VFMCRP shall have the right, but not the obligation, to initiate such lawsuit or take such other action, after providing [***] notice to Cara and giving good faith consideration to the Cara's reason(s) for not initiating a lawsuit or taking other action, and shall keep Cara reasonably informed of the progress and results of such action. The Party that conducts an action against a Mark Infringement shall retain any recoveries (including by settlement) of such action.

7.9 Patent Invalidity Claim.

(a) Each Party shall promptly notify the other in the event of any legal or administrative action by any Third Party against a Licensed Patent Right or Joint Patent of which it becomes aware challenging the validity or enforceability thereof, including any opposition, post-grant review, inter-partes review, nullity, revocation, reexamination, third party observations, or compulsory license proceeding.

(b) Cara shall have the first right, but not the obligation, at its expense, to defend against any such action relating to a Licensed Patent Right or Joint Patent in the Licensed Territory. In such case, Cara shall keep VFMCRP reasonably informed of the progress and results of such action and defense, including providing copies of all substantive filings and orders in any such action. If Cara does not initiate a defense against any such action involving a Licensed Patent Right or Joint Patent within [***] following such notice, then VFMCRP shall have the right, but not the obligation, to defend such action at its expense, provided that VFMCRP shall keep Cara regularly informed of all actions taken and results of such defense.

7.10 Patent Marking. VFMCRP shall ensure that all Licensed Products sold in the Licensed Territory are appropriately marked to indicate all relevant Patent Rights claiming the Licensed Product or its use, in accordance with Applicable Law.

ARTICLE VIII

CONFIDENTIALITY AND PUBLICATION

8.1 Nondisclosure and Limited Use Obligations. Each of the Parties agree that during the Term, and for a period of [***] thereafter, each Party and its Affiliates (and, with respect to VFMCRP, its Sublicensees) shall (a) maintain in confidence the Confidential Information of the other Party, using efforts to protect such information that are at least as strong as those that such Party uses to maintains its own confidential information (but in no event less than reasonable efforts), (b) not disclose such Confidential Information to any Third Party without the prior written

consent of the other Party, or as otherwise expressly permitted in this Agreement, and (c) not use such Confidential Information for any purpose except those permitted by this Agreement.

8.2 Authorized Disclosure. Notwithstanding anything to the contrary in this Article 8, a Party may disclose particular Confidential Information of the other Party to the extent such disclosure is reasonably necessary in the following instances:

(a) Prosecuting, enforcing or defending applicable Patent Rights that are the subject of this Agreement in accordance with Article 7 of this Agreement;

(b) making filings covering Licensed Products with Regulatory Authorities in accordance with this Agreement;

(c) complying with Applicable Law (including securities laws and the requirements of the securities exchange on which Cara's stock is traded) or submitting information to tax or other Governmental Authorities; provided that if a Party is required by Law to make any public disclosure of Confidential Information of the other Party, to the extent it may legally do so, it will give reasonable advance notice to the other Party of such disclosure and will use its reasonable efforts to secure confidential treatment of such Confidential Information prior to its disclosure (whether through protective orders or otherwise);

(d) to its Affiliates, and to employees, accountants, and lawyers, on a need to know basis, each of whom prior to disclosure must be subject to appropriate obligations of confidentiality and non-use equivalent in scope to those set forth in this ARTICLE VIII and that are of reasonable duration in view of the circumstances of the disclosure; or

(e) to the extent mutually agreed to in writing by the Parties.

8.3 Press Releases and Other Permitted Disclosures.

(a) Cara and VFMCRP each agree not to disclose any of the terms and conditions of this Agreement to any Third Party, except as described below in this Section 8.3. The Parties will cooperate in the release of a mutually agreed upon press release, within thirty (30) days following execution of the Agreement, announcing the collaboration contemplated by this Agreement as soon as practicable after the Effective Date. Subject to the other provisions of this Agreement, no other press release, public statement or public disclosure concerning the existence or terms of this Agreement shall be made, either directly or indirectly, by either Party, without first obtaining the written approval of the other Party, such approval not to be unreasonably withheld; provided, however, the foregoing limitation does not apply to the extent a press release, public statement or public disclosure contains information that was previously disclosed publicly.

(b) Either Party may disclose the existence and terms of this Agreement in confidence to its attorneys, professional accountants, auditors or other professional advisors, under an agreement with terms of confidentiality and non-use no less rigorous than the terms contained in this Agreement (or pursuant to ethical requirements of the professional that require the recipient to preserve the confidentiality of the disclosed information).

(c) Notwithstanding the foregoing provisions of this ARTICLE VIII, a Party may disclose the existence and terms of this Agreement (however, with it seeking to exclude, as far as legally possible, any and all technical or financial information and terms contained within the Agreement, including applicable information in Exhibits hereto, to the extent such information and terms may be redacted under a Confidential Treatment Request or similar application under Applicable Law), or the Parties' activities under this Agreement, where such disclosure is required, as determined by the legal counsel of the disclosing Party, by Applicable Law, by applicable stock exchange regulation or by order or other ruling of a competent court, although, to the extent practicable, the other Party shall be given [***] advance notice of any such legally required disclosure to provide comments to the disclosing Party, and the disclosing Party shall use its good faith diligent efforts to reasonably consider such comments provided by such other Party on the proposed disclosure and seek to further redact the information and terms contained within the Agreement in a consistent manner, to the extent such redactions are permitted under Applicable Law. In case either

Party is obliged to publish the Agreement as a "material agreement" in accordance with the U.S. stock exchange regulations ("**SEC Filing**"), the Agreement shall be redacted by the filing Party as far as legally possible, as determined reasonably by the filing Party's legal counsel, and the filing Party shall cooperate with the other Party reasonably in advance to such SEC Filing to enable the other Party to review and comment on the scope of such redaction, all in accordance with the requirements found in the immediately preceding sentence.

8.4 Data Security. During the Term of this Agreement, each Party will maintain (and, as applicable, cause its Affiliates to maintain) reasonable environmental, safety and facility procedures, data security procedures and other safeguards against the disclosure, destruction, loss, or alteration of the other Party's Confidential Information in the possession of such Party or its Affiliates, which efforts shall in any event be no less rigorous than those maintained by such Party for its own Confidential Information of a similar nature.

ARTICLE IX

REPRESENTATIONS AND WARRANTIES; INDEMNIFICATION

9.1 Representations and Warranties of the Parties. VFMCRP and Cara each represent, warrant and covenant to each other Party that as of the Effective Date:

(a) it has the authority and right to enter into and perform this Agreement and grant the rights embodied herein, and it is not aware of any legal impediment that could inhibit its ability to perform its obligations under this Agreement;

(b) its execution, delivery and performance of this Agreement does not constitute a breach of any order, judgment, agreement or instrument to which it is a party or is otherwise bound;

(c) such Party is a corporation duly organized, validly existing and in good standing under the laws of the state or other jurisdiction of incorporation or formation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof except where failure to be in good standing would not materially impact the Party's ability to meet its obligations hereunder;

(d) as of the Effective Date, no consent of any Third Party is required for such Party to grant the licenses and rights granted to the other Party under this Agreement or to perform its obligations hereunder;

(e) all of such Party's personnel and employees and Third Parties, including agents and consultants, hired by such Party and involved in the Development, manufacture or Commercialization of Compounds or Licensed Products hereunder are, or when hired will be, under a written agreement whereby they have presently assigned to such Party any right they may have in any Invention first invented, discovered, made, conceived or reduced to practice in the conduct of activities pursuant to the Global Development Program or in the Development, manufacture or Commercialization of any of such Compounds or Licensed Products, and all intellectual property rights therein;

(f) it will not, after the Effective Date, enter into any written or oral contractual obligation with any Third Party that would conflict with the obligations that arise on its part out of this Agreement; and

(g) no consent, approval, order or authorization of, or registration, qualification, designation, declaration or filing with, any federal, state or local governmental authority is required on the part of such Party in connection with the valid execution, delivery and performance of this Agreement.

(h) In performing under this Agreement, it and its Affiliates agree to comply with all applicable anti- corruption laws, including the Foreign Corrupt Practices Act of 1977, as amended from time to time ("**FCPA**"); the anti-corruption laws of the Territory; and all laws enacted to implement the Organization for Economic Co-operation and Development Convention on Combating Bribery of Foreign Officials in International Business Transactions;

(i) It is not aware of any Government Official or Other Covered Party having any financial interest in the subject matter of this Agreement or in any way personally benefiting, directly or indirectly, from this Agreement.

(j) No political contributions or charitable donations will be given, offered, promised or paid by a Party (or its Affiliate) at the request of any Government Official or Other Covered Party that is in any way related to this Agreement or any activity conducted pursuant to this Agreement by such Party (or its Affiliate), without the other Party's prior written approval.

(k) It has not been debarred by the FDA, is not the subject of a conviction described in Section 306 of the FD&C Act, and is not subject to any similar sanction of other Governmental Authorities outside the Territory, and neither it nor any of its Affiliates has used, in any capacity, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction. Neither Party will engage, in any capacity in connection with this Agreement or any ancillary agreements, any person who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction. Each Party will inform the other Party in writing promptly if it or any person engaged by it or any of its Affiliates who is performing services under this Agreement, or any ancillary agreements, is debarred or is the subject of a conviction described in Section 306 of the FD&C Act, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to each Party's knowledge, is threatened, relating to the debarment or conviction of a Party, any of its Affiliates or any such person performing services hereunder or thereunder.

(l) It has been and will, for the Term, be in compliance with all applicable global trade laws (including the Global Trade Control Laws), including those related to import controls, export controls or economic sanctions, and it will cause each of its Affiliates to remain in compliance with the same during the Term. Neither Party, nor any of its Affiliates or its or their respective directors, officers, employees, agents or representatives is, or in the last five years was, a Restricted Party. Neither Licensee nor its Affiliates or sublicensees will export, transfer, or sell the Licensed Product (i) to any country or territory that is subject to comprehensive economic sanctions administered by OFAC, which currently includes Cuba, Iran, North Korea, Sudan and Syria, as well the Crimea region of Ukraine, unless the sale of the product would be permissible if Licensee, its Affiliates or sublicensees were subject to OFAC's jurisdiction, (ii) to any Restricted Party unless the sale of the product would be permissible if Licensee, its Affiliates or sublicensees was subject to OFAC's jurisdiction or (iii) in such a manner that would violate the Global Trade Control Laws.

(m) It will comply with all Applicable Law in performing its activities hereunder.

9.2 Representations and Warranties of Cara. Cara represents, warrants and covenants to VFMCRP, as of the Effective Date, that:

(a) the existing Licensed Patents Rights and Product Trademarks have been duly filed in the applicable countries in the Licensed Territory (i.e., where such rights exist);

(b) all applicable filing, maintenance and other fees have been timely paid for all of the Licensed Patent Rights the Product Trademarks and any Local Trademarks (if applicable), including all issued patents or registered trademarks, and, to Cara's Knowledge, all of the Licensed Patent Rights and Product Trademarks that are issued patents or registered trademarks are in full force and effect;

(c) (i) there is no pending or, to Cara's Knowledge, threatened (in writing) re-examination, opposition, interference, *inter partes* review or claim challenging the inventorship, ownership, validity, enforceability or patentability of the Licensed Patent Rights owned by Cara or other litigation or proceeding relating to any of the Licensed Patents Rights owned by Cara and (ii) to Cara's Knowledge, there is no pending or threatened (in writing) re-examination, opposition, interference, *inter partes* review or claim challenging the inventorship, ownership, validity, enforceability or patentability of the Licensed Patent Rights in-licensed by Cara or other litigation or proceeding relating to any of the Licensed Patent Rights in-licensed to Cara;

(d) to Cara's Knowledge, the making, having made, selling, offering for sale, using or importing of a Compound or Licensed Product (as currently existing) does not infringe any valid Patent Right or other intellectual property rights of any Third Party in the Licensed Territory or the U.S.;

(e) Cara has received no written notice of any claim that a patent or trade secret owned or controlled by a Third Party is or would be infringed or misappropriated by the Development, manufacture, use, sale, offer or sale, import or other Commercialization of the Licensed Compound or the Licensed Products in the Territory or the U.S.;

(f) to Cara's Knowledge, all inventors of any Inventions that are claimed by the Licensed Patent Rights have assigned their entire right, title and interest in and to such Inventions and the corresponding Licensed Patent Rights to Cara (or to its licensor);

(g) Cara has not assigned, transferred, conveyed, granted rights to a Third Party or otherwise encumbered its right, title and interest in Cara Product Technology in a manner inconsistent with the license rights granted to VFMCRP under this Agreement;

(h) Cara is the legal and beneficial owner of the Licensed Patent Rights existing as of the Effective Date, free and clear of all liens, charges and encumbrances (other than encumbrances that do not breach the warranty in Section 9.2(g));

(i) to Cara's Knowledge, the conception, development and reduction to practice of the material Cara Product Technology has not constituted or involved the misappropriation of Know-How of any Third Party or the infringement of the Patent Rights of any Third Party;

(j) Cara has not received any written notice of any unauthorized use, infringement, or misappropriation of any material Cara Product Technology by any person or entity, including any current or former employee or consultant of Cara;

(k) Cara has no Knowledge of any information that it believes would render unenforceable or unpatentable any claim in the Licensed Patent Rights existing as of the Effective Date.

(l) the research, Development and manufacture of the Licensed Product conducted by Cara or its Affiliates has been conducted in material compliance with Applicable Law, and to Cara's Knowledge, the research, Development and manufacture of the Licensed Product conducted by Cara's Third Party contractors has been conducted in material compliance with Applicable Law.

As used herein, "**Knowledge**" means that, based on the actual knowledge of the executive officers (including General Counsel and the Head of IP) of Cara, such officers are not aware of facts that make the statement, by which the term Knowledge is qualified, materially untrue.

9.3 Representations and Warranties of VFMCRP. VFMCRP represents, warrants and covenants to Cara that:

(a) as of the Effective Date, it and its Affiliates do not have any ongoing program to identify, research or Develop any drug products that may be competitive with Licensed Product.

9.4 No Other Warranties. EXCEPT AS EXPRESSLY SET FORTH IN SECTIONS 9.1 - 9.3, NEITHER OF THE PARTIES MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING AND PARTICULARLY THAT THE INTELLECTUAL PROPERTY LICENSED HEREUNDER IS NON-INFRINGING OR THAT PRODUCT(S) WILL BE SUCCESSFULLY DEVELOPED HEREUNDER, AND FURTHER, THE PARTIES HEREBY DISCLAIM ALL OTHER WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTIES OF TITLE, NON-INFRINGEMENT, MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE.

9.5 Indemnification by VFMCRP. VFMCRP shall indemnify, hold harmless and defend Cara, its Affiliates and all of their respective officers, directors, employees, agents, licensors and shareholders (collectively, the "**Cara Indemnitees**") from and against any and all losses, damages, liabilities, judgments, fines, amounts paid in settlement, expenses and costs of defense (including reasonable attorneys' fees) ("**Losses**") resulting from any allegation, demand, claim, suit, action or proceeding brought or initiated by a Third Party (each a "**Third Party Claim**") against any Cara Indemnitee to the extent arising out of (a) a Default by VFMCRP or its Affiliates ; (b) the gross negligence or willful misconduct of, or violation of Applicable Law by, VFMCRP or its Affiliate or Sublicensee; or (c) the Development, offer for sale, sale or use or other Commercialization of any Compound or Licensed Product by, on behalf of or under authority of, VFMCRP or its Affiliate, Sublicensee, Third Party distributor, or end user; *provided that* the foregoing defense, hold harmless and indemnity obligations shall not apply to the extent such Third Party Claim is caused by the gross negligence, willful misconduct or violation of Applicable Law by Cara or is due to any action, omission or activity covered by Section 9.6(a) or (b) below, or by an action or omission of Cara for which Cara has an indemnity obligation under the terms of the Supply Agreement with respect to defective Licensed Product supplied by Cara.

9.6 Indemnification by Cara. Cara shall indemnify, hold harmless and defend VFMCRP and its Affiliates and all of their respective officers, directors, employees, agents, licensors and shareholders (collectively, the "**VFMCRP Indemnitees**") from and against any and all Losses resulting from any Third Party Claim against any VFMCRP Indemnitee to the extent arising out of (a) a Default by Cara or its Affiliates; (b) the gross negligence or willful misconduct of, or violation of Applicable Law by, Cara or its Affiliates; or (c) the Development, offer for sale, sale or use or other Commercialization of any Compound or Licensed Product by, or on behalf of or under the authority of Cara or its Affiliate or Third Party licensee (for clarity, other than VFMCRP or its Affiliate or Sublicensee), or the manufacture of any Compound or Licensed Product by, on behalf of or under authority of, Cara or its Affiliate (for clarity, other than VFMCRP or its Affiliate or Sublicensee); *provided that* the foregoing defense, hold harmless and indemnity obligations shall not apply to the extent such Third Party Claim is caused by the gross negligence, willful misconduct or violation of Law by a VFMCRP Indemnitee or is due to any action, omission or activity covered by Section 9.5(a) or (b) above.

9.7 Indemnification Procedure.

(a) To be eligible for the Cara Indemnitees to be indemnified hereunder, Cara shall provide VFMCRP with prompt notice of the Third Party Claim giving rise to the indemnification obligation under Section 9.5 (provided that any delay in giving such notice shall not exempt VFMCRP from its indemnity, hold harmless and defense obligations if such delay does not cause any material prejudice to VFMCRP) and the exclusive (provided that VFMCRP timely undertakes and continues to fully defend against the Third Party Claim) ability to defend or settle any such claim; *provided however* that VFMCRP shall not enter into any settlement for damages, or that imposes upon any Cara Indemnitee any obligation or liability, without Cara's prior written consent, such consent not to be unreasonably withheld, delayed or conditioned. Cara shall have the right to participate, at its own expense and with counsel of its choice, in the defense of any claim or suit that has been assumed by VFMCRP, *provided that* VFMCRP shall in any event control the defense of the claim or suit.

(b) To be eligible for the VFMCRP Indemnitees to be indemnified hereunder, VFMCRP shall provide Cara with prompt notice of the Third Party Claim giving rise to the indemnification obligation under Section 9.6 (provided that any delay in giving such notice shall not exempt Cara from its indemnity, hold harmless and defense obligations if such delay does not cause any material prejudice to Cara) and the exclusive (provided that Cara timely undertakes and continues to fully defend against the Third Party Claim) ability to defend or settle any such claim; *provided however* that Cara shall not enter into any settlement for damages, or that imposes upon any VFMCRP Indemnitee any obligation or liability, without VFMCRP's prior written consent, such consent not to be unreasonably withheld, delayed or conditioned. VFMCRP shall have the right to participate, at its own expense and with counsel of its choice, in the defense of any claim or suit that has been assumed by Cara, provided that Cara shall in any event control the defense of the claim or suit.

9.8 Insurance. Each Party will, at its own expense, obtain and maintain insurance with respect to the Development and Commercialization of the Compound and the Licensed Products under this Agreement in such amount and subject to such deductibles and other limitations as biopharmaceutical companies in the Territory

customarily maintain with respect to the research, development, and commercialization of similar products. Each Party will provide a copy of such insurance policy to the other Party upon request.

9.9 No Consequential or Punitive Damages. EXCEPT FOR DAMAGES RESULTING FROM (a) A BREACH OF THE CONFIDENTIALITY OBLIGATIONS OF ARTICLE VIII, OR (b) A PARTY'S WILLFUL MISCONDUCT OR GROSS NEGLIGENCE, NEITHER PARTY HERETO WILL BE LIABLE TO THE OTHER PARTY FOR ANY INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL, EXEMPLARY OR PUNITIVE DAMAGES, INCLUDING LOST PROFITS, ARISING FROM OR RELATING TO THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF SUCH DAMAGES. FOR CLARITY, THIS SECTION 9.9 SHALL NOT LIMIT EITHER PARTY'S RIGHTS OR OBLIGATIONS UNDER SECTIONS 9.5 OR 9.6.

ARTICLE X

TERM AND TERMINATION

10.1 Term and Expiration. This Agreement shall be effective as of the Effective Date and shall continue in effect until expiration upon the expiration of all Royalty Terms, or until earlier termination of the Agreement pursuant to Section 10.2 (the "**Term**"). Upon expiration (but not earlier termination) of this Agreement, VFMCRP shall have a fully paid-up, royalty-free, perpetual and non-exclusive license (with the right to assign to Affiliates and Sublicensees), to manufacture, import, market, promote, use, develop and sell the Licensed Product in the Licensed Territory. Following such expiration (but not earlier termination) of this Agreement and for a period of [***] thereafter, Cara agrees not to commercialize (whether directly or indirectly) the Licensed Product in countries in the Licensed Territory in which VFMCRP has launched commercial sales of the Licensed Product during the term of the Agreement

10.2 Termination.

(a) Termination of Agreement for Cause. If at any time during the Term a Party (the "**Non- Defaulting Party**") believes that the other Party (the "**Defaulting Party**") has committed a Default, then the Non-Defaulting Party may provide written notice (a "**Breach Notice**") to the Defaulting Party, which Breach Notice shall identify in detail the Default, the intent to terminate the Agreement if the Default is not cured, and the actions or conduct that it considers would be a cure of such Default. If such a Breach Notice has been provided, and such Default is not cured by the date sixty (60) days (thirty (30) days for breach of a payment obligation) after such Breach Notice was provided, then the Non-Defaulting Party may terminate the Agreement on written notice of termination to Defaulting Party.

(b) Termination for Bankruptcy. Either Party shall have the right to terminate this Agreement in the event of the commencement of any proceeding in or for bankruptcy, insolvency, dissolution or winding up by or against the other Party (other than pursuant to a corporate restructuring) that is not dismissed or otherwise disposed of within sixty (60) days thereafter, subject to a Party's rights and licenses that are retained under Section 2.7.

(c) Termination by Consent. The Parties may terminate this Agreement by mutual written consent.

(d) Termination for Patent Challenge. Except to the extent the following is unenforceable under the laws of a particular jurisdiction, Cara may terminate this Agreement on written notice if VFMCRP or its Affiliates or Sublicensees, individually or in association with any other person or entity, commences a legal action challenging the validity or enforceability of any of the Licensed Patent Rights (a "**Patent Challenge**"); provided, however, that Cara may not terminate this Agreement pursuant to this Section 10.2(d) as a result of any Patent Challenge brought in response to an action brought against VFMCRP or its Affiliates or Sublicensees by Cara for infringement of any Licensed Patent in the Licensed Territory.

(e) Termination by VFMCRP for Convenience. Upon the earlier of (i) the acceptance for filing of an NDA covering Licensed Product filed with the FDA (after completion of the phase 3 program), or (ii) the

third anniversary of the Effective Date, VFMCRP may terminate this Agreement in its entirety, or in part only with respect to particular countries within the Licensed Territory, by providing written notice to Cara thereof, which termination will be effective 12 months following the date of such notice; *provided*, *however*, that such 12 month notice period may be shortened by mutual agreement of the Parties.

10.3 Effect of Termination. If this Agreement terminates early in its entirety pursuant to a termination under Section 10.2 (that is, prior to expiration under Section 10.1), then:

(a) Cara shall, within [***] after the effective date of such termination, return or cause to be returned to VFMCRP copies of all VFMCRP's Confidential Information (*other than* VFMCRP Product Technology); for clarity, Cara may retain (i) all copies of Joint Know-How, (ii) one copy of such returned VFMCRP Confidential Information solely for legal archive purposes, and (iii) copies of all VFMCRP Product Technology (for use in exercising the license rights granted to Cara under the Agreement that survive termination of this Agreement;

(b) VFMCRP's licenses pursuant to Sections 2.1, 2.2 and 2.3 shall terminate as of the effective date of termination;

(c) within [***] after the effective date of termination VFMCRP shall return or cause to be returned to Cara, all copies of all Cara's Confidential Information and all Licensed Know-How; except that VFMCRP may retain (i) all copies of Joint Know-How, and (ii) one copy of the Cara Confidential Information solely for legal archive purposes;

(d) all of VFMCRP's rights to use Cara Confidential Information and Cara Know-How, including with respect to Compounds and Licensed Products, shall terminate and revert exclusively to Cara, and VFMCRP covenants that, for [***] after the date of such termination, VFMCRP and its Affiliates and Sublicensees shall not market, promote, use, offer for sale or sell Compound or Licensed Product (except as may otherwise be permitted in Section 10.3(f) with respect to remaining inventory);

(e) immediately and automatically upon termination, VFMCRP will be deemed to grant to Cara, effective solely upon, and exercisable from and after, such termination: (A) the exclusive, worldwide license, with full rights to grant sublicenses through multiple tiers, under VFMCRP's and its Affiliates' interest in all applicable Joint Patents as specified by Cara, such license solely to research, Develop, make, have made, use, offer for sale, sell, export and import all Compounds and Licensed Products, in the Field in the Licensed Territory; and (B) a worldwide, fully sublicenseable (through multiple tiers), non- exclusive license, under all applicable VFMCRP Product Technology, including all regulatory documentation and applications relating to Compound or Licensed Product, such license to research, Develop, make, have made, use, offer for sale, sell, export and import Compound and Licensed Products existing for all purposes in the Licensed Territory.

(f) Cara shall have the option, exercisable within [***] following such termination, to purchase and obtain VFMCRP's and VFMCRP's Affiliate's or Sublicensee's existing inventory of Licensed Products (or a portion of any such inventory) at the supply price paid for such Licensed Products by, and/or any costs for manufacturing, formulating, tableting and packaging the Licensed Products incurred by, VFMCRP, its Affiliates or their permitted Sublicensees (such supply price or costs, the "**Product Price**" for the applicable Licensed Product), *provided that* if Cara desires to exercise such option, VFMCRP shall provide to Cara, within [***] of request, a listing of the expiration dates for each lot in such inventory (with each lot identified by lot number), and for any such inventory purchased by Cara hereunder, VFMCRP shall provide to Cara a typical product warranty as to remaining shelf life, storage in accordance with cGMP, and compliance with specifications and Applicable Law. Cara may exercise such option by written notice to VFMCRP during such [***] period. In addition, if this Agreement is terminated by Cara pursuant to Section 10.2(a), then the purchase price for any Licensed Product purchased by Cara by exercise of this option shall be [***] of the Product Price for the applicable Licensed Product purchased hereunder by Cara. If Cara does not exercise such option, VFMCRP, its Affiliates or their respective permitted sublicensees will be permitted to sell, subject to the payment to Cara in full of applicable royalties and any other amounts due under this Agreement, any Licensed Products in inventory (including completion for sale of any work in progress) as of the date of termination, such sales solely during the [***] period following such termination, and *provided that* VFMCRP covenants and warrants that any such sale of Licensed Product after such termination shall comply with all Applicable Laws.

(g) Automatically and immediately upon termination of this Agreement in its entirety VFMCRP shall assign and transfer and hereby assigns and transfers to Cara all right, title and interest in any and all regulatory applications (such as INDs and NDAs) and Regulatory Approval applications and Regulatory Approvals in the Licensed Territory covering Licensed Product. VFMCRP and VFMCRP's Affiliates each shall sign all documents and instruments and take all such actions as reasonable needed to effect and perfect such assignments and transfers.

(h) If VFMCRP terminates this Agreement solely with respect to a particular country or countries in the Licensed Territory, rather than in its entirety, pursuant to Section 10.2(e), then such countries are automatically excluded from the Licensed Territory, and all rights hereunder as to Compound and Licensed Product in such countries revert automatically and exclusively to Cara, and the definition of the Licensed Territory for the purposes of this Agreement will automatically be amended to remove such terminated country or countries.

10.4 Partial Termination for Cara Uncured Material Breach. If at any time during the Term, Cara has committed a Default, then in lieu of proceeding under Section 10.2(a), VFMCRP may proceed under this Section 10.4, by providing to written notice (a "**Default Notice**") to Cara, which Default Notice shall identify in detail the Default, the intent to terminate partially (pursuant to this Section 10.4) the Agreement if the Default is not cured, and the actions or conduct that it considers would be a cure of such Default. If such a Default Notice has been provided with respect to an actual Default by Cara, and such Default is not cured by the date sixty (60) days after such Default Notice was provided, then on written notice to Cara VFMCRP may effect a partial, limited termination of the Agreement, having the following effects: (a) the Development provisions under Article IV with respect to Cara conducted Development activities for Licensed Product in the Field, with respect to Licensed Territory, shall be terminated and subject to the following provisions of this Section 10.4; (b) VFMCRP shall undertake and commit to conduct such Development of Licensed Product with respect to Licensed Territory, at its cost, and subject and pursuant to the terms of Article 14, with each of the Party's respective roles under the terms of Article IV that apply to Cara conducting such Development activities being reversed and (c) VFMCRP's royalty obligations under Section 6.3 shall be reduced by [***]. For clarity, after a partial termination under this Section 10.4, all terms of this Agreement, except as modified pursuant to the foregoing sentence of this Section 10.4, shall remain in full force and effect.

10.5 Effect of Expiration or Termination; Survival.

(a) Expiration or termination of the Agreement shall not relieve the Parties of any obligation accruing prior to such expiration or termination. Any expiration or termination of this Agreement shall be without prejudice to the rights of either Party against the other Party accrued or accruing under this Agreement prior to expiration or termination, including the obligation to pay royalties for Licensed Product(s) sold prior to such expiration or termination. Termination of this Agreement shall be in addition to, and shall not prejudice, the Parties' remedies at law or in equity, including the Parties' ability to receive legal damages or equitable relief with respect to any breach of this Agreement, regardless of whether or not such breach was the reason for the termination.

(b) On a country-by-country and Licensed Product-by-Licensed Product basis, if VFMCRP uses any Product Trademark or any Local Trademark in connection with the Commercialization of the Licensed Products in a particular country of the Licensed Territory, then following the expiration during the Term of the applicable Royalty Term in such country and completion of payment of all amounts owed to Cara for sales of Licensed Product in such country, the licenses granted to VFMCRP under Sections 2.4 and 5.5 to use the Product Trademarks and Local Trademarks in such will remain exclusive, subject to payment by VFMCRP of a royalty of [***] of Net Sales of all Licensed Products in such country thereafter.

(c) The following Articles and Sections: Articles I, VI (until completion of all payments owed to Cara), VIII, X, XI and XII, and Sections 2.6, 2.8(a), 7.1, 7.2, 9.5, 9.6, 9.7 and 9.9, shall survive the expiration or termination of the Agreement.

ARTICLE XI

DISPUTE RESOLUTION

11.1 Seeking Consensus. If any dispute or issue between the Parties arises out of, in connection with or related to this Agreement, including disputes over the interpretation, performance, enforcement or breach of this Agreement, including any disagreements at the JSC level described in Section 3.2(c), (any such dispute or issue, a "**Dispute**"), then upon the written request of either Party, the matter shall be referred to the Senior Executives, who shall meet in a good faith effort to resolve the Dispute. Any final decision mutually agreed to by the Senior Executives shall be conclusive and binding on the Parties. If the Senior Executives are not able to agree on the resolution of any such Dispute within [***] (or such other period of time as mutually agreed by the Senior Executives) after such Dispute was first referred to them, then such Dispute shall be resolved (if at all) pursuant to the provisions of Section 11.2.

11.2 Courts. If the Parties do not fully settle or otherwise resolve a Dispute pursuant to Section 11.1, and a Party wishes to pursue the further resolution of such Dispute, each such Dispute shall be finally and exclusively resolved by litigation in the courts in the State of New York. Each Party hereby consents to the jurisdiction and proper venue of the courts in the State of New York for any such action or claim initiated by a Party in accordance with this Article XI.

11.3 Preliminary Relief. Notwithstanding Section 11.1, a Party may seek and apply for preliminary and/or permanent injunctive relief through the equitable powers of courts in the State of New York at any time to prevent ongoing or threatened harm due to an applicable breach of this Agreement or other good cause.

ARTICLE XII

MISCELLANEOUS

12.1 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of New York and applicable federal laws of the U.S., other than any principle of conflict or choice of laws that would cause the application of the laws of any other jurisdiction.

12.2 Waiver. Waiver by a Party of a breach hereunder by the other Party shall not be construed as a waiver of any succeeding breach of the same or any other provision. No delay or omission by a Party to exercise or avail itself of any right, power or privilege that it has or may have hereunder shall operate as a waiver of any right, power or privilege by such Party. No waiver shall be effective unless made in writing with specific reference to the relevant provision(s) of this Agreement and signed by a duly authorized representative of the Party granting the waiver.

12.3 Notices. Unless otherwise provided for in this Agreement, all notices, instructions and other communications hereunder or in connection herewith shall be in writing, shall be sent to the address specified in this Section 12.3 and shall be: (a) delivered personally; (b) transmitted by facsimile; (c) sent by registered or certified mail, return receipt requested, postage prepaid; or (d) sent via a reputable international overnight delivery service. Any such notice, instruction or communication shall be deemed to have been delivered (i) upon receipt if delivered by hand or when transmitted with electronic confirmation of receipt, if transmitted by facsimile (if such transmission is on a Business Day; otherwise, on the next Business Day following such transmission), *provided that* an original document is sent via an internationally recognized overnight delivery service (receipt requested), (ii) three (3) Business Days after it is sent by registered or certified mail, return receipt requested, postage prepaid, or (iii) one (1) Business Day after it is sent via a reputable international overnight delivery service.

If to Cara, to:

Cara Therapeutics, Inc.
4 Stamford Plaza
107 Elm Street, 9th Floor
Stamford, CT 06902

Attention: Chief Executive Officer

Facsimile: +1 (203) 406-3770

with a copies to: Cara Therapeutics, Inc.
4 Stamford Plaza
107 Elm Street, 9th Floor
Stamford, CT 06902

Attention: Office of the General Counsel
Facsimile: +1 (203) 406-3770

and: Cooley LLP
3175 Hanover St.
Palo Alto, CA 94306 USA
Attn: Babak Yaghmaie, Esq.

If to VFMCRP, to: Vifor Fresenius Medical Care Renal Pharma Ltd
Rechenstrasse 37
9014 St. Gallen
Switzerland Attn: CEO
Fax: +41 58 851 8001
Vifor Pharma Management Ltd

with a copy to: Flughofstrasse 61
8152 Glattbrugg
Switzerland
Attn: Group General Counsel
Fax: +41 58 851 8001

or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith.

12.4 Entire Agreement; Amendment. This Agreement (including its Exhibits and Schedules) contains the complete understanding of the Parties with respect to the subject matter of this Agreement and supersedes all prior understandings and writings relating to such subject matter. No amendment, change or addition to this Agreement will be effective or binding on either Party unless reduced to writing and duly executed on behalf of both Parties.

12.5 Headings. Headings in this Agreement are for convenience of reference only and shall not be considered in construing this Agreement.

12.6 Severability. If any provision or portion thereof in this Agreement is for any reason held to be invalid, illegal or unenforceable, the same shall not affect any other portion of this Agreement, as it is the intent of the Parties that this Agreement shall be construed in such fashion as to maintain its existence, validity and enforceability to the greatest extent possible. In any such event, this Agreement shall be construed as if such clause of portion thereof had never been contained in this Agreement, and there shall be deemed substituted therefor such provision as will most nearly carry out the intent of the Parties as expressed in this Agreement to the fullest extent permitted by Applicable Law.

12.7 Assignment. Neither this Agreement nor any right or obligation hereunder may be assigned or otherwise transferred by any Party without the consent of the other Party, which consent shall not be unreasonably withheld; *provided*, *however*, that (a) a Party may, without such consent, assign this Agreement, in whole or in part to any of its respective Affiliates; *provided that* the assigning Party shall remain jointly and severally liable with such Affiliate in respect of all obligations so assigned, and (b) a Party may assign this Agreement, without such consent, to its successor in interest in connection with the merger, acquisition, sale of all or substantially all of the assets of or similar transaction of such Party. In addition, if a Party is acquired by or mergers with a Third Party, any Patent Rights

or other intellectual property rights owned or controlled by such Third Party, as of just prior to the closing of such transaction, shall be excluded from all rights licensed by such Party to the other Party under this Agreement.

12.8 Counterparts. This Agreement may be executed in any number of counterparts, each of which shall be deemed an original but all of which together shall constitute one and the same instrument.

12.9 Force Majeure. No Party shall be liable for failure of or delay in performing obligations (other than payment obligations) set forth in this Agreement, and no Party shall be deemed in breach of its obligations, if such failure or delay is due to God, a public or natural disaster, explosion, fire, flood, tornado, thunderstorm, hurricane, earthquake, war, terrorism, riot, embargo, loss or shortage of power, labor stoppage, substance or material shortage, events caused by reason of laws of any Governmental Authority, events caused by acts or omissions of a Third Party or any other cause reasonably beyond the control of such Party, if the Party affected gives prompt notice of any such cause to the other Party. The Party giving such notice shall thereupon be excused from such of its obligations hereunder as it is thereby disabled from performing for so long as it is so disabled; provided, however, that such affected Party commences and continues to use its Commercially Reasonable Efforts to cure or avoid the effects of such cause. If any such delay resulting from such a force majeure exceeds [***] (from the date the applicable obligation was required to be performed), then the Party not affected by the force majeure will have the right to terminate this Agreement on written notice to the other Party, with the consequences set out in Section 10.3.

12.10 Third Party Beneficiaries. None of the provisions of this Agreement shall be for the benefit of or enforceable by any Third Party, other than an Cara Indemnitee under Section 9.5 or VFMCRP Indemnitee under Section 9.6. No such Third Party shall obtain any right under any provision of this Agreement or shall by reason of any such provision make any claim in respect of any debt, liability or obligation (or otherwise) against either Party.

12.11 Relationship of the Parties. Each Party shall bear its own costs incurred in the performance of its obligations hereunder without charge or expense to the other, except as expressly provided in this Agreement. Neither Party shall have any responsibility for the hiring, termination or compensation of the other Party's employees or for any employee compensation or benefits of the other Party's employees. No employee or representative of a Party shall have any authority to bind or obligate the other Party for any sum or in any manner whatsoever, or to create or impose any contractual or other liability on the other Party without said other Party's approval. For all purposes, and notwithstanding any other provision of this Agreement to the contrary, the legal relationship under this Agreement of each Party to the other Party shall be that of independent contractor. Nothing in this Agreement shall be construed to establish a relationship of partners or joint ventures between the Parties, or to grant a Party the right to bind the other Party to any obligations to any Third Party.

12.12 Performance by Affiliates. To the extent that this Agreement imposes obligations on Affiliates of a Party or permits a Party to exercise its rights or perform its obligations through its Affiliates, such Party agrees to cause its Affiliates to perform such obligations and shall guarantee performance of this Agreement by its Affiliates. If any disagreement arises out of the performance of this Agreement by an Affiliate of a Party, or the alleged failure of an Affiliate to comply with the conditions and obligations of this Agreement, the Party seeking to resolve such dispute shall have the right do so directly with the other Party, without any obligation to first pursue an action against, or recovery from, the Affiliate which is alleged to have caused a breach of this Agreement.

12.13 Construction. Each Party acknowledges that it has been advised by counsel during the course of negotiation of this Agreement, and, therefore, that this Agreement shall be interpreted without regard to any presumption or rule requiring construction against the Party causing this Agreement to be drafted. Any reference in this Agreement to an ARTICLE, Section, subsection, paragraph, clause, Schedule or Exhibit shall be deemed to be a reference to any article, section, subsection, paragraph, clause, schedule or exhibit, of or to, as the case may be, this Agreement. Except where the context otherwise requires, (a) wherever used, the use of any gender will be applicable to all genders; (b) the word "or" is used in the inclusive sense (and/or); (c) any definition of or reference to any agreement, instrument or other document refers to such agreement, instrument other document as from time to time amended, supplemented or otherwise modified (subject to any restriction on such amendments, supplements or modifications set forth herein or therein); (d) any reference to any Law refers to such Law as from time to time enacted, repealed or amended; (e) the words "herein", "hereof" and hereunder", and words of similar import, refer to this Agreement in its entirety and not to any particular provision hereof; and (f) the words "include", "includes" and

“including” shall not limit the scope of the matter coming before such words and shall be deemed to be followed by the phrase “but not limited to”, “without limitation” or words of similar import.

[*Signature page follows*]

IN WITNESS WHEREOF, the Parties have executed this Collaboration and License Agreement as of the Effective Date.

Cara Therapeutics, Inc.

BY: /s/ Derek Chalmers
NAME: Derek Chalmers
TITLE: CEO

Vifor Fresenius Medical Care Renal Pharma Ltd.

BY:/s/ Stefan Schulze
NAME:Stefan Schulze
TITLE:President of the Executive Committee and COO

Vifor Fresenius Medical Care Renal Pharma Ltd.

BY:/s/ Dr. Oliver P. Kronenberg
NAME:D. Oliver P. Kronenberg
TITLE:Group General Counsel

[Signature Page to License Agreement]

[Signature Page to License Agreement]

Exhibit 1.18

[***]

Exhibit 1.34

Excluded Clinics and Programs

[***]

Exhibit 1.62

Product Trademark

KORSUVA

Exhibit 2.5(a)

Permitted Sublicensees

(a) VFMCRP Affiliates;

[***]

(b) Vifor Pharma Affiliates;

[***]

(c) Third Parties

[***]

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: August 8, 2022

By: /s/ Christopher Posner
CHRISTOPHER POSNER
CHIEF EXECUTIVE OFFICER

EXHIBIT 31.2

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

I, Richard Makara, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 8, 2022

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

EXHIBIT 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended June 30, 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 Richard Makara, as VP, Head of Accounting & Controller of the Company, each hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his knowledge, based upon a review of the Report:

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

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

/s/ CHRISTOPHER POSNER
Name: Christopher Posner
Title: Chief Executive Officer
Date: August 8, 2022

/s/ RICHARD MAKARA
Name: Richard Makara
Title: VP, Head of Accounting & Controller
(*Principal Financial Officer*)
Date: August 8, 2022