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

FORM 10-Q

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2018

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**	
(Address of registrant's principal executive offices)	**06902** **(Zip Code)**

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

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). ☒ Yes ☐ No.

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

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☐
Emerging growth company	☒		

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

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

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of August 1, 2018 was: 39,290,464.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2018

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PART I
FINANCIAL INFORMATION

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

CARA THERAPEUTICS, INC.

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

	June 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 17,802	$ 9,388
Marketable securities	114,159	83,181
Income tax receivable	473	731
Other receivables	116	123
Prepaid expenses	5,615	1,635
Restricted cash, current	361	—
Total current assets	138,526	95,058
Property and equipment, net	959	1,177
Restricted cash	408	769
Total assets	$ 139,893	$ 97,004
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 12,553	$ 8,506
Current portion of deferred revenue	22,270	—
Total current liabilities	34,823	8,506
Deferred revenue, non-current	30,299	—
Deferred lease obligation	1,695	1,718
Commitments and contingencies (Note 15)		
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at June 30, 2018 and December 31, 2017, zero shares issued and outstanding at June 30, 2018 and December 31, 2017	—	—
Common stock; $0.001 par value; 100,000,000 shares authorized at June 30, 2018 and December 31, 2017, 34,059,214 shares and 32,662,255 shares issued and outstanding at June 30, 2018 and December 31, 2017, respectively	34	33
Additional paid-in capital	327,401	307,158
Accumulated deficit	(254,302)	(220,341)
Accumulated other comprehensive loss	(57)	(70)
Total stockholders' equity	73,076	86,780
Total liabilities and stockholders' equity	$ 139,893	$ 97,004

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, 2018	June 30, 2017	June 30, 2018	June 30, 2017
Revenue:				
License and milestone fees	$ 2,874	$ —	$ 2,874	$ 530
Collaborative revenue	—	—	—	313
Clinical compound revenue	—	—	—	68
Total revenue	2,874	—	2,874	911
Operating expenses:				
Research and development	17,002	6,961	30,429	27,797
General and administrative	3,685	2,672	7,382	5,072
Total operating expenses	20,687	9,633	37,811	32,869
Operating loss	(17,813)	(9,633)	(34,937)	(31,958)
Other income	467	331	778	421
Loss before benefit from income taxes	(17,346)	(9,302)	(34,159)	(31,537)
Benefit from income taxes	152	2	198	33
Net loss	$ (17,194)	$ (9,300)	$ (33,961)	$ (31,504)
Net loss per share:				
Basic and Diluted	$ (0.52)	$ (0.29)	$ (1.03)	$ (1.06)
Weighted average shares:				
Basic and Diluted	33,315,809	32,239,877	33,000,487	29,783,424
Other comprehensive income (loss), net of tax of $0:				
Change in unrealized gains (losses) on available-for-sale marketable securities	57	(37)	13	(16)
Total comprehensive loss	$ (17,137)	$ (9,337)	$ (33,948)	$ (31,520)

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2016	27,296,863	$ 27	$ 212,866	$ (162,171)	$ 3	$ 50,725
Sale of common stock in a follow-on public offering ($18.00 per share), net of underwriting discounts and commissions and offering expenses of $5,891	5,117,500	5	86,219	—	—	86,224
Stock-based compensation expense	—	—	2,426	—	—	2,426
Shares issued upon exercise of stock options	153,122	1	1,364	—	—	1,365
Cumulative effect adjustment upon adoption of ASU 2016-09	—	—	45	(45)	—	—
Net loss	—	—	—	(31,504)	—	(31,504)
Other comprehensive loss	—	—	—	—	(16)	(16)
Balance at June 30, 2017	32,567,485	$ 33	$ 302,920	$ (193,720)	$ (13)	$ 109,220

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2017	32,662,255	$ 33	$ 307,158	$ (220,341)	$ (70)	$ 86,780
Sale of common stock under license agreement	1,174,827	1	14,555	—	—	14,556
Stock-based compensation expense	—	—	3,940	—	—	3,940
Shares issued upon exercise of stock options	222,132	—	1,748	—	—	1,748
Net loss	—	—	—	(33,961)	—	(33,961)
Other comprehensive income	—	—	—	—	13	13
Balance at June 30, 2018	34,059,214	$ 34	$ 327,401	$ (254,302)	$ (57)	$ 73,076

See Notes to Condensed Financial Statements.

CARA THERAPEUTICS, INC.

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

	Six Months Ended	
	June 30, 2018	June 30, 2017
Operating activities		
Net loss	$ (33,961)	$ (31,504)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Stock-based compensation expense	3,940	2,426
Depreciation and amortization	239	245
Amortization/accretion of available-for-sale marketable securities	(559)	(163)
Realized loss (gain) on sale of available-for-sale marketable securities	15	(3)
Realized gain on sale of property and equipment	—	(13)
Deferred rent costs	(23)	(7)
Deferred revenue	52,569	—
Changes in operating assets and liabilities:		
Income tax receivable	258	292
Other receivables	7	(88)
Prepaid expenses	(3,980)	(405)
Accounts payable and accrued expenses	4,047	(4,343)
Net cash provided by (used in) operating activities	22,552	(33,563)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	56,700	35,906
Proceeds from sale of available-for-sale marketable securities	11,150	5,430
Purchases of available-for-sale marketable securities	(98,271)	(98,021)
Purchases of property and equipment	(21)	(30)
Proceeds from sale of property and equipment	—	13
Net cash used in investing activities	(30,442)	(56,702)
Financing activities		
Proceeds from sale of common stock in a follow-on public offering	—	86,224
Proceeds from the sale of common stock under license agreement	14,556	—
Proceeds from the exercise of stock options	1,748	1,365
Net cash provided by financing activities	16,304	87,589
Net increase (decrease) in cash, cash equivalents and restricted cash	8,414	(2,676)
Cash, cash equivalents and restricted cash at beginning of period	10,157	13,561
Cash, cash equivalents and restricted cash at end of period	$ 18,571	$ 10,885

See Notes to Condensed Financial Statements.

1. Business

Cara Therapeutics, Inc., or the Company, is a clinical-stage biopharmaceutical corporation formed on July 2, 2004. The Company is focused on developing and commercializing new chemical entities designed to alleviate pruritus and pain by selectively targeting kappa opioid receptors. The Company's primary activities to date have been organizing and staffing the Company, developing its product candidates, including conducting preclinical studies and clinical trials of CR845/difelikefalin-based product candidates and raising capital.

As of June 30, 2018, the Company had raised aggregate net proceeds of approximately $291,100 from several rounds of equity financing, including its initial public offering, or IPO, which closed in February 2014 and two follow-on public offerings of common stock, which closed in April 2017 and August 2015, and the issuance of convertible preferred stock and debt prior to the IPO. The Company had also received approximately $88,900 under its license agreements for CR845/difelikefalin, primarily with Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceutical Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and an earlier product candidate for which development efforts ceased in 2007. Additionally, in May 2018, the Company received net proceeds of $14,556 from the issuance and sale of 1,174,827 shares of the Company's common stock to Vifor (International) Ltd., or Vifor, in connection with the license agreement with VFMCRP (see Note 10, *Collaborations and Licensing Agreements*).

As of June 30, 2018, the Company had unrestricted cash and cash equivalents and marketable securities of $131,961 and an accumulated deficit of $254,302. 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 $17,194 and $9,300 for the three months ended June 30, 2018 and 2017, respectively, and $33,961 and $31,504 for the six months ended June 30, 2018 and 2017, respectively, and had net cash provided by (used in) operating activities of $22,552 and $(33,563) for the six months ended June 30, 2018 and 2017, respectively.

In July 2018, the Company received net proceeds of approximately $92,026 from the issuance and sale of 5,175,000 shares of its common stock in a follow-on public offering, including the full exercise of the underwriters' option to purchase 675,000 additional shares of its common stock (see Note 16, *Subsequent Event*).

The Company is subject to risks common to other life science companies including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, product liability, protection of proprietary technology, ability to raise additional financing, and compliance with Food and Drug Administration, or FDA, and other government regulations. If the Company does not successfully commercialize any of its product candidates, it will be unable to generate recurring product revenue or achieve profitability.

2. Basis of Presentation

The unaudited interim condensed financial statements included herein have been prepared pursuant to the rules and regulations of the Securities and Exchange Commission, or SEC. Accordingly, they do not include all information and disclosures necessary for a presentation of the Company's financial position, results of operations and cash flows in conformity with generally accepted accounting principles in the United States of America, or GAAP. In the opinion of management, these unaudited interim financial statements reflect all adjustments, consisting primarily of normal recurring accruals, necessary for a fair presentation of results for the periods presented. Certain amounts in the prior year's condensed financial statements have been reclassified to conform to the current-year presentation due to the adoption of certain accounting standards (see Note 2, *Accounting Pronouncements Recently Adopted: ASU 2016-18, Statement of Cash Flows (Topic 230), Restricted Cash*). 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 for the year ended December 31, 2017 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, 2017.

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. Actual results could differ materially from the Company's estimates and assumptions. Significant estimates include the fair value of marketable securities that are classified as level 2 of the fair value hierarchy, useful lives of fixed assets, the periods over which certain revenues will be recognized, including licensing and collaborative revenue recognized from non-refundable up-front and milestone payments, the determination of prepaid research and development, or R&D, clinical costs and accrued research projects, the amount of non-cash compensation costs related to share-based payments to employees and non-employees and the periods over which those costs are expensed and the likelihood of realization of deferred tax assets.

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, 2017, except for the recent adoption of new accounting pronouncements as disclosed below.

Accounting Pronouncements Recently Adopted

Revenue Recognition

On January 1, 2018, the Company adopted Accounting Standards Update, or ASU, 2014-09, *Revenue from Contracts with Customers (Topic 606)*, or ASC 606, as amended by ASU 2016-08, 2016-10, 2016-12 and 2016-20 using the full retrospective method. Under ASC 606, the Company recognizes revenue in an amount that reflects the consideration to which it expects to be entitled in exchange for the transfer of promised goods or services to customers. To determine revenue recognition for contracts with customers that are within the scope of ASC 606, the Company performs the following steps: (1) identifies the contract with the customer, (2) identifies the performance obligations in the contract, (3) determines the transaction price, (4) allocates the transaction price to the performance obligations in the contract, and (5) recognizes revenue when (or as) the entity satisfies a performance obligation. The Company has concluded that upon adoption of ASC 606, as amended, there was no impact on its results of operations, financial position or cash flows for any period presented from its only two revenue-related contracts, which were in effect at that time: the CKDP Agreement or the Maruishi Agreement (see Note 10, *Collaboration and Licensing Agreements* and Note 11, *Revenue Recognition)*.

The Company has entered into agreements to license its intellectual property, or IP, related to CR845/difelikefalin to develop, manufacture and/or commercialize drug products. These agreements typically contain multiple performance obligations, including licenses of IP and R&D services. Payments to the Company under these agreements may include nonrefundable license fees, payments for research activities, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The Company identifies agreements as contracts that create enforceable rights and obligations when the agreement is approved by the parties, identifies the rights of the parties and the payment terms, has commercial substance and it is probable that the Company will collect the consideration to which it will be entitled in exchange for the goods and services that will be transferred to the customer. The counterparty is considered to be a customer when it has contracted with the Company to obtain goods and services that are the output of the Company's ordinary activities (i.e., development of pharmaceutical products) in exchange for consideration.

A performance obligation is a promise to transfer distinct goods or services to a customer. Performance obligations that are both capable of being distinct and distinct within the context of the contract are considered to be separate performance obligations. Performance obligations are capable of being distinct if the counterparty is able to benefit from the good or service on its own or together with other resources that are readily available to it. Performance obligations are distinct within the context of the contract when each performance obligation is separately identifiable from each other; i.e., the Company is not using the goods or services as inputs to produce or deliver the combined output or outputs specified by the customer; one or more of the goods or services does not significantly modify or customize one of the other goods or services in the contract; and goods or services are not highly interdependent or not highly interrelated. Performance obligations that are not distinct are accounted for as a single performance obligation over the period that goods or services are transferred to the customer. The determination of whether performance obligations in a contract are distinct may require significant judgment.

The transaction price is the amount of consideration that the Company expects to be entitled to in exchange for transferring promised goods or services to the customer based on the contract terms at inception of a contract. There is a constraint on inclusion of variable consideration related to licenses of IP, such as milestone payments or sales-based royalty payments, in the transaction price if there is uncertainty at inception of the contract as to whether such consideration will be recognized in the future because it is probable that there will be a significant reversal of revenue in the future when the uncertainty is resolved. The determination of whether or not it is probable that a significant reversal of revenue will occur in the future depends on the likelihood and magnitude of the reversal. Factors that could increase the likelihood or magnitude of a reversal of revenue include (a) the susceptibility of the amount of consideration to factors outside the entity's influence, such as the outcome of clinical trials, the timing of initiation of clinical trials by the counterparty and the approval of drug product candidates by regulatory agencies, (b) situations in which the uncertainty is not expected to be resolved for a long period of time and (c) level of the Company's experience in the field. When it becomes probable that events will occur, for which variable consideration was constrained at inception of the contract, the Company allocates the related consideration to the separate performance obligations in the same manner as described below.

At inception of a contract, the Company allocates the transaction price to the distinct performance obligations based upon their relative standalone selling prices. Standalone selling price is the price at which an entity would sell a promised good or service separately to a customer. The best evidence of standalone selling price is an observable price of a good or service when sold separately by an entity in similar circumstances to similar customers. Since the Company typically does not have such evidence, it estimates standalone selling price so that the amount that is allocated to each performance obligation equals the amount that the Company expects to receive for transferring goods or services. The methods that the Company uses to make such estimates include (1) the adjusted market assessment approach, under which the Company forecasts and analyzes CR845/difelikefalin in the appropriate market, the phase of clinical development as well as considering recent similar license arrangements within the same phase of clinical development, therapeutic area, type of agreement, etc. and (2) the expected cost of satisfying the performance obligations plus a margin, or the expected cost plus a margin approach.

The Company recognizes revenue when, or as, it satisfies a performance obligation by transferring a promised good or service to a customer and the customer obtains control of the good or service. Revenue related to the grant of a license that is a distinct performance obligation and that is deemed to be functional IP is recognized at the point in time that the Company has the right to payment for the license, the customer has legal title to the license and can direct the use of the license (for example, to grant sublicenses), the customer has the significant risks and rewards of ownership of the license and the customer has accepted the asset (license) by signing the license agreement.

Recognition of revenue related to R&D services that are a distinct performance obligation or that are combined with granting of a license as a single performance obligation is deferred at inception of a contract and is recognized as those services are performed based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation.

Milestone payments are considered to be variable consideration and are not included in the transaction price at inception of the contract if it is uncertain that the milestone will be achieved. Rather, when it becomes probable that the milestone will be achieved and, therefore, there will not be a significant reversal of revenue in future periods, the respective amount to be earned is included in the transaction price, allocated to the distinct performance obligations based on their relative standalone selling price and recognized as revenue, as described above. Sales milestones and sales-based royalty payments related to a license of IP are recognized as revenue when the respective sales occur.

Other Accounting Pronouncements Recently Adopted

As of January 1, 2018, the Company adopted ASU No. 2017-09, *Compensation – Stock Compensation (Topic 718) - Scope of Modification Accounting*, or ASU 2017-09, which clarifies that a change to the terms or conditions of a share-based payment award should be accounted for as a modification only if the fair value, vesting conditions or classification (as equity or liability) of the award changes as a result of the change in terms or conditions. Modification of a share-based payment award may result in the Company recognizing additional compensation expense. The Company generally has not modified, and does not expect to frequently modify, the fair value, vesting conditions or classification of its share-based payment awards. The Company does not expect this guidance to have a material effect on its financial position, results of operations or cash flows. However, if and when modifications occur, their effect could be material to the Company's financial position, results of operations or cash flows (see Note 13, *Stock-based Compensation*).

As of January 1, 2018, the Company adopted ASU No. 2017-01, *Business Combinations (Topic 805), Clarifying the Definition of a Business*, or ASU 2017-01, that clarifies the definition of a business to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. ASU 2017-01 requires an entity to evaluate if substantially all of the fair value of the gross assets acquired or disposed of is concentrated in a single identifiable asset or a group of similar identifiable assets; if so, the set of transferred assets and activities is not a business. ASU 2017-01 also requires a business to include at least an input and one substantive process that together significantly contribute to the ability to create output and removes the evaluation of whether a market participant could replace missing elements. The adoption of ASU 2017-01 did not have a material effect on the Company's financial position, results of operations or cash flows.

As of January 1, 2018, the Company adopted ASU No. 2016-18, *Statement of Cash Flows (Topic 230), Restricted Cash* (a consensus of the Emerging Issues Task Force), or ASU 2016-18, which changes the presentation of the cash flow statement to include amounts generally described as restricted cash or restricted cash equivalents, together with cash and cash equivalents, when reconciling the beginning-of-period and end-of-period amounts shown on the statement of cash flows. ASU 2016-18 also requires additional disclosures concerning the nature of the restrictions on cash and cash equivalents and a reconciliation between amounts of cash, cash equivalents and restricted cash on the balance sheet and statement of cash flows for each period presented. Upon adoption, ASU 2016-18 was applied retrospectively to all periods presented. The Company historically presented changes in restricted cash as an investing activity in the statement of cash flows. Upon adoption of ASU 2016-18, such changes are reflected in the beginning and ending balances of cash, cash equivalents and restricted cash for all periods presented (see Note 6, *Restricted Cash*).

Accounting Pronouncements Not Yet Adopted

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*, or ASU 2018-07, which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. ASU 2018-07 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. Accordingly, under ASU 2018-07, the fair value of stock options granted to nonemployees will be measured only on the grant date, the amount of which will be recognized as compensation expense over the nonemployee's service (vesting) period in the same period(s) and in the same manner as if the Company had paid cash for the goods or services instead of paying with or using share-based payment awards. On an award-by-award basis, the Company may elect to use the contractual term as the expected term when estimating the fair value of a nonemployee award to satisfy the measurement objective. Prior guidance under Subtopic 505-50 required the fair value of nonemployee stock options to be marked to market at each reporting period during the service period, which resulted in volatility of compensation expense during that period. ASU 2018-07 is effective for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The Company will adopt ASU 2018-07 on January 1, 2019 on a modified retrospective basis through a cumulative-effect adjustment to equity by remeasuring, on that date, the fair value of all outstanding unvested stock options that had been granted to nonemployees. The Company expects that the adoption of ASU 2018-07 will not have a material effect on its results of operations, financial position or cash flows because grants of stock options to non-employees have been insignificant.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, or ASU 2016-02, which amends the current guidance for the accounting and disclosure of leases (ASC 840) for both lessees and lessors. The Company is currently identifying its contracts that contain leases. The primary effect of adoption will be the requirement to record right-of-use assets and corresponding lease obligations for those current operating leases. ASU 2016-02 is effective for interim and annual periods beginning after December 31, 2018 but may be adopted earlier. ASU 2016-02 requires modified retrospective adoption. However, the FASB issued ASU 2018-11, *Leases (Topic 842): Targeted Improvements*, or ASU 2018-11, which allows entities to elect to continue to apply the guidance in ASC 840, including its disclosure requirements, in the comparative periods presented in the year that they adopt the new leases guidance in ASC 842. Entities that elect this option would record the cumulative effect of adoption on the effective date rather than at the beginning of the earliest comparative period presented. The Company does not expect that ASU 2016-02 or ASU 2018-11 will have a material impact on its Condensed Statements of Comprehensive Loss or its Condensed Statements of Cash Flows, but it does expect that upon adoption, it will have a material impact on the assets and liabilities on the Condensed Balance Sheets.

(amounts in thousands, except share and per share data)

3. Available-for-Sale Marketable Securities

As of June 30, 2018 and December 31, 2017, the Company's available-for-sale marketable securities consisted of money market funds and debt securities issued by the U.S. Treasury, U.S. government-sponsored entities and by investment grade institutions.

The following tables summarize the Company's available-for-sale marketable securities by major type of security as of June 30, 2018 and December 31, 2017:

As of June 30, 2018

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 68,195	$ —	$ (57)	$ 68,138
U.S. Treasury securities	1,495	—	—	1,495
U.S. government agency obligations	1,096	—	—	1,096
Corporate bonds	6,735	—	(1)	6,734
Commercial paper	36,695	3	(2)	36,696
Total available-for-sale marketable securities	$ 114,216	$ 3	$ (60)	$ 114,159

As of December 31, 2017

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds	$ 39,988	$ —	$ (37)	$ 39,951
U.S. government agency obligations	7,799	—	(5)	7,794
Corporate bonds	15,919	—	(12)	15,907
Commercial paper	19,545	—	(16)	19,529
Total available-for-sale marketable securities	$ 83,251	$ —	$ (70)	$ 83,181

All available-for-sale marketable securities are classified in the Company's Condensed Balance Sheets as Marketable securities.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of June 30, 2018, the Company's marketable debt securities mature at various dates through January 2019. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows. The table does not include money market funds that are classified as available-for-sale marketable securities.

Contractual maturity	As of June 30, 2018 Amortized Cost	As of June 30, 2018 Fair Value	As of December 31, 2017 Amortized Cost	As of December 31, 2017 Fair Value
Less than one year	$ 46,021	$ 46,021	$ 43,263	$ 43,230

During the six months ended June 30, 2018, the Company sold shares of a money market fund, that is classified as an available-for-sale marketable security, with a total fair value of $11,150. The cost of the money market fund shares that were sold was determined by specific identification. The sales of the shares of the money market fund resulted in a realized loss of $15.

(amounts in thousands, except share and per share data)

The following tables show the fair value of the Company's available-for-sale marketable securities that have unrealized losses and that are deemed to be only temporarily impaired, aggregated by investment category and length of time that the individual investments have been in a continuous unrealized loss position.

As of June 30, 2018

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Money market funds	$ 68,138	$ (57)	$ —	$ —	$ 68,138	$ (57)
Corporate bonds	5,334	(1)	—	—	5,334	(1)
Commercial paper	12,672	(2)	—	—	12,672	(2)
Total	$ 86,143	$ (60)	$ —	$ —	$ 86,143	$ (60)

As of December 31, 2017

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
Money market funds	$ 39,951	$ (37)	$ —	$ —	$ 39,951	$ (37)
U.S. government agency obligations	7,794	(5)	—	—	7,794	(5)
Corporate bonds	15,907	(12)	—	—	15,907	(12)
Commercial paper	19,031	(16)	—	—	19,031	(16)
Total	$ 82,683	$ (70)	$ —	$ —	$ 82,683	$ (70)

As of June 30, 2018 and December 31, 2017, the Company held a total of 11 out of 26 positions and 30 out of 31 positions, respectively, that were in an unrealized loss position, none of which had been in an unrealized loss position for 12 months or greater. 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 and that, therefore, it had no other-than-temporary impairments on these securities as of June 30, 2018 and December 31, 2017. The Company does not intend to sell these debt securities before maturity and the Company believes it is not more likely than not that it will be required to sell these securities before the recovery of their amortized cost basis, which may be maturity.

(amounts in thousands, except share and per share data)

4. Accumulated Other Comprehensive Income (Loss)

The following table summarizes the changes in accumulated other comprehensive income (loss), or AOCI, net of tax, from unrealized gains (losses) on available-for-sale marketable securities, the Company's only component of AOCI, for the six months ended June 30, 2018 and June 30, 2017.

	Total Accumulated Other Comprehensive Income (Loss)
Balance, December 31, 2017	$ (70)
Other comprehensive loss before reclassifications	(2)
Amount reclassified from accumulated other comprehensive loss	15
Net current period other comprehensive income	13
Balance, June 30, 2018	$ (57)
Balance, December 31, 2016	$ 3
Other comprehensive loss before reclassifications	(13)
Amount reclassified from accumulated other comprehensive loss	(3)
Net current period other comprehensive loss	(16)
Balance, June 30, 2017	$ (13)

The reclassifications out of AOCI and into net loss were as follows:

Component of AOCI	Three Months Ended June 30, 2018	Three Months Ended June 30, 2017	Six Months Ended June 30, 2018	Six Months Ended June 30, 2017	Affected Line Item in the Statements of Operations
Unrealized gains (losses) on available-for-sale marketable securities	$ —	$ —	$ (15)	$ 3	Other income
	—	—	—	—	Benefit from income taxes
	$ —	$ —	$ (15)	$ 3	

The amounts reclassified out of AOCI into net loss were determined by specific identification.

5. Fair Value Measurements

As of June 30, 2018 and December 31, 2017, the Company’s financial instruments consisted of cash and cash equivalents, available-for-sale marketable securities, restricted cash, accounts payable and accrued liabilities. The fair values of cash and cash equivalents, restricted cash, accounts payable and accrued liabilities approximate their carrying values due to the short-term nature of these financial instruments. Available-for-sale marketable securities are reported on the Company’s Condensed Balance Sheets as Marketable Securities at their fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services, as described below.

(amounts in thousands, except share and per share data)

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

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

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

Valuation Techniques - Level 2 Inputs

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

The Company validates the prices provided by its third-party pricing services by reviewing their pricing methods, obtaining market values from other pricing sources and comparing them to the share prices presented by the third-party pricing services. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by its third-party pricing services as of June 30, 2018 or December 31, 2017.

The following tables summarize the Company's financial assets measured at fair value on a recurring basis as of June 30, 2018 and December 31, 2017.

Fair value measurement as of June 30, 2018:

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 fund and checking accounts	$ 17,802	$ 17,802	$ —	$ —
Available-for-sale marketable securities:				
Money market funds	68,138	—	68,138	—
U.S. Treasury securities	1,495	—	1,495	—
U.S. government agency obligations	1,096	—	1,096	—
Corporate bonds	6,734	—	6,734	—
Commercial paper	36,696	—	36,696	—
Restricted cash:				
Commercial money market account	769	769	—	—
Total financial assets	$ 132,730	$ 18,571	$ 114,159	$ —

(amounts in thousands, except share and per share data)

Fair value measurement as of December 31, 2017:

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 fund and checking accounts	$ 9,388	$ 9,388	$ —	$ —
Available-for-sale marketable securities:				
Money market fund	39,951	—	39,951	—
U.S. government agency obligations	7,794	—	7,794	—
Corporate bonds	15,907	—	15,907	—
Commercial paper	19,529	—	19,529	—
Restricted cash:				
Commercial money market account	769	769	—	—
Total financial assets	$ 93,338	$ 10,157	$ 83,181	$ —

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 for the six months ended June 30, 2018. There were no transfers of financial assets between Levels 1, 2, or 3 classifications during the six months ended June 30, 2018.

6. Restricted Cash

The Company is required to maintain a stand-by letter of credit as a security deposit under its lease for its office space in Stamford, Connecticut (refer to Note 15, *Commitments and Contingencies*). 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, 2018, the restricted cash balance for the Stamford lease was invested in a commercial money market account. This balance is required to remain at $769 through May 2019 and may, upon request from the Company, thereafter be reduced to $408 through the end of the lease term in 2023. The reduction in the balance of the letter of credit for the Stamford lease is contingent upon the Company not being in default of any provisions of that lease prior to the request for the reduction. As of June 30, 2018, the Company had $361 of restricted cash related to the Stamford lease in current assets and $408 in long-term assets. As of December 31, 2017, the Company had $769 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, 2018	December 31, 2017
Cash and cash equivalents	$ 17,802	$ 9,388
Restricted cash, current assets	361	—
Restricted cash, long-term assets	408	769
Total cash, cash equivalents, and restricted cash shown in the Condensed Statements of Cash Flows	$ 18,571	$ 10,157

(amounts in thousands, except share and per share data)

7. Prepaid expenses

As of June 30, 2018, prepaid expenses were $5,615, consisting of $4,923 of prepaid R&D clinical costs, $479 of prepaid insurance and $213 of other prepaid costs. As of December 31, 2017, prepaid expenses were $1,635, consisting of $1,287 of prepaid R&D clinical costs, $124 of prepaid insurance, and $224 of other prepaid costs.

8. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	June 30, 2018	December 31, 2017
Accounts payable	$ 3,692	$ 3,829
Accrued research projects	6,941	2,356
Accrued professional fees	356	384
Accrued compensation and benefits	1,478	1,864
Accrued other	86	73
Total	$ 12,553	$ 8,506

9. Stockholders' Equity

On April 5, 2017, the Company closed an underwritten follow-on offering for 5,117,500 shares of its common stock, including the full exercise of the underwriters' option to purchase 667,500 additional shares of its common stock. The Company received net proceeds of approximately $86,224, after deducting $5,891 relating to underwriting discounts and commissions and offering expenses. This offering was made pursuant to the Company's Registration Statement on Form S-3 (File No. 333-216657), filed with the SEC on March 13, 2017 and declared effective on March 24, 2017, and a related prospectus dated March 24, 2017 and prospectus supplement dated March 30, 2017, which was filed with the SEC on March 31, 2017.

On May 18, 2018, the Company issued 1,174,827 shares of its common stock to Vifor in connection with the license agreement entered into with VFMCRP (refer to Note 10, *Collaboration and Licensing Agreements*).

On July 23, 2018, the Company closed an underwritten follow-on offering for 5,175,000 shares of its common stock, including the full exercise of the underwriters' option to purchase 675,000 additional shares of its common stock. The Company received net proceeds of approximately $92,026, after deducting $6,300 relating to underwriting discounts and commissions and estimated offering expenses. This offering was made pursuant to the Company's Registration Statement on Form S-3 (File No. 333-216657) filed with the SEC on March 13, 2017 and declared effective on March 24, 2017, and a related prospectus supplement dated July 18, 2018, which was filed with the SEC on July 20, 2018 (see Note 16, *Subsequent Event*).

10. Collaboration and Licensing Agreements

Vifor Fresenius Medical Care Renal Pharma Ltd.

On May 17, 2018, the Company entered into a license agreement, or the VFMCRP Agreement, with VFMCRP under which the Company granted VFMCRP an exclusive, royalty-bearing license, or the VFMCRP License, to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize CR845/difelikefalin injection, or the Licensed Product, for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients, or the Field, worldwide (excluding the United States, Japan and South Korea), or the Territory. VFMCRP cannot perform development activities on their own unless specifically allocated to VFMCRP by the Joint Development Committee, or JDC, and Joint Steering Committee, or JSC. The Company's membership on the JSC or JDC is at its sole discretion and is not its obligation.

The Company is responsible, at its own cost, to undertake clinical and non-clinical development, or the R&D services. The Company is also responsible to provide all content and subject matter expertise required for registration with the European Medicines Agency, or EMA, in the European Union, or the EU, that will be needed by VFMCRP for such registration, including participation in regulatory meetings, as needed. If third-party costs incurred by the Company with respect to its clinical development for the EMA registration exceed $20,000, such excess costs will be shared equally by the Company and VFMCRP. VFMCRP will contribute, at its own cost, its clinical development expertise as reasonably useful for such development activities, such as preparing the clinical results that the Company presents to it in a format acceptable to the EMA to obtain marketing approval in the EU.

The Company has identified two performance obligations under ASC 606: (1) granting of the VFMCRP License and (2) the R&D services. The Company has determined that these two performance obligations are not capable of being distinct (i.e., do not have standalone value for VFMCRP) because VFMCRP cannot benefit (derive potential cash flows) from either one on its own or together with other resources that are readily available to it since VFMCRP is relying on the Company's expertise in investigating chronic kidney disease-associated pruritus, or CKD-aP, and its know-how obtained from multiple years of pre-clinical and clinical development, and years of interactions with the FDA which other companies or CROs would not have. The VFMCRP License does not provide benefit to VFMCRP until and unless the Company conducts the pivotal clinical trials and other supportive trials in CKD-aP to gather sufficient clinical data for VFMCRP to obtain marketing approval in the Territory. Furthermore, VFMCRP does not have the right to perform development activities on its own unless specifically allocated by the JDC or JSC.

The two identified performance obligations are also not distinct within the context of the contract, (i.e., are not separately identifiable from each other) because of the nature of the promise within the context of the contract. The nature of the promise is to transfer a combined deliverable to VFMCRP based on the agreement (to support the ability of VFMCRP to commercialize the Licensed Product) and the Company determined that the VFMCRP License and the R&D services are inputs rather than a transfer of each of these goods and services individually. In addition, the two identified performance obligations are highly interrelated and interdependent because satisfaction of both performance obligations is required for VFMCRP to derive benefit from the VFMCRP Agreement for commercialization of the Licensed Product in the Territory. Therefore, the two performance obligations are not distinct from each other and are accounted for as a single performance obligation.

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

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

At inception of the VFMCRP Agreement, there was significant uncertainty as to whether marketing approval would be obtained in the Territory for the Licensed Product. Therefore, at that time, there was a significant probability that any potential revenue from sales of the Licensed Product that would be included in the transaction price would be reversed when the uncertainty is resolved. Consequently, any sales royalties and sales milestones are constrained from the transaction price at inception of the VFMCRP Agreement and will be recognized as revenue if, and when, such sales transactions occur in the future.

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

The license also requires VFMCRP to promote and take orders in the U.S. for sale by the Company to FMC U.S. Dialysis Clinics and allows VFMCRP to grant sub-licenses, which, in certain cases, requires the Company's prior written consent. The Company retains the rights to import, distribute, promote, sell and otherwise commercialize the Licensed Product outside of the Field and outside of the Territory.

The Company retains the rights to make and have made the Licensed Product in the Territory for commercial sale by VFMCRP in the Field in or outside the Territory and for supply of Licensed Product to VFMCRP under the terms of a supply agreement, or the Supply Agreement. The supply price will be the Company's cost of goods sold, as calculated under U.S. GAAP, plus an appropriate margin. The Supply Agreement will co-terminate with the VFMCRP Agreement. In regards to a supply agreement, the VFMCRP Agreement only includes a requirement for the Company to negotiate in good faith with VFMCRP. After the execution of the VFMCRP Agreement, a separate agreement to supply them with the Licensed Product would be entered into, although the Company has no obligation to execute a supply agreement. In the event that the parties fail to enter into a Supply Agreement or if the Company fails to provide Licensed Product on a timely basis, VFMCRP has the right to manufacture or have manufactured the Licensed Product in and outside the Territory.

The Supply Agreement will be accounted for as a customer option that is not a material right because the selling price of the Licensed Product under the Supply Agreement is the Company's cost of goods sold plus an appropriate margin, which is commensurate with the "cost of goods sold plus" model that the Company would charge other parties under similar agreements (the standalone selling price) and not at a discount. Therefore, the sale of clinical compound to VFMCRP is not a performance obligation under the VFMCRP Agreement but rather the Supply Agreement is a separate agreement from the VFMCRP Agreement. The only performance obligation under the Supply Agreement is the delivery of the Licensed Product to VFMCRP for commercialization. Revenue from the sale of the Licensed Product to VFMCRP will be recognized as Clinical Supply revenue in the Company's Statements of Comprehensive Loss as sales of the Licensed Product occur.

The VFMCRP Agreement terminates upon the expiration of all royalty terms with respect to the Licensed Products, which expire on a Product-by-Product and country-by-country basis, at the latest of (a) the expiration of all patent rights licensed to VFMCRP covering such Licensed Product; (b) the expiration of all regulatory and data exclusivity applicable to such Licensed Product in such country and (c) the tenth anniversary of the first commercial sale of such Product in such country.

The VFMCRP Agreement may be terminated earlier by either party for material breach that is not cured within 60 days and bankruptcy and by both parties upon mutual written consent. The Company may terminate the VFMCRP Agreement if VFMCRP challenges the validity of any licensed patent rights, except if such patent challenge results from the Company's action against VFMCRP for infringement of any licensed patent in the Territory. In addition, upon the earlier of (1) the acceptance for filing of an NDA covering Licensed Product filed with the FDA (after completion of the Phase 3 program) or (2) the third anniversary of the Effective Date, the VFMCRP Agreement may be terminated by VFMCRP in its entirety or with respect to any countries within the Territory upon written notice to the Company. Such termination will be effective twelve months following the date of such notice.

If the VFMCRP Agreement terminates early for any reason stated above, VFMCRP's licenses will terminate, VFMCRP's rights to use the Company's confidential information and the Company's know-how will revert to the Company and VFMCRP will assign and transfer to the Company all right, title and interest in all regulatory applications (IND's and NDA's), regulatory approval applications and regulatory approvals in the Territory covering Licensed Product.

Maruishi Pharmaceutical Co., Ltd.

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

Under the Maruishi Agreement, the Company identified two performance obligations in accordance with ASC 606: (1) the license; and (2) the R&D services specific to the uremic pruritus field of use (specified as Phase 1 and proof-of-concept clinical trials), both of which were determined to have standalone value. The Company determined that these performance obligations had standalone value due to the fact that Maruishi obtained the right to develop the compound on its own and the Company was specifically contracted to perform specific R&D services as noted above. The Company believes that these early stage R&D services performed by the Company did not require any specific expertise or know-how, but rather could have been completed by outside third parties, therefore providing standalone value to Maruishi.

In March 2017, Maruishi entered into a sub-license agreement with Kissei Pharmaceutical Co. Ltd. for the development and sales/marketing of CR845/difelikefalin (called MR13A9 by Maruishi) for the treatment of uremic pruritus in dialysis patients in Japan. Consequently, for the six months ended June 30, 2017, the Company recognized revenue of $843 related to the sub-license fee. The Company allocated the amount of the sub-license fee to each of the two identified performance obligations in the same proportion as the upfront license fee that the Company received at inception of the Maruishi Agreement. Accordingly, $530 was recognized as license and milestone fees revenue and $313 was recognized as collaborative revenue.

During the six months ended June 30, 2017, the Company recognized clinical compound revenue of $68 from the sale of clinical compound to Maruishi. There were no sales of clinical compound during the six months ended June 30, 2018.

The Company incurred R&D expense related to the Maruishi Agreement of $61, consisting of cost of clinical compound, during the six months ended June 30, 2017. The Company did not incur any R&D expense for clinical compound during the six months ended June 30, 2018.

Chong Kun Dang Pharmaceutical Corporation

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

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

11. Revenue Recognition

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

Contract balances

As of June 30, 2018, the Company had deferred revenue, current of $22,270 and deferred revenue, non-current of $30,299 related to the performance obligations from the VFMCRP Agreement and had no balances of receivables or other assets related to the VFMCRP Agreement. There were no balances of receivables, other assets or deferred revenue relating to the Maruishi and CKDP agreements as of June 30, 2018. As of December 31, 2017, the Company had no balances of receivables, other assets or deferred revenue related to the Maruishi and CKDP Agreements.

Performance obligations

Under the VFMCRP Agreement, the Company's performance obligations of granting a license to allow VFMCRP to commercialize CR845/difelikefalin injection worldwide, except in the United States, Japan and South Korea, which occurred at inception of the contract in May 2018, and performing R&D services by the Company to obtain sufficient clinical data which will be shared with VFMCRP to allow them to receive regulatory approval to sell CR845/difelikefalin in the licensed territory, are not distinct, and are accounted for as a single performance obligation during the period that the R&D services are rendered (see Note 10, *Collaboration and Licensing Agreements*).

The Company's distinct performance obligations under the Maruishi Agreement include transfer of the license to the Company's IP, which allowed Maruishi to develop and commercialize CR845/difelikefalin, for acute pain and uremic pruritus indications in Japan, which occurred at inception of the contract in 2013, and performance of R&D services, which occurred from 2013 to 2015, as those services were rendered. The Company agreed to conduct limited work on an oral tablet formulation of CR845/difelikefalin and to conduct Phase 1 and proof-of-concept Phase 2 clinical trials of an intravenous formulation of CR845/difelikefalin to be used to treat patients with uremic pruritus. The Company agreed to transfer the data and information from such development to Maruishi for its efforts to obtain regulatory approval in Japan. These activities are referred to as R&D services.

The Company's only performance obligation under the supply agreement with Maruishi is to deliver clinical compound to Maruishi in accordance with the receipt of purchase orders. If and when the Company enters into a supply agreement with VFMCRP, the Company's only performance obligation under this supply agreement would be to deliver CR845/difelikefalin injection to VFMCRP in accordance with the receipt of purchase orders.

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

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

Transaction price allocated to the remaining performance obligations

At inception of the VFMCRP Agreement, the entire transaction price of $55,444 was allocated to the one combined performance obligation, as described above. As of June 30, 2018, $2,874 of that amount was recognized as license and milestone fees revenue based on the percentage of R&D services that had been completed. As of June 30, 2018, there were no remaining performance obligations under either the Maruishi Agreement or the CKDP Agreement, although the Company is eligible to receive milestone payments and sales royalties in the future.

Significant judgments

In applying ASC 606, as amended, to its three contracts, the Company made the following judgments that significantly affect the timing and amount of revenue recognition:

1. Determination of the number of distinct performance obligations in a contract

The VFMCRP Agreement contains one distinct performance obligation, which includes the Company's two performance obligations to grant a license to VFMCRP and conduct R&D services. Both of those performance obligations are inputs to the promise, within the context of the contract, to transfer a combined output for which VFMCRP has contracted (the ability of VFMCRP to commercialize the Licensed Product) (see Note 10, *Collaboration and Licensing Agreements*, for further discussion).

The Maruishi Agreement contains two distinct performance obligations: the granting of the license and the promise to deliver defined R&D services. Under the Maruishi Agreement, the license and the R&D services represent distinct goods or services from each other because Maruishi is able to benefit from the license on its own or together with other resources that are readily available to it (i.e., capable of being distinct). Maruishi's ability to benefit from the license without the R&D services is indicated by its ability to conduct clinical trials of CR845/difelikefalin on its own and by the provision in the Maruishi Agreement whereby if the Company suspends or discontinues its development activity, the Company will provide information regarding its development efforts up to that point so that Maruishi may continue development and commercialization of the product in Japan. Therefore, the R&D services do not significantly affect Maruishi's ability to use and benefit from the license.

In addition, the Company's promise in the Maruishi contract to transfer the license is separately identifiable from the promise to provide defined R&D services (i.e., distinct within the context of the contract) because the Company is not using the goods or services as inputs to produce or deliver the combined output or outputs specified by the customer. The combined output specified by Maruishi is its right to conduct development activities related to CR845/difelikefalin in Japan, which could result in regulatory approval in Japan. That right is derived from the Company's grant of the license. Maruishi is conducting clinical trials on its own and does not require the R&D services provided by the Company. Furthermore, the R&D services do not significantly modify or customize the license and vice versa. Finally, the license and R&D services are not highly interdependent or highly interrelated because the Company is able to fulfill its promise to transfer the initial license independently from its promise to subsequently provide the R&D services, which Maruishi can obtain on its own.

The only performance obligation in the CKDP Agreement is the granting of the license.

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

The transaction price is the amount of consideration that the Company expects to be entitled to in exchange for transferring promised goods or services to the customer. The transaction price must be determined at inception of a contract and may include amounts of variable consideration. However, there is a constraint on inclusion of variable consideration, such as milestone payments or sales-based royalty payments, in the transaction price related to licenses of IP, if there is uncertainty at inception of the contract as to whether such consideration will be recognized in the future (see Note 2, *Accounting Pronouncements Recently Adopted: Revenue Recognition*).

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

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

Under the VFMCRP Agreement, the single combined performance obligation will be satisfied as the R&D services are rendered and the transaction price, including the upfront payment of $50,000 and the premium on the common stock purchased by VFMCRP of $5,444, will be recognized as revenue as the R&D services are performed based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation. The remaining potential consideration was considered to be variable consideration and was constrained at inception of the contract, including regulatory and sales milestones and sales royalties (see Note 10, *Collaboration and Licensing Agreements*).

All performance obligations under the Maruishi Agreement and the CKDP Agreement were satisfied by the end of 2015. In the future, any milestone event will be recognized in accordance with Note 2, *Accounting Pronouncements Recently Adopted: Revenue Recognition*, as milestone and license fee revenue and collaboration revenue based upon the relative standalone selling prices of the two performance obligations at inception of the Maruishi Agreement, and as milestone and license fee revenue under the CKDP Agreement.

Under the Maruishi Agreement, the transaction price includes only the non-refundable and non-creditable upfront license fee of $15,337, including the premium of $337 from the sale of Company stock to Maruishi, that was paid to the Company at inception of the contract. The remaining potential consideration was considered to be variable consideration and was constrained at inception of the contract, including an aggregate of up to $10,500, which the Company is eligible to receive upon achievement of clinical development and regulatory milestones, a one-time sales milestone of one billion Yen when a certain sales level is attained; a mid-double-digit percentage of all non-royalty payments received by Maruishi from its sub-licensees, if any; and tiered royalties based on net sales of products containing CR845/difelikefalin in Japan, if any, with minimum royalty rates in the low double digits and maximum royalty rates in the low twenties.

Under the CKDP Agreement, the transaction price includes only the non-refundable and non-creditable upfront license fee of $646, including the premium of $83 from the sale of Company stock to CKDP, that was paid to the Company at inception of the contract. The remaining consideration was considered to be variable consideration and was constrained at inception of the contract, including an aggregate of up to $3,750, which the Company is eligible to earn upon achievement of clinical development and regulatory milestones. The Company is also eligible to receive a mid-double-digit percentage of all non-royalty payments received by CKDP from its sub-licensees, if any, and tiered royalties ranging from the high single digits to the high teens based on net sales of products containing CR845/difelikefalin in South Korea, if any.

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

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

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

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

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

Since both the VFMCRP Agreement and the CKDP Agreement each contain only one distinct performance obligation, at the inception of each of those agreements, the entire transaction price was allocated to the respective performance obligation.

5. Determination of the timing of revenue recognition for contracts

Revenue should be recognized when, or as, an entity satisfies a performance obligation by transferring a promised good or service to a customer; i.e., when the customer obtains control of the good or service. The licenses granted to both Maruishi and CKDP are being accounted for as distinct performance obligations. As discussed below, both licenses relate to functional IP for which revenue is recognized at a point in time – in the case of these two license agreements, the point in time is at inception of the contract because the customer obtained control of the license at that point.

The licenses grant Maruishi and CKDP the right to use the Company’s IP relating to CR845/difelikefalin as it existed at the point in time that the licenses were granted. That IP has significant standalone functionality as it provides the customer with the ability to perform a function or task, such as to manufacture CR845/difelikefalin and conduct clinical trials, and is considered to be functional IP.

During the license periods, the Company is continuing to develop and advance CR845/difelikefalin by conducting clinical trials. Those development efforts are for its own benefit and do not substantively change the significant standalone functionality of the licensed IP granted to Maruishi or CKDP. Therefore, the Company’s ongoing development efforts do not significantly affect the IP’s utility to which Maruishi or CKDP have rights. Furthermore, if the Company abandons its development efforts, Maruishi or CKDP may still continue to develop CR845/difelikefalin in their respective countries.

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

Similarly, under the VFMCRP Agreement, revenue related to the single distinct performance obligation, which includes both granting of the license and performance of the R&D services, will be recognized as the R&D services are performed, based on the costs incurred as a percentage of the estimated total costs to be incurred to complete the performance obligation. The Company expects that the remaining amount of the transaction price that was allocated to the combined performance obligation of $52,569 at June 30, 2018 will be recognized by 2020, as the R&D services are performed, subject to certain development and regulatory uncertainties.

6. Determination of consideration as variable consideration, including factors related to inclusion in the transaction price at inception of the contract and timing of recognition as revenue.

The VFMCRP Agreement, the Maruishi Agreement and the CKDP Agreement contain potential payments related to achievement of defined milestone events and royalties upon net sales of future products, which are considered to be variable consideration because of the uncertainty of occurrence of any of those events specified in those agreements at inception of the agreements. Therefore, those potential payments were not included in the transaction price at the inception of the agreements.

Revenue related to achievement of milestone events is recognized when the Company has determined that it is probable that a milestone event will be achieved and there will not be a significant reversal of revenue in future periods. Upon probability of achievement of a milestone event, the most likely amount of variable consideration is included in the transaction price. Subsequent changes to the transaction price, after contract initiation, are allocated to the performance obligations in the contract on the same basis as at contract inception. Revenue for variable consideration is recognized in the same manner (point in time or over time) as for the performance obligations to which the payment amounts were allocated.

The Maruishi Agreement and the CKDP Agreement specify that certain development milestones will be achieved at pre-specified defined phases of a clinical trial (such as initiation or completion or other pre-specified time during a clinical trial as specified in the agreements).

During the six months ended June 30, 2018 and 2017, no milestone events were probable of occurrence or achieved.

Sublicense payments

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

In March 2017, Maruishi entered into a sub-license agreement to the Maruishi Agreement with another pharmaceutical company in Japan for development and sales/marketing of CR845/difelikefalin for the treatment of uremic pruritus in dialysis patients in Japan. The Company first learned that the terms of the sub-license agreement had been finalized less than a month before the sub-licensee publicly announced the agreement. At that time, the Company determined that the sub-license fee would not be constrained from inclusion in the transaction price. Consequently, the Company included the amount of the sub-license fee in the transaction price and recognized revenue of $843 in the same manner as described above for milestone payments.

Sales-based Royalty Payments

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

a. The subsequent sale or usage occurs.

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

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

(amounts in thousands, except share and per share data)

12. Net Loss Per Share

The Company computes basic net income (loss) per share by dividing net income (loss) by the weighted-average number of shares of common stock outstanding. Diluted net income per share includes the potential dilutive effect of common stock equivalents as if such securities were exercised during the period, when the effect is dilutive. Common stock equivalents may include outstanding stock options, which are included using the treasury stock method when dilutive. For the three and six months ended June 30, 2018 and 2017, the Company excluded the effects of potentially dilutive shares that were outstanding during those respective periods from the denominator as their inclusion would be anti-dilutive due to the Company's net losses during those periods.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Basic:				
Weighted average common shares outstanding	33,315,809	32,239,877	33,000,487	29,783,424
Diluted:				
Weighted average common shares outstanding - Basic	33,315,809	32,239,877	33,000,487	29,783,424
Common stock options*	—	—	—	—
Denominator for diluted net loss per share	33,315,809	32,239,877	33,000,487	29,783,424

* 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,	
	2018	2017	2018	2017
Net loss	$ (17,194)	$ (9,300)	$ (33,961)	$ (31,504)
Weighted-average common shares outstanding:				
Basic and Diluted	33,315,809	32,239,877	33,000,487	29,783,424
Net loss per share, Basic and Diluted	$ (0.52)	$ (0.29)	$ (1.03)	$ (1.06)

As of June 30, 2018 and 2017, 3,871,194 and 3,118,786 stock options, respectively, were outstanding, which could potentially dilute basic earnings per share in the future, but were not included in the computation of diluted net loss per share because to do so would have been anti-dilutive.

On July 23, 2018, the Company issued and sold 5,175,000 shares of its common stock in a follow-on public offering, including the full exercise of the underwriters' option to purchase 675,000 additional shares of its common stock (see Note 16, *Subsequent Event*).

(amounts in thousands, except share and per share data)

13. Stock-Based Compensation

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. However, as of January 1, 2015 for officers and January 1, 2016 for employees and non-employee consultants, subsequent grants of Stock Awards vest monthly over a period of four years from the grant date. Stock options initially granted to members of the Company's Board of Directors vest on the date of the Annual Meeting of Stockholders at which their initial term expires based on the class of Director. Subsequent grants to Directors that are made automatically at Annual Meetings of Stockholders vest fully on the first anniversary of the date of grant. The Plan administrator determines the term of Stock Awards granted under the 2014 Plan up to a maximum of ten years.

The aggregate number of shares of the Company's common stock reserved for issuance under the 2014 Plan has automatically increased on January 1 of each year, beginning on January 1, 2015 and will continue to increase on January 1 of each year through and including January 1, 2024, by 3% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the Company's Board of Directors. On January 1, 2018, the aggregate number of shares of common stock that may be issued pursuant to stock awards under the 2014 Plan automatically increased from 3,920,613 to 4,900,481. 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.

Under the 2014 Plan, the Company granted 136,500 and 90,000 stock options during the three months ended June 30, 2018 and 2017, respectively, and 732,500 and 838,500 stock options during the six months ended June 30, 2018 and 2017, respectively. The fair values of stock options granted during the three and six months ended June 30, 2018 and 2017 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,	
	2018	2017	2018	2017
Risk-free interest rate	2.85% - 2.94%	1.85% - 1.88%	2.51% - 2.94%	1.85% - 2.57%
Expected volatility	85.7% - 92.8%	83.3%	85.7% - 92.8%	75.3% - 83.3%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee options (in years)	6.25	6.25	6.25	6.25
Expected life of non-employee options (in years)	NA	10	NA	10

The weighted-average grant date fair value of options granted to employees, non-employee members of the Company's Board of Directors for their Board service and non-employee consultants during the three months ended June 30, 2018 and 2017 was $10.49 and $13.53, respectively, and during the six months ended June 30, 2018 and 2017 was $10.51 and $12.41, respectively.

(amounts in thousands, except share and per share data)

As of June 30, 2018 and 2017, the Company used the Black-Scholes option valuation model with the following ranges of assumptions to re-measure the fair value of all outstanding options that had been granted to non-employee consultants during the vesting period of each tranche in accordance with ASC 505-50:

	June 30,	
	2018	2017
Risk-free interest rate	1.92% - 2.82%	2.02% - 2.28%
Expected volatility	60.4% - 96.2%	76.4% - 81.3%
Expected dividend yield	0%	0%
Expected life of non-employee options (in years)	0.25 - 8.69	6.58 - 9.69

The weighted-average fair value of outstanding options that had been granted to non-employee consultants, as re-measured during the vesting period of each tranche in accordance with ASC 505-50, was $9.97 and $12.18 as of June 30, 2018 and 2017, respectively.

On January 1, 2017, the Company adopted ASU No. 2016-09, *Improvements to Employee Share-Based Payment Accounting*, or ASU 2016-09. On the date of adoption of ASU 2016-09, the Company began to account for forfeitures of unvested stock options as they occur rather than estimate forfeiture rates that were applied to unvested stock option awards, as under the previous accounting guidance. Accordingly, on the date of adoption, the Company recorded a cumulative effect adjustment to stockholders' equity of $45 for all stock option awards that were unvested as of that date.

During the three and six months ended June 30, 2018 and 2017, the Company recognized compensation expense in the accompanying Condensed Statements of Comprehensive Loss relating to stock options, as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Research and development	$ 852	$ 603	$ 1,500	1,166
General and administrative	1,217	715	2,440	1,260
Total stock option expense	$ 2,069	$ 1,318	$ 3,940	$ 2,426

Included in the table above are the following amounts of compensation expense recognized with regard to stock options that were granted to non-employee consultants, including the effect of re-measurement of the fair values of those options, as described above:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Research and development	$ 93	$ 3	$ 121	$ 146
General and administrative	40	(7)	179	32
Total stock option expense	$ 133	$ (4)	$ 300	$ 179

(amounts in thousands, except share and per share data)

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, 2018 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2017	3,492,141	$ 11.75
Granted	732,500	14.13
Exercised	(222,132)	7.87
Expired	(6,562)	17.41
Forfeited	(124,753)	10.95
Outstanding, June 30, 2018	3,871,194	$ 12.44
Options exercisable, June 30, 2018	1,746,033	

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, 2018 and 2017.

14. Income Taxes

For the three months ended June 30, 2018 and 2017, pre-tax losses were $17,346 and $9,302, respectively, and for the six months ended June 30, 2018 and 2017, pre-tax losses were $34,159 and $31,537, respectively. The Company recognized a full tax valuation allowance against its deferred tax assets as of June 30, 2018 and December 31, 2017. Upon adoption of ASU 2016-09 on January 1, 2017, the tax benefit related to the exercise of stock options is recognized as a deferred tax asset that is offset by a corresponding valuation allowance.

The benefit from income taxes of $152 and $2 for the three months ended June 30, 2018 and 2017, respectively, and $198 and $33 for the six months ended June 30, 2018 and 2017, respectively relates to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, which permits qualified small businesses engaged in R&D activities within Connecticut to exchange their unused R&D tax credits for a cash amount equal to 65% of the value of the exchanged credits.

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act, or the Act. The Act, which is also commonly referred to as "U.S. tax reform", significantly changed U.S. corporate income tax laws by, among other provisions, reducing the maximum U.S. corporate income tax rate from 35% to 21% starting in 2018. In accordance with the reduction in U.S. corporate income tax rate during the period of enactment, the Company reduced its deferred tax assets, which were offset by a corresponding reduction to its valuation allowance. On June 30, 2018 and December 31, 2017, the Company did not have any foreign subsidiaries and the international aspects of the Act are not applicable for the respective periods.

On December 22, 2017, Staff Accounting Bulletin 118, or SAB 118, was issued by the SEC due to the complexities involved in accounting for the Act. SAB 118 requires the Company to include in its financial statements a reasonable estimate of the impact of the Act on earnings to the extent such estimate has been determined. Accordingly, the Company's annual estimated effective tax rate for the year ending December 31, 2018 is based on the reasonable estimate guidance provided by SAB 118. The Company is continuing to assess the impact from the Act and will record adjustments in 2018, if necessary.

(amounts in thousands, except share and per share data)

15. Commitments and Contingencies

Contractual obligations and commitments as of June 30, 2018, consisting of future minimum lease payments under the Company's Stamford lease, were as follows:

	Payment Due for the Year Ending December 31,						
	2018	2019	2020	2021	2022	2023	Total
Stamford operating lease	$ 601	$ 1,215	$ 1,240	$ 1,264	$ 1,288	$ 1,164	$ 6,772

Stamford Operating Lease

In December 2015, the Company entered into a lease agreement, or the Stamford Lease, with Four Stamford Plaza Owner LLC, or the Landlord, for office space in Stamford, Connecticut, or the Premises, for the purpose of relocating its headquarters. The initial term of the Stamford Lease commenced in May 2016, or the Commencement Date, and ends in November 2023. The Stamford Lease requires monthly lease payments, including rent escalations and rent holidays, during the initial lease term. The Company began to make rental payments from the Commencement Date. The Company records monthly rent expense on a straight-line basis from March 2016, upon taking possession of the Premises, through November 2023. As of June 30, 2018 and December 31, 2017, the balance of deferred lease obligation, representing the difference between cash rent paid and straight-line rent expense, was $925 and $876, respectively. The Stamford Lease is renewable for one five-year term.

As of the Commencement Date, the Stamford landlord had made tenant improvements of approximately $1,094 to the leased premises. Such amount was included in Property and equipment, net and in Deferred lease obligation on the Company's Balance Sheet on that date. The portion of Deferred lease obligation that is related to tenant improvements is being amortized as a reduction to rent expense over the same term as rent expense. As of June 30, 2018 and December 31, 2017, the balance of Deferred lease obligation related to tenant improvements was $770 and $842, respectively.

In connection with the signing of the Stamford Lease, the Company entered into a standby letter of credit agreement for $769, which serves as a security deposit for the Premises. The standby letter of credit is automatically renewed annually through November 2023. This standby letter of credit is secured with restricted cash in a money market account (refer to Note 6, *Restricted Cash*).

16. Subsequent Event

On July 18, 2018, the Company entered into an underwriting agreement with Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, as representatives of the several underwriters named therein, relating to the issuance and sale by the Company of up to 5,175,000 shares of its common stock, including 675,000 shares of common stock the underwriters had the option to purchase, at a public offering price of $19.00 per share. This offering was made pursuant to the Company's Registration Statement on Form S-3 (File No. 333-216657), filed with the SEC on March 13, 2017 and declared effective on March 24, 2017, and a related prospectus dated March 24, 2017 and prospectus supplement dated July 18, 2018, which was filed with the SEC on July 20, 2018.

On July 23, 2018, the Company closed the offering, including the full exercise of the underwriters' option to purchase 675,000 additional shares of common stock. The Company received net proceeds of approximately $92,026, after deducting $6,300 relating to underwriting discounts and commissions and estimated offering expenses.

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

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

- the success and timing of our clinical trials, including our clinical trial programs for KORSUVA™ (CR845/difelikefalin) injection in chronic kidney disease associated pruritus, or CKD-aP, and Oral KORSUVA (CR845/difelikefalin) in CKD-aP, and chronic liver disease associated pruritus, or CLD-aP, and other investigational indications, and the reporting of clinical trial results;
- the potential regulatory development pathway for KORSUVA (CR845/difelikefalin) injection in CKD-aP and CR845/difelikefalin injection in acute post-operative pain;
- our plans to develop and commercialize KORSUVA (CR845/difelikefalin) injection, Oral KORSUVA (CR845/difelikefalin) and our other product candidates;
- the potential results of ongoing and planned preclinical studies and clinical trials and future regulatory and development milestones for our product candidates;
- the size and growth of the potential markets for pruritus management, including CKD-aP in hemodialysis and non-dialysis markets, CLD-aP markets as well as pain management markets, and for our other product candidates and our ability to serve those markets;
- our ability to obtain and maintain regulatory approval of our product candidates, including intravenous, or I.V., and Oral CR845/difelikefalin, and the labeling under any approval we may obtain;
- the anticipated commercial launch of our lead product candidate, KORSUVA (CR845/difelikefalin) injection;
- the potential of future scheduling of KORSUVA (CR845/difelikefalin) injection by the United States Drug Enforcement Administration, or DEA, if regulatory approval is received;
- the performance of our current and future collaborators and licensees, including Vifor Fresenius Medical Care Renal Pharma Ltd., or VFMCRP, Maruishi Pharmaceuticals Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and our ability to maintain such collaborations;
- our ability to establish additional collaborations for our product candidates;
- the continued service of our key scientific or management personnel;
- our ability to establish commercialization and marketing capabilities;
- regulatory developments in the United States and foreign countries;
- the rate and degree of market acceptance of any approved products;
- our ability to obtain and maintain coverage and adequate reimbursement from third-party payers for any approved products;
- our planned use of our cash and cash equivalents and marketable securities and the clinical milestones we expect to fund with such proceeds;
- the accuracy of our estimates regarding expenses, future revenues and capital requirements;

- our ability to obtain funding for our operations;
- our ability to obtain and maintain intellectual property protection for our product candidates and our ability to operate our business without infringing on the intellectual property rights of others;
- the success of competing drugs that are or may become available; and
- the performance of third-party manufacturers and clinical research organizations.

You should refer to Part I Item 1A. “Risk Factors” of our Annual Report on Form 10-K for the year ended December 31, 2017 for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Quarterly Report on Form 10-Q will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

You should read this Quarterly Report on Form 10-Q and the documents that we reference in this Quarterly Report on Form 10-Q and have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

The following *Management's Discussion and Analysis of Financial Condition and Results of Operations* should be read in conjunction with: (i) the Condensed Financial Statements and related notes thereto which are included in this Quarterly Report on Form 10-Q; and (ii) our Annual Report on Form 10-K for the year ended December 31, 2017.

Introduction

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

In Phase 2 trials, KORSUVA (CR845/difelikefalin) injection (intravenous formulation) has demonstrated statistically significant reductions in itch intensity and concomitant improvement in pruritus-related quality of life measures in hemodialysis patients with moderate-to-severe CKD-aP, and is currently being investigated in Phase 3 trials in hemodialysis patients with CKD-aP. We have partnered with VFMCRP, a joint venture between Vifor Pharma Group and Fresenius Medical Care, to commercialize KORSUVA (CR845/difelikefalin) injection in dialysis patients with CKD-aP worldwide, excluding the United States, Japan (Maruishi), and South Korea (CKDP). We retain all rights in the United States and will promote KORSUVA (CR845/difelikefalin) injection, if approved, with VFMCRP in U.S. Fresenius Medical Care North America, or FMCNA, dialysis clinics under a profit share agreement. CR845/difelikefalin has also demonstrated efficacy in patients with moderate-to-severe pain in the post-operative setting, without inducing many of the undesirable side effects typically associated with currently available opioid pain therapeutics. We retain rights to all KORSUVA/CR845 formulations and indications worldwide, excluding KORSUVA (CR845/difelikefalin) injection in dialysis patients with CKD-aP under our agreement with VFMCRP for certain ex-U.S. territories and our other license agreements for CR845/difelikefalin in Japan (Maruishi) and South Korea (CKDP).

The U.S. Food and Drug Administration, or FDA, has conditionally accepted KORSUVA as the trade name for CR845/difelikefalin injection and its safety and efficacy have not been fully evaluated by any regulatory authority.

We commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our product candidates, including conducting preclinical studies and clinical trials of CR845/difelikefalin-based product candidates, and raising capital. To date, we have financed our operations primarily through sales of our equity and debt securities and payments from license agreements. We have no products currently available for sale, and substantially all of our revenue to date has been revenue from license agreements, although we have received nominal amounts of revenue under research grants.

Recent Developments

Equity Offering

On July 18, 2018, we entered into an underwriting agreement with Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, as representatives of the several underwriters named therein, relating to the issuance and sale by us of up to 5,175,000 shares of our common stock, including 675,000 shares of common stock the underwriters had the option to purchase, at a public offering price of $19.00 per share. This offering was pursuant to Registration Statement on Form S-3 (File No. 333-216657), filed with the SEC on March 13, 2017 and declared on March 24, 2017, and a related prospectus dated March 24, 2017 and prospectus supplement dated July 18, 2018, which was filed with the SEC on July 20, 2018.

On July 23, 2018, we closed the offering, including the full exercise of the underwriters' option to purchase 675,000 additional shares of common stock. We received net proceeds of approximately $92.0 million, after deducting $6.3 million relating to underwriting discounts and commissions and estimated offering expenses.

Vifor Fresenius Medical Care Renal Pharma Ltd. License Agreement

On May 17, 2018, we entered into a license agreement, or the VFMCRP Agreement, with VFMCRP, a joint venture between Vifor Pharma Group and Fresenius Medical Care, under which we granted VFMCRP a license to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA (CR845/difelikefalin) injection for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients worldwide (excluding the United States, Japan and South Korea). We retain full development and commercialization rights for KORSUVA injection for the treatment of CKD-aP in the U.S. except in the dialysis clinics of Fresenius Medical Care North America (FMCNA), where we and VFMCRP will promote KORSUVA injection under a profit-sharing arrangement.

Upon entry into the VFMCRP Agreement, VFMCRP made a non-refundable, non-creditable $50 million upfront payment to us and Vifor (International) Ltd., or Vifor, purchased 1,174,827 shares of our common stock for $20 million, at a premium for the price of $17.024 per share. In addition, we are eligible to receive from VFMCRP regulatory and commercial milestone payments in the aggregate of up to $470 million, consisting of up to $30 million in regulatory milestones and up to $440 million in tiered commercial milestones, all of which are sales-related. We are also eligible to receive tiered double-digit royalty payments based on annual net sales, as defined, of KORSUVA (CR845/difelikefalin) injection in the licensed territories. In the United States, we and VFMCRP will promote KORSUVA (CR845/difelikefalin) injection in the dialysis clinics of FMCNA under a profit-sharing arrangement (subject to the terms and conditions of the VFMCRP Agreement) based on net FMCNA clinic sales recorded by us.

Our Product Candidates

Our product candidate, CR845/difelikefalin, is a new chemical entity, which is designed to selectively stimulate kappa, rather than mu, and delta opioid receptors outside of the central nervous system, or CNS. CR845/difelikefalin has been designed with specific chemical characteristics to restrict its entry into the CNS and further limit its mechanism of action to kappa opioid receptors in the peripheral nervous system, or nerves outside of the brain and spinal cord and certain immune cells. In addition to the side effects associated with activation of mu opioid receptors in the CNS, activation of kappa receptors in the CNS is also known to result in some undesirable effects, including dysphoria. CR845/difelikefalin is designed to specifically target kappa receptors located on peripheral nervous system and certain immune cells that results in modulation of pain signals as well as relief from pruritus or itch associated with certain chronic diseases. Since CR845/difelikefalin is designed to modulate 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 (i.e. dysphoria and hallucinations). CR845/difelikefalin has been administered to more than 2,000 human subjects in Phase 1, Phase 2, Phase 2/3 and Phase 3 clinical trials as an I.V. infusion, rapid intravenous injection or oral capsule or tablet, and thus far has been observed to be generally well tolerated in these clinical trials.

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

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

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

Program	Product Candidate	Primary Indication	Status	Commercialization Rights
Pruritus	KORSUVA (CR845/ difelikefalin) Injection	Pruritus Chronic Kidney Disease-Hemodialysis	• Global Phase 3 efficacy trial initiated • Phase 3 U.S. efficacy trial ongoing; Phase 3 long term safety trial ongoing • Phase 2/3 adaptive trial completed • Breakthrough Therapy Designation granted by FDA in June 2017	Cara (United States); Maruishi (Japan); CKDP (South Korea); VFMCRP (Worldwide, other than United States, Japan and South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus CKD (Stage III - V) (non-hemodialysis)	• Phase 2 efficacy trial ongoing • Phase 1 safety and PK study - daily dosing completed	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral KORSUVA (CR845/difelikefalin)	Pruritus Chronic Liver Disease (CLD)	• Phase 1 safety and PK trial ongoing	Cara (Worldwide, other than South Korea); CKDP (South Korea)
Pain	CR845/difelikefalin Injection	Acute Post Operative Pain	• Adaptive Phase 2/3 trial completed; Top-line data released	Cara (Worldwide, other than Japan and South Korea); Maruishi (Japan); CKDP (South Korea)
	Oral CR845/difelikefalin	Chronic Pain	• Phase 2b osteoarthritis, or OA, clinical trial completed and data reported	Cara (Worldwide, other than South Korea); CKDP (South Korea)
	CR701	Chronic Pain	• Preclinical	Cara (Worldwide)

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

Pruritus, or itch, is associated with certain chronic conditions such as kidney disease, atopic dermatitis, eczema, liver disease and psoriasis. Based on KORSUVA (CR845/difelikefalin)'s effect on the peripheral nervous system and immune cells as well as KORSUVA (CR845/difelikefalin)'s anti-pruritic and anti-inflammatory effects in non-clinical models, we believe KORSUVA (CR845/difelikefalin) has the potential to treat pruritus associated with multiple medical conditions.

CKD-associated pruritus, or CKD-aP, also known as uremic pruritus, is an intractable systemic itch condition with high prevalence in patients with CKD for which there are no approved therapeutics in the United States.

In the first quarter of 2018, we initiated the first pivotal Phase 3 efficacy trial of KORSUVA (CR845/difelikefalin) injection in the United States for the treatment of CKD-aP in patients undergoing hemodialysis. In August 2018, we initiated a Global Phase 3 efficacy trial of KORSUVA (CR845/difelikefalin) injection that is expected to enroll patients in the United States and multiple countries outside the United States. In addition to the efficacy trials, we are also conducting a 52-week Phase 3 safety study of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP.

In June 2017, the FDA granted breakthrough therapy designation for KORSUVA (CR845/difelikefalin) injection for the treatment of moderate-to-severe uremic pruritus in patients with CKD undergoing hemodialysis. This regulatory decision was supported by positive results from Phase 2 clinical trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP. Breakthrough therapy designation is granted to expedite the development and review process for new therapies addressing serious or life-threatening conditions, where preliminary clinical evidence indicates that the drug candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints.

KALM™-1 and KALM-2 Phase 3 Efficacy Trial of KORSUVA (CR845/Difelikefalin) Injection

In January 2018, we initiated the first Phase 3 efficacy trial to support regulatory filings for the approval of KORSUVA (CR845/difelikefalin) injection. This U.S study is a multicenter, randomized, double-blind, placebo-controlled 12-week treatment trial (with a 52-week open label extension phase) that is designed to evaluate the safety and efficacy of 0.5 mcg/kg of KORSUVA (CR845/difelikefalin) injection to be administered three times per week after dialysis in 350 hemodialysis patients with moderate-to-severe pruritus, with a pre-specified interim assessment that allows for expansion of the study to up to 500 patients, if needed. The primary efficacy endpoint is the proportion of patients achieving at least a 3-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. Secondary endpoints of the Phase 3 trial include assessment of itch-related quality of life changes measured using self-assessment 5-D Itch and Skindex-10 scales, as well as the proportion of patients achieving at least 4-point improvement from baseline in weekly mean of the daily 24-hour worst itching NRS score at week 12.

In August 2018, we initiated the second Phase 3 efficacy trial (KALM-2) to support regulatory filings worldwide that is matching in design and size to the KALM-1. This second Phase 3 trial will enroll hemodialysis patients with moderate-to-severe pruritus in the United States as well as in multiple countries in Europe and Asia Pacific. The primary and secondary endpoints are equivalent to those in the KALM-1 trial.

Phase 3 Safety Trial of KORSUVA (CR845/Difelikefalin) Injection

In the second quarter of 2017, we initiated a 52-week Phase 3 safety trial that is expected to enroll up to 240 hemodialysis patients with CKD-aP who completed one of our prior Phase 2/3 trials of KORSUVA (CR845/difelikefalin) injection as well as patients who have not been previously exposed to CR845/difelikefalin. This open-label trial is evaluating the long-term safety of KORSUVA (CR845/ difelikefalin) injection at the dose of 0.5mcg/kg and has currently enrolled over 100 patients with CKD-aP.

The design and dose selection for our Phase 3 trials are based on results of the previously completed Phase 2 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients with CKD-aP in consultation with the FDA as part of our End of Phase 2 meeting with the FDA that was held in September 2017.

Phase 2/3 Adaptive Design Trial of KORSUVA (CR845/Difelikefalin) Injection in Dialysis Patients

In June 2016, we initiated a two-part Phase 2/3 adaptive design trial of KORSUVA (CR845/difelikefalin) injection in dialysis patients suffering from moderate-to-severe uremic pruritus. In March 2017, we announced top-line data from the Phase 2 trial, which was a randomized, double-blind, placebo-controlled trial of three doses of intravenous KORSUVA (CR845/difelikefalin) injection (0.5mcg/kg, 1.0 mcg/kg and 1.5 mcg/kg) administered three times per week after dialysis over an eight-week treatment period in 174 patients with moderate-to-severe uremic pruritus.

The primary endpoint of this trial was the change from baseline of the mean worst itching score for week eight measured on a patient reported 24-hour worst itching intensity 11-point NRS scale. Patients receiving KORSUVA (CR845/difelikefalin) injection experienced a 68% greater reduction from baseline in worst itch scores than those receiving placebo ($p<0.0019$). The secondary endpoints of this trial focused on itch-related quality of life measures assessed using the Skindex-10 scale, 5-D itch scale, sleep disturbance subscale and others. In addition to reduction of pruritus, patients experienced substantial improvement in multiple itch-related quality of life (Skindex-10, 5-D Itch scale) measures and sleep over two months of treatment. Additionally, in a post-hoc analysis, (1) 64% of the patients treated at the 0.5 mcg/kg dose experienced at least a 3-point improvement from baseline with respect to the weekly mean NRS score versus 29% of patients on placebo ($p<0.01$), and (2) 51% of the patients treated at the 0.5 mcg/kg dose experienced at least a 4-point improvement from baseline with respect to the weekly mean NRS score versus 24% of patients on placebo ($p<0.05$).

Overall, KORSUVA (CR845/difelikefalin) was observed to be generally well tolerated over the eight-week treatment period and the unblinded Drug Safety Monitoring Board did not raise any safety concerns during the course of the trial. The most common treatment-emergent adverse events were somnolence, headache, dizziness, mental status changes, nausea and diarrhea, generally in line with what has been observed in previous clinical studies of KORSUVA (CR845/difelikefalin).

Phase 2 Efficacy Trial in Dialysis Patients (Part B)

In 2014, we conducted a Phase 2 randomized, double-blind, placebo-controlled proof-of-concept trial (Part B), which measured the efficacy of KORSUVA (CR845/difelikefalin) injection at the dose of 1.0 mcg/kg compared to placebo in reducing the intensity of itch in 65 dialysis patients with uremic pruritus over a two-week dosing period, who had baseline "worst itching" scores of greater than 40 mm on a visual analog scale, or VAS ranging from 0 to 100 mm. In July 2015, we reported positive top-line efficacy results from this trial, in which we observed that KORSUVA (CR845/difelikefalin) injection demonstrated statistically significant reduction in worst itch intensity as measured by VAS, the primary endpoint of the trial, as well as statistically significant improvement in quality of life measures such as Skindex-10, the trial's secondary endpoint**.** The overall safety and tolerability profile was favorable. The dose of the Phase 2 study was informed by Phase 1 safety and pharmacokinetic, or PK, trial (Part A) that was conducted in subjects undergoing hemodialysis at doses ranging from 0.5 mcg/kg to 2.5 mcg/kg after each dialysis session up to three times per week.

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

In July 2018, we announced the dosing of first patients in a Phase 2 trial of Oral KORSUVA (CR845/difelikefalin) for the treatment of pruritus in stage III-V (moderate-to-severe) CKD patients. The Phase 2, multicenter, randomized, double-blind, placebo-controlled 12-week trial is designed to evaluate the safety and efficacy of three dose levels (0.25 mg, 0.5 mg and 1 mg, once daily) of Oral KORSUVA versus placebo in approximately 240 stage III-V CKD patients with moderate-to-severe pruritus, with a pre-specified interim assessment that allows for expansion of the study to up to 480 patients, if needed. The primary efficacy endpoint is the change from baseline in the weekly mean of the daily 24-hour Worst Itch Numeric Rating Scale (NRS) score at Week 12 of the treatment period. Secondary endpoints include change from baseline in itch-related quality of life scores at the end of Week 12, as assessed by the total Skindex-10 and 5-D itch scores, as well as the proportion of patients achieving an improvement from baseline ≥3 points with respect to the weekly mean of the daily 24-hour Worst Itch NRS score at week 12.

The dosing of the above Phase 2 trial was informed by the results of our Phase 1 trial of Oral KORSUVA (CR845/difelikefalin) in patients with Stage III - V CKD (non-hemodialysis). The Phase 1 trial was designed to examine the PK and safety of different tablet strengths of Oral KORSUVA (CR845/difelikefalin) (0.25 mg, 0.5 mg and 1.0 mg), dosed daily over a one-week treatment period in three groups of patients with moderate renal impairment and three groups of patients with severe renal impairment (six groups total). The exposure levels achieved with Oral KORSUVA tablets were approximately equivalent to the exposure level achieved with 0.5 mcg/kg dose of I.V. KORSUVA that exhibited statistically significant and clinically meaningful reduction in itch intensity in hemodialysis patients with moderate to severe CKD-aP in a previous Phase 2 trial.

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

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

In the fourth quarter of 2017, we submitted an investigational new drug application, or IND, to the FDA for Oral KORSUVA (CR845/difelikefalin) for symptomatic relief of CLD-aP and initiated a Phase 1 safety and PK clinical trial of Oral KORSUVA (CR845/difelikefalin) in patients with CLD in the first quarter of 2018. The open-label study is designed to evaluate the safety and PK profile of repeated doses of Oral KORSUVA (twice daily) in up to 60 patients with CLD and up to 12 matched healthy control subjects. Oral KORSUVA will be evaluated over an eight-day treatment period in patients with mild, moderate or severe CLD based on their Child-Pugh classification (i.e, Class A, B and C). We aim to initiate a Phase 2 trial of Oral KORSUVA for the treatment of CLD-aP later this year/early next year.

Intravenous CR845/Difelikefalin for Treatment of Acute Postoperative Pain

We are also investigating CR845/difelikefalin for the treatment of pain in an acute care setting. CR845/difelikefalin is designed to provide pain relief without stimulating mu opioid receptors and therefore potentially without mu opioid-related side effects, such as nausea, vomiting, respiratory depression and euphoria.

Phase 2/3 Efficacy and Safety Trial of CR845/Difelikefalin Injection in Patients Undergoing Abdominal Surgery

In June 2018, we reported positive top-line date from the adaptive Phase 2/3 study of CR845/difelikefalin in patients undergoing abdominal surgery. This trial was initiated in September 2015 and was designed as a multi-center, randomized, double-blind, placebo-controlled, parallel-group adaptive design trial with repeated doses of CR845/difelikefalin injection or placebo administered both prior to and following abdominal surgery. The trial protocol initially included three dose levels of CR845/difelikefalin injection (1.0 mcg/kg, 2.0 mcg/kg and 5.0 mcg/kg versus placebo) that was subsequently modified in June 2016 to test two doses of I.V. CR845/difelikefalin (1.0 mcg/kg and 0.5 mcg/kg) versus placebo, based on a safety review by us, the trial's Independent Data Monitoring Committee, or IDMC, and the FDA, of unblinded safety data from the first 90 patients dosed. The safety review was conducted in response to a clinical hold that the FDA placed on the trial in February 2016 and removed in April 2016 following the safety review. The clinical hold was based on a pre-specified stopping rule related to elevated serum sodium levels of greater than 150 mmol/L that was included in the clinical trial protocol. The trial enrolled 444 patients undergoing abdominal surgery, composed of 228 patients who underwent ventral hernia surgery and 216 patients who completed a hysterectomy procedure. The primary endpoint was pain relief as measured by Area Under the Curve (AUC) of the NRS pain intensity scores collected over the first 24-hour period after the baseline dose (0 hour) post-surgery for all combined surgeries. The secondary endpoints included incidence of vomiting, improvement in impact scores of post-operative nausea and vomiting (PONV), reduction in use of rescue analgesic medication, as well as patient global assessment at 24 hours post baseline dose after surgery.

- CR845 injection achieved statistical significance for the primary endpoint of pain relief over 24 hours (AUC 0-24) post-surgery with the 1.0 mcg/kg dose versus placebo (p=0.032). The 0.5 mcg/kg dose did not achieve statistical significance over the 0-24 hour period (p=0.076). In addition, improvement in pain AUC was statistically significant for both the 0.5 and 1.0 mcg/kg doses over 0 to 6 hours (p=0.041, p=0.001) and 0 to 12 hours (p=0.035, p=0.004) periods and also statistically significant for the 1.0 mcg/kg dose over the 0 to 18-hour period (p=0.013) post-surgery.
- At 6 and 24 hours after baseline dose post-surgery, there were statistically significant improvements in PONV impact scores with both doses of CR845 injection compared to placebo: 0.5 mcg/kg (6 hrs.: p=0.0072, 24 hrs.: p<0.006) and 1.0 mcg/kg (6 hrs.: p<0.0001, 24 hrs.: p<0.0001).
- There were statistically significant differences between placebo and both doses of CR845 with respect to the total use of anti-emetic medication over the first 24 hours post-surgery (0.5 mcg/kg: p=0.0003; 1.0 mcg/kg: p< 0.0001).

- There was a 73% reduction in the incidence of patient-reported vomiting in the group receiving the 1.0 mcg/kg dose versus placebo (p=0.029). Although the 0.5 mcg/kg also showed reduction in vomiting, it did not reach statistical significance. Both doses of CR845 exhibited numerical trends toward reduced use of rescue analgesic medication compared to placebo, but did not achieve statistical significance.
- There was no significant effect, compared to placebo, on patient's global assessment of medication for either dose of CR845 over the 24-hour period.

Common adverse effects reported in the placebo and both CR845 groups were generally low and similar in incidence, and included nausea, constipation, vomiting, flatulence, headache and dyspepsia.

The next steps for the acute post-operative pain program will be determined after we have completed detailed analysis of the data and consulted with the FDA.

Phase 1 Safety and PK and Phase 2 Acute Pain Clinical Trials (Post-Surgery) of CR845/Difelikefalin Injection

Previously, in three different randomized, double-blind, placebo-controlled Phase 2 clinical trials, CR845/difelikefalin injection has been shown to be well tolerated and demonstrated efficacy of pain relief. Two of these trials were conducted in patients undergoing laparoscopic hysterectomy, a soft tissue surgical procedure, and a third trial was in patients undergoing bunionectomy, a hard tissue surgical procedure. Intravenous administration of CR845/difelikefalin resulted in statistically significant reductions in pain intensity, as measured by the sum of pain intensity difference. In addition, in both surgical models, CR845/difelikefalin injection exhibited an ability to decrease the opioid-related adverse events, or AEs, of nausea and vomiting associated with current therapies, along with no evidence of drug-related respiratory depression.

The safety profile of CR845/difelikefalin injection has been demonstrated in multiple studies. CR845/difelikefalin injection was considered to be generally safe and well tolerated in all of these clinical trials. The most common treatment-emergent adverse events, or TEAEs, across evaluated populations in acute pain trials were transient facial tingling or numbness, dizziness and fatigue. In addition, a transient increase in urine output in the absence of electrolyte loss, otherwise known as aquaresis, was also observed, which in some subjects in acute pain trials was accompanied by asymptomatic elevations in plasma sodium that were generally considered to be clinically unimportant. No clinically significant changes in electrocardiogram characteristics have been observed in any of these studies. Importantly, there appeared to be no cases of dysphoria/hallucinations typically observed with prior-generation CNS-active kappa agonists.

Human Abuse Liability Trial of CR845/Difelikefalin Injection

In the fourth quarter of 2014, we successfully completed a Human Abuse Liability, or HAL, trial of CR845/difelikefalin injection. The results from this HAL trial indicate that CR845/difelikefalin injection met the trial's primary endpoint by demonstrating highly statistically significant lower "drug liking" scores as measured by VAS Emax ($p < 0.0001$) when compared to pentazocine, an approved Schedule IV opioid receptor agonist. I.V. CR845 also demonstrated highly statistically significant lower "feeling high," "overall liking," and "take drug again" scores ($p < 0.0001$) as compared to pentazocine. Additionally, CR845/difelikefalin injection showed no "drug liking" dose response as both doses of CR845/difelikefalin injection were the same. Those scores represent standard subjective measures recommended by the FDA to assess a drug's abuse liability. We believe that the totality of the results from the HAL trial are supportive of the potential for CR845/difelikefalin to be the first non-scheduled or low (Schedule V) scheduled peripheral kappa opioid for acute pain or pruritus.

Respiratory Safety Phase 1 Trial of CR845/Difelikefalin Injection

In April 2017, we announced summary results from our quantitative Phase 1 trial evaluating respiratory safety of CR845/difelikefalin injection. Respiratory depression remains the most life-threatening side effect of traditional, centrally acting, opioid analgesics, the most commonly used drug class for current treatment of postoperative pain in the United States. The Phase 1 trial was a randomized, double-blind, placebo-controlled, three-way crossover trial of two doses of CR845/difelikefalin injection versus placebo on three measures of respiratory drive in 15 healthy volunteers. Each subject was randomized to one of three treatment sequences and was administered I.V. bolus placebo, I.V. CR845/difelikefalin (1.0 mcg/kg) and I.V. CR845/difelikefalin (5.0 mcg/kg) on sequential 24-hour periods, with I.V. CR845/difelikefalin (5.0 mcg/kg) representing a projected five-fold supra-therapeutic dose. After each administration, and continuing through four hours post-dosing, end-tidal CO_2, or $ETCO_2$, oxygen saturation, or SpO_2, and respiratory rate were continuously monitored. The primary safety endpoints were: a >10 mmHg sustained ($\geq$30 seconds duration) increase in $ETCO_2$ above baseline or to >50 mmHg, and a sustained reduction in SpO_2 to <92 percent.

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

Oral CR845/Difelikefalin for Treatment of Osteoarthritis

We also investigated an oral version of CR845/difelikefalin, or Oral CR845/difelikefalin for pain relief, which we believe could be used to provide pain relief to patients with acute or chronic pain in an outpatient setting and also as an I.V.-to-oral transition, or step-down, therapy for hospital patients being prepared for discharge.

Phase 2b Trial of Oral CR845/Difelikefalin

In the third quarter of 2016 we initiated a Phase 2b trial with Oral CR845/difelikefalin, which was designed to evaluate three tablet strengths (1.0 mg, 2.5 mg and 5.0 mg), dosed twice-daily over an eight-week treatment period in 476 patients with osteoarthritis, or OA, of the knee or hip experiencing moderate-to-severe pain across the United States. The primary efficacy endpoint was the change from baseline at week eight, with respect to the weekly mean of the daily pain intensity score using an NRS score. Secondary endpoints included overall Patient Global Assessment, or PGA, score, and overall improvement in Western Ontario and McMaster Osteoarthritis Index, or WOMAC, scores, two commonly used patient-reported outcome measures, as well as mean reduction in rescue medication.

In June 2017, we announced top-line results from the Phase 2b trial. The results of the primary efficacy analysis of change from baseline in pain intensity NRS score comparing Oral CR845/difelikefalin (all doses) vs. placebo were not statistically significant across all patients (OA of the knee or hip). However, patients with OA of the hip maintained on the 5.0 mg dose to the end of the eight-week treatment period exhibited a statistically significant 39% reduction in mean joint pain score versus placebo ($p=0.043$); although this effect did not reach statistical significance in a combined analysis of all patients with OA of the knee or hip maintained on the 5.0 mg dose ($p=0.111$). For patients maintained on the 5.0 mg dose, there was a statistically significant increase in the proportion of patients whose OA pain was “very much improved” or “much improved” as indicated by PGA score in both the total patient group ($p <0.005$ vs. placebo) and in patients with primary OA of the hip ($p<0.006$ vs. placebo). The reduction in pain score in the 5.0 mg dose group in hip patients was accompanied by a reduction in mean rescue medication of 41% at week eight versus placebo. Patients maintained on the 1.0 mg and 2.5 mg tablet strengths did not exhibit significant reductions in mean joint pain scores compared to placebo. All tablet strengths were generally well tolerated with no drug-related serious adverse events. For the 5.0 mg dose, the most common adverse events reported at the >5 percent incidence level were dry mouth (6%) and constipation (12%). There were no clinically significant changes in serum sodium levels observed during the eight-week treatment period for any dose group.

In 2015, we completed a Phase 2a trial of Oral CR845/difelikefalin in 80 patients with OA of the knee or hip with moderate-to-severe pain evaluating four tablet strengths (0.25 mg, 0.5 mg, 1.0 mg and 5.0 mg) administered twice a day over a two-week treatment period. We reported data that showed dose related reduction in mean joint pain score and that all four tablet strengths were safe and well tolerated.

We do not intend to develop Oral CR845/difelikefalin in pain associated with OA on our own and will likely seek one or more potential partner(s) for further development of Oral CR845/difelikefalin in this indication.

CR701

In addition to our CR845/difelikefalin family of peripheral kappa agonists, we have discovered lead molecules that selectively modulate peripheral cannabinoid receptors. Studies on the effects of cannabis have led to the discovery of an endogenous system of ligands in humans involved in a number of physiological processes, including pain and inflammation. The main naturally occurring ligands for this system, anandamide and 2-arachidonoylglycerol (2-AG), activate a number of cannabinoid receptors, including CB1 and CB2 receptors. Like opioid receptors, CB1 and CB2 receptors are members of the G protein-coupled receptor superfamily. CB1 receptors and associated ligands are mainly localized in the brain, whereas CB2 receptors are found mainly in peripheral tissues, particularly immune cells such as leukocytes and mast cells, which have been shown to be involved in pain and inflammatory responses.

Our most advanced CB compound, CR701, is a peripherally-restricted, mixed-CB1/CB2 receptor agonist that selectively interacts with these cannabinoid receptor subtypes, with no off-target activities. The compound is orally bioavailable, active in preclinical models of inflammatory and neuropathic pain, and does not produce the side effects characteristic of centrally-active cannabinoids, such as sedation and hypothermia. Accordingly, CR701 would be expected to have substantially less abuse potential than centrally-active cannabinoids, but retain activity against therapeutically valuable peripheral targets, similar in principle to CR845/difelikefalin.

Components of Operating Results

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the foreseeable future. Substantially all of our revenue recognized to date has consisted of upfront payments under license agreements with VFMCRP, Maruishi and CKDP, and milestone and sub-license payments under license agreements with CKDP and Maruishi for CR845/difelikefalin, some or all of which was deferred upon receipt, as well as license agreements for CR665, our first-generation drug program for which development efforts have ceased. To date, excluding the upfront payments received under our three license agreements, we have earned a total of $5.2 million in clinical development or regulatory milestone payments and sub-license fees under our Maruishi and CKDP collaborations, net of contractual foreign currency adjustments and South Korean withholding taxes, but have not yet received any milestone payments under the VFMCRP Agreement. We have not received any royalties, under any of our collaborations.

Research and Development (R&D)

Our R&D expenses relate primarily to the development of CR845/difelikefalin. R&D expenses consist of expenses incurred in performing R&D activities, including compensation and benefits for full-time R&D employees, clinical trial and related clinical manufacturing expenses, third-party formulation expenses, fees paid to contract research organizations, or 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 2018 will increase over those for 2017. 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:

- per patient trial costs;
- the number of patients that participate in the trials;
- the number of sites included in the trials;
- the countries in which the trial is conducted;
- the length of time required to enroll eligible patients;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring or other studies requested by regulatory agencies;

- the duration of patient follow-up; and
- the efficacy and safety profile of the product candidate.

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

General and Administrative

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, legal, business development 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 2018 will approximate those for 2017 to support our continued R&D activities and potential commercialization of our product candidates. These expenses will likely include costs related to the hiring of additional personnel, fees to outside consultants, lawyers and accountants, and investor relations costs. In addition, if I.V. CR845/difelikefalin, Oral CR845/difelikefalin or any future product candidate obtains regulatory approval for marketing, we expect to incur expenses associated with building a sales and marketing team.

Other Income

Other income consists of interest and dividend income earned on our cash, cash equivalents, marketable securities and restricted cash and realized gains and losses on the sale of marketable securities and property and equipment.

Benefit from Income Taxes

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

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2018 and 2017

Revenue

	Three Months Ended June 30,			Six Months Ended June 30,		
	2018	2017	% change	2018	2017	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
License and milestone fees revenue	$ 2,874	$ —	N/A	$ 2,874	$ 530	442%
Collaborative revenue	—	—	0%	—	313	-100%
Clinical compound revenue	—	—	0%	—	68	-100%
Total revenue	$ 2,874	$ —	N/A	$ 2,874	$ 911	216%

License and milestone fees revenue

License and milestone fees revenue for the three and six months ended June 30, 2018 was $2.9 million. There was no license and milestone fees revenue for the three months ended June 30, 2017. License and milestone fees revenue for the three and six months ended June 30, 2018 was related to license fees earned by us during the period in connection with the VFMCRP Agreement. License and milestone fees revenue for the six months ended June 30, 2017 included $530 thousand of the $843 thousand sub-license fee earned by us in connection with Maruishi's sub-license agreement with Kissei Pharmaceuticals, Co. Ltd. that was allocated to the license fee performance obligation under the Maruishi Agreement (see Note 10 of Notes to Condensed Financial Statements, *Collaborations and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

Collaborative revenue

There was no collaborative revenue for the three and six months ended June 30, 2018 or the three months ended June 30, 2017. Collaborative revenue for the six months ended June 30, 2017 included $313 thousand of the $843 thousand sub-license fee earned by us in connection with Maruishi's sub-license agreement with Kissei Pharmaceuticals, Co. Ltd. that was allocated to the R&D services performance obligation under the Maruishi Agreement (see Note 10 of Notes to Condensed Financial Statements, *Collaborations and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

Clinical compound revenue

There was no clinical compound revenue for the three or six months ended June 30, 2018 or the three months ended June 30, 2017. Clinical compound revenue for the six months ended June 30, 2017 included $68 thousand from the sale of clinical compound to Maruishi.

Research and Development Expense

	Three Months Ended June 30,			Six Months Ended June 30,		
	2018	2017	% change	2018	2017	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 12,739	$ 3,544	259%	$ 22,087	$ 20,746	6%
Consultant services in support of clinical trials	914	539	69%	1,456	911	60%
Stock-based compensation	852	603	41%	1,500	1,166	29%
Depreciation and amortization	94	104	-10%	199	207	-4%
Other R&D operating expenses	2,403	2,171	11%	5,187	4,767	9%
Total R&D expense	$ 17,002	$ 6,961	144%	$ 30,429	$ 27,797	9%

For the three months ended June 30, 2018 compared to the three months ended June 30, 2017, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $9.9 million, mainly from activities related to the two Phase 3 studies of I.V. KORSUVA (CR845/difelikefalin) in CKD patients undergoing hemodialysis, the Phase 3 long-term safety study of I.V. KORSUVA (CR845/difelikefalin) in hemodialysis patients with CKD-aP, and the Phase 2 trial of Oral CR845 in CKD-aP patients. There was also an increase of $2.2 million in drug manufacturing costs. Those costs were partially offset by a decrease of $2.4 million, mainly from the Phase 2b clinical trial of Oral CR845/difelikefalin in patients with osteoarthritis, the Phase 2 clinical trial of I.V. KORSUVA (CR845/difelikefalin) in hemodialysis patients with moderate-to-severe uremic pruritus, and the Phase 1 safety and PK trial of multiple doses of Oral CR845/difelikefalin in hemodialysis patients, all of which are complete and no longer ongoing. The increase in stock-based compensation expense relates primarily to an increase in the number of options outstanding and stock option awards granted to non-employee consultants, which are marked to market each quarter, and resulted from an increase in the market price of our common stock. The increase in other R&D operating expenses was primarily the result of an increase in payroll and related costs associated with R&D personnel.

For the six months ended June 30, 2018 compared to the six months ended June 30, 2017, the net increase in direct clinical trial costs and related consultant costs primarily resulted from increases totaling $14.4 million, mainly from activities related to the two Phase 3 studies of I.V. KORSUVA (CR845/difelikefalin) in CKD patients undergoing hemodialysis, the Phase 3 long-term safety study of I.V. KORSUVA (CR845/difelikefalin) in hemodialysis patients with CKD-aP, the Phase 2

trial of Oral CR845 in CKD-aP patients, the Phase 1 safety and PK trial of multiple doses of Oral CR845/difelikefalin in moderate-to-severe CKD patients and the Phase 1 safety and PK trial of Oral CR845/difelikefalin in patients with liver disease. There was also an increase of $1.4 million in drug manufacturing costs. Those costs were partially offset by a decrease of $13.7 million, mainly from the Phase 2b clinical trial of Oral CR845/difelikefalin in patients with osteoarthritis, the Phase 2/3 I.V. CR845/difelikefalin adaptive clinical trial in postoperative pain, the Phase 2 clinical trial of I.V. KORSUVA (CR845/difelikefalin) in hemodialysis patients with moderate-to-severe uremic pruritus, and the Phase 1 safety and PK trial of multiple doses of Oral CR845/difelikefalin in hemodialysis patients, all of which are complete and no longer ongoing. The increase in stock-based compensation expense relates primarily to an increase in the number of options outstanding. The increase in other R&D operating expenses was primarily the result of an increase in payroll and related costs associated with R&D personnel.

The following table summarizes our R&D expenses by programs for the three and six months ended June 30, 2018 and 2017:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2018	2017	% change	2018	2017	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
I.V. CR845 - Pruritus	$ 8,187	$ 990	727%	$ 11,858	$ 4,366	172%
I.V. CR845 - Pain	699	86	713%	3,968	8,730	-55%
Oral CR845 - Pruritus	3,317	1,142	190%	5,563	2,606	113%
Oral CR845 - Pain	1,450	1,865	-22%	2,153	5,955	-64%
Internal research and development expenses	3,349	2,878	16%	6,887	6,140	12%
Total research and development expenses	$ 17,002	$ 6,961	144%	$ 30,429	$ 27,797	9%

General and Administrative Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2018	2017	% change	2018	2017	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 889	$ 568	56%	$ 1,482	$ 1,102	34%
Stock-based compensation	1,217	715	70%	2,440	1,260	94%
Depreciation and amortization	20	19	4%	40	38	3%
Other G&A operating expenses	1,559	1,370	14%	3,420	2,672	28%
Total G&A expense	$ 3,685	$ 2,672	38%	$ 7,382	$ 5,072	46%

For the three months ended June 30, 2018 compared to the three months ended June 30, 2017, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs, legal fees, accounting and auditing fees and patents. The increase in stock-based compensation expense resulted from additional stock option grants to employees and higher expense relating to Board of Directors' stock options. The increase in other G&A operating expenses was primarily the result of an increase in payroll and related costs associated with G&A personnel.

For the six months ended June 30, 2018 compared to the six months ended June 30, 2017, the increase in professional fees and public/investor relations expenses was primarily the result of increased consultants' costs, legal fees, accounting and auditing fees and patents. The increase in stock-based compensation expense resulted from additional stock option grants to employees and higher expense relating to Board of Directors' stock options. The increase in other G&A operating expenses was primarily the result of an increase in payroll and related costs associated with G&A personnel.

Other Income

	Three Months Ended June 30,			Six Months Ended June 30,		
	2018	2017	% change	2018	2017	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other Income	$ 467	$ 331	41%	$ 778	$ 421	85%

During the three months ended June 30, 2018 compared to the three months ended June 30, 2017, the increase in other income was primarily due to an increase in dividend and interest income resulting from a higher average balance of our portfolio of investments in the 2018 period.

During the six months ended June 30, 2018 compared to the six months ended June 30, 2017, the increase in other income was primarily due to an increase in dividend and interest income resulting from a higher average balance of our portfolio of investments in the 2018 period.

Benefit from Income Taxes

For the three months ended June 30, 2018 and 2017, pre-tax losses were $17.3 million and $9.3 million, respectively, and we recognized a benefit from income taxes of $152 thousand and $2 thousand, respectively. For the six months ended June 30, 2018 and 2017, pre-tax losses were $34.2 million and $31.5 million, respectively, and we recognized a benefit from income taxes of $198 thousand and $33 thousand, respectively.

The benefit from income taxes relates to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, as discussed above. We recognized a full valuation allowance against deferred tax assets at June 30, 2018 and December 31, 2017.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception and through June 30, 2018, we have raised an aggregate of approximately $394.6 million to fund our operations, including (1) net proceeds of $217.8 million from the sale of shares of our common stock in three 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 $88.9 million under our license agreements, primarily with VFMCRP, Maruishi and CKDP, and an earlier product candidate for which development efforts ceased in 2007; and (4) net proceeds of $14.6 million from the purchase of our common stock in relation to the license agreement with VFMCRP (see Note 10 of Notes to Condensed Financial Statements, *Collaborations and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

In order to fund future operations, including our planned clinical trials, we filed a shelf registration statement on Form S-3 (File No. 333-216657), which the Securities and Exchange Commission, or SEC, declared effective on March 24, 2017. The shelf registration statement provides for aggregate offerings of up to $250 million of common stock, preferred stock, debt securities, warrants or any combination thereof. The securities registered under this shelf registration statement include unsold securities that had been registered under our previous shelf registration statement (File No. 333-203072) that was declared effective on May 13, 2015.

On April 5, 2017, we completed a public offering of 5,117,500 shares of our common stock, including 667,500 shares sold upon the full exercise by the underwriters of their option to buy additional shares pursuant to our shelf registration statement. We received net proceeds of $86.2 million after deducting the underwriting discounts and commissions and offering expenses paid by us. The proceeds of the offering are being used to fund our clinical and research development activities, including the ongoing Phase 3 program for I.V. KORSUVA (CR845/difelikefalin) in CKD-aP or uremic pruritus, additional trials of Oral CR845/difelikefalin in other diseases associated with pruritus, the recently completed Phase 2/3 I.V. CR845/difelikefalin adaptive clinical trial in postoperative pain, as well as for working capital and general corporate purposes.

On July 18, 2018, we entered into an underwriting agreement with Jefferies LLC and Merrill Lynch, Pierce, Fenner & Smith Incorporated, as representatives of the several underwriters named therein, relating to the issuance and sale by us of up to 5,175,000 shares of our common stock, including 675,000 shares of common stock the underwriters had the option to purchase, at a public offering price of $19.00 per share. This offering was made by pursuant to our Registration Statement on Form S-3 (File No. 333-216657), filed with the SEC on March 13, 2017 and declared effective on March 24, 2017, and a related prospectus dated March 24, 2017 and a prospectus supplement dated July 18, 2018, which was filed with the SEC on July 20, 2018.

On July 23, 2018, we closed the offering, including the full exercise of the underwriters' option to purchase 675,000 additional shares of common stock. We received net proceeds of approximately $92.0 million, after deducting $6.3 million relating to underwriting discounts and commissions and estimated offering expenses.

We intend to use the net proceeds from this most recent underwritten offering to fund our clinical and research development activities, including the completion of our Phase 3 program and submission of a new drug application to the FDA for KORSUVA (CR845/difelikefalin) injection for the treatment of CKD-aP in hemodialysis patients, the advancement of Oral KORSUVA (CR845/difelikefalin) into Phase 2 trials for the treatment of CKD-aP in Stage III-V patients and CLD patients, the expansion of our Oral KORSUVA program into certain dermatologic conditions and the exploration of further development of CR845/difelikefalin injection in the post-operative setting after consultation with the FDA, as well as for working capital and other general corporate purposes.

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. We believe that the use of a shelf registration statement provides us with the flexibility to raise additional capital to finance our operations as needed.

As of June 30, 2018, we had $132.0 million in unrestricted cash and cash equivalents and available-for-sale marketable securities. Additionally, in July 2018, we completed a follow-on public offering pursuant to which we received net proceeds of approximately $92.0 million. We believe our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient to fund our currently anticipated operating expenses and capital expenditures into 2021, without giving effect to any potential milestone payments we may receive under our licensing and collaboration agreements with VFMCRP, Maruishi and CKDP. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs.

Under the VFMCRP Agreement, we are eligible to receive regulatory and commercial milestone payments in the aggregate of up to $470 million, consisting of up to $30 million in regulatory milestones and up to $440 million in tiered commercial milestones, all of which are sales-related. We are also eligible to receive tiered double-digit royalty payments based on annual net sales, as defined in the VFMCRP Agreement, of CR845/difelikefalin injection in the Licensed Territories.

Under the Maruishi Agreement, we are also potentially eligible to earn up to an aggregate of $6.0 million in clinical development milestones and $4.5 million in regulatory milestones, before any foreign exchange adjustment, as well as tiered royalties, with percentages ranging from the low double digits to the low twenties, based on net sales of products containing CR845/difelikefalin in Japan, if any, and share in any sub-license fees. As of June 30, 2018, we have received milestone payments of $2.5 million before contractual foreign currency exchange adjustments.

During the first quarter of 2017, Maruishi entered into a sub-license agreement with another Japanese pharmaceutical company for the development and sales/marketing of CR845/difelikefalin in patients with uremic pruritus in Japan, as a result of which we received a payment of $843 thousand.

The next potential milestones that could result in us receiving payments under the Maruishi Agreement will be a clinical development milestone associated with the recently completed first pivotal Phase 3 trial of CR845/difelikefalin in acute pain in the United States and the potential initiation by Maruishi of a Phase 3 clinical trial of CR845/difelikefalin in Japan for uremic pruritus. If achieved, these milestones will result in payments of $1.0 million and $2.0 million, respectively, before contractual foreign currency exchange adjustments, being due to us.

Under the CKDP Agreement, we are potentially eligible to earn up to an aggregate of $2.25 million in clinical development milestones and $1.5 million in regulatory milestones, before South Korean withholding tax, as well as tiered royalties with percentages ranging from the high single digits to the high teens, based on net sales of products containing CR845/difelikefalin in South Korea, if any, and share in any sub-license fees. As of June 30, 2018, we have received milestone payments of $1.5 million before South Korean withholding tax.

The next potential milestone that could result in us receiving payment under the CKDP Agreement will be for a clinical development milestone for the completion by us in the United States of a Phase 3 trial of CR845/difelikefalin in uremic pruritus. If achieved, this milestone will result in a payment of $750 thousand, before South Korean withholding tax, being due to us.

Our ability to earn these payments and their timing is dependent upon the outcome of I.V. and Oral CR845/difelikefalin development activities and, potentially, commercialization. However, our receipt of any further such amounts is uncertain at this time and we may never receive any more of these amounts.

Funding Requirements

Our primary uses of capital have been, and we expect will continue to be, compensation and related expenses, third-party clinical R&D services and clinical costs. In the past, we have also previously used capital for laboratory and related supplies.

Since inception, we have incurred significant operating and net losses. Our net losses were $17.2 million and $9.3 million for the three months ended June 30, 2018 and 2017, respectively, and $34.0 million and $31.5 million for the six months ended June 30, 2018 and 2017, respectively. As of June 30, 2018, we had an accumulated deficit of $254.3 million. We expect to continue to incur significant expenses and operating and net losses in the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials, the receipt of additional milestone payments, if any, under our licensing and collaborations with VFMCRP, Maruishi and CKDP, the receipt of payments under any future collaborations and/or licensing agreements we may enter into, and our expenditures on other R&D activities.

We anticipate that our expenses will increase as we:

- continue the development of KORSUVA (CR845/difelikefalin) injection for CKD-aP in dialysis patients;
- continue the development of Oral KORSUVA (CR845/difelikefalin) for CKD-aP and other diseases associated with pruritus, such as CLD-aP;
- explore the potential to further develop I.V. CR845/difelikefalin in the post-operative setting;
- conduct R&D of any potential future product candidates;
- seek regulatory approvals for I.V. CR845/difelikefalin and any product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our global intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development and potential future commercialization efforts.

The successful development of any of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of I.V. CR845/difelikefalin, Oral CR845/difelikefalin or our other current and future programs. We are also unable to predict when, if ever, we will generate any further material net cash inflows from CR845/difelikefalin. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- achieving meaningful penetration in the markets which we seek to serve; and
- obtaining adequate coverage or reimbursement by third parties, such as commercial payers and government healthcare programs, including Medicare and Medicaid.

A change in the outcome of any of these variables with respect to the development of I.V. CR845/difelikefalin, Oral CR845/difelikefalin or any of our future product candidates would significantly change the costs and timing associated with the development of that product candidate.

Because our product candidates are still in clinical development and the outcome of these efforts is uncertain, we cannot estimate the total amounts necessary to successfully complete the development and commercialization of all our product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements, including our existing licensing and collaboration agreements with VFMCRP, Maruishi and CKDP.

We will require additional capital beyond our current balances of cash and cash equivalents and available-for-sale marketable securities and anticipated amounts as described above, and this additional capital may not be available when needed, on reasonable terms, or at all. In particular, because we do not have sufficient financial resources to meet all of our development objectives, especially the completion of our planned development of I.V. and Oral CR845/difelikefalin for the treatment of pruritus, we will need to raise additional capital. If we are not able to do so, we could be required to postpone, scale back or eliminate some, or all, of these objectives. To the extent that we raise additional capital through the future sale of equity or convertible debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on timing expectations and projected costs for our current clinical development plans, which include completing our Phase 3 trials of KORSUVA (CR845/difelikefalin) injection in hemodialysis patients suffering from moderate-to-severe CKD-aP to enable an NDA submission, and conducting Phase 1 and Phase 2 trials of Oral (CR845/difelikefalin) in patients with CKD-aP and CLD-aP, we expect that our existing cash and cash equivalents and available-for-sale marketable securities as of June 30, 2018, as well as $92.0 million of net proceeds that we received in July 2018 related to the issuance and sale by us of 5,175,000 shares of our common stock, will be sufficient for us to fund our currently anticipated operating expenses and capital expenditures into 2021, without giving effect to any potential milestone payments we may receive under our collaboration agreements with VFMCRP, Maruishi and CKDP. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that may be delayed or not initiated and other non-committed controllable costs. Because the process of testing product candidates in clinical trials is costly and the timing of progress in these trials is uncertain, it is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we presently expect.

The Tax Cuts and Jobs Act of 2017

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act, or the Act. The Act, which is also commonly referred to as "U.S. tax reform", significantly changed U.S. corporate income tax laws by, among other provisions, reducing the maximum U.S. corporate income tax rate from 35% to 21% starting in 2018. In accordance with the reduction in U.S. corporate income tax rate during the period of enactment, we reduced our deferred tax assets, which were offset by a corresponding reduction to our valuation allowance. On June 30, 2018 and December 31, 2017, we did not have any foreign subsidiaries and the international aspects of the Act are not applicable for the respective periods.

On December 22, 2017, Staff Accounting Bulletin 118, or SAB 118, was issued by the SEC due to the complexities involved in accounting for the Act. SAB 118 requires us to include in our financial statements a reasonable estimate of the impact of the Act on earnings to the extent such estimate has been determined. Accordingly, our annual estimated effective tax rate for the year ending December 31, 2018 is based on the reasonable estimate guidance provided by SAB 118. We are continuing to assess the impact from the Act and will record adjustments in 2018, if necessary.

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, 2018 and 2017:

	Six Months Ended June 30,	
	2018	2017
	Dollar amounts in thousands	
Net cash provided by (used in) operating activities	$ 22,552	$ (33,563)
Net cash used in investing activities	(30,442)	(56,702)
Net cash provided by financing activities	16,304	87,589
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 8,414	$ (2,676)

Net cash provided by (used in) operating activities

Net cash provided by operating activities for the six months ended June 30, 2018 consisted primarily of a $56.2 million cash inflow from net non-cash charges and a $0.4 million inflow from net changes in operating assets and liabilities, partially offset by a net loss of $34.0 million. Net non-cash charges primarily consisted of an increase in deferred revenue of $52.6 million related to the VFMCRP Agreement and stock-based compensation expense of $3.9 million. The net change in operating assets and liabilities primarily consisted of a cash inflow of $4.0 million from an increase in accounts payable and accrued expenses, partially offset by a cash outflow of $4.0 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs.

Net cash used in operating activities for the six months ended June 30, 2017 consisted primarily of a net loss of $31.5 million, and a $4.5 million outflow from net changes in operating assets and liabilities, partially offset by a $2.5 million cash inflow from net non-cash charges. The net change in operating assets and liabilities primarily consisted of a cash outflow of $4.3 million from a decrease in accounts payable and accrued expenses and a cash outflow of $0.4 million from an increase in prepaid expense, primarily related to an increase in prepaid clinical costs. Those cash outflows were partially offset by a cash inflow of $0.3 million due to a decrease in income tax receivable from the State of Connecticut under the Connecticut R&D Tax Credit Exchange Program. Net non-cash charges primarily consisted of $2.4 million of stock-based compensation expense and $0.2 million of depreciation and amortization expense.

Net cash used in investing activities

Net cash used in investing activities was $30.4 million for the six months ended June 30, 2018, which primarily included cash outflows of $98.3 million for the purchase of available-for-sale marketable securities, partially offset by cash inflows of $56.7 million from maturities of available-for-sale marketable securities and $11.1 million from the sale of available-for-sale marketable securities.

Net cash used in investing activities for the six months ended June 30, 2017, primarily included cash outflows of $98.0 million for the purchase of available-for-sale marketable securities, partially offset by cash inflows of $35.9 million from maturities of available-for-sale marketable securities and $5.4 million from the sale 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, 2018 consisted of proceeds of $14.6 million from the sale of our common stock relating to the VFMCRP Agreement and $1.7 million received from the exercise of stock options.

Net cash provided by financing activities for the six months ended June 30, 2017 consisted of proceeds, net of issuance costs, of $86.2 million from our public offering of common stock completed in April 2017 and $1.4 million received from the exercise of stock options.

Significant Contractual Obligations and Commitments

Contractual obligations and commitments as of June 30, 2018 consisted of an operating lease obligation in connection with our operating facility in Stamford, Connecticut. See Note 15 of Notes to Condensed Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q.

Recent Accounting Pronouncements

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

Off-Balance Sheet Arrangements

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

Discussion of Critical Accounting Policies

The preparation of financial statements in conformity with GAAP requires us to use judgment in making certain estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities and the reported amounts of revenues and expenses in our condensed financial statements and accompanying notes. Critical accounting policies are those that are most important to the portrayal of our financial condition and results of operations and require difficult, subjective and complex judgments by management in order to make estimates about the effect of matters that are inherently uncertain. During the six months ended June 30, 2018, there were no significant changes to our critical accounting policies from those described in our Annual Report on Form 10-K for the year ended December 31, 2017, except as disclosed in Note 2, *Basis of Presentation*, of Notes to Condensed Financial Statements, included in this Quarterly Report on Form 10-Q regarding revenue recognition.

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

Interest Rate Risk

As of June 30, 2018, we invested a majority of our cash reserves in a variety of available-for-sale marketable securities, including money market funds and investment-grade debt instruments, principally corporate notes, commercial paper 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, 2018, we had invested $114.2 million of our cash reserves in such marketable securities. Those marketable securities include $46.0 million of investment grade debt instruments with a yield of approximately 2.22% and maturities through January 2019 and $68.2 million of money market funds with an average annual return of 1.52%. As of December 31, 2017, we had invested $83.2 million of our cash reserves in such marketable securities. Those marketable

securities included $43.2 million of investment grade debt instruments with a yield of approximately 1.70% and maturities through July 2018 and $40.0 million of money market funds with an average annual return of 1.32%.

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

Duration is a sensitivity measure that can be used to approximate the change in the fair value of a security that will result from a change in interest rates. Applying the duration model, a hypothetical 1% increase in interest rates as of June 30, 2018 and December 31, 2017, would have resulted in immaterial decreases in the fair values of our portfolio of marketable securities at those dates. We do not currently use interest rate derivative instruments to manage exposure to interest rate changes.

Credit Quality Risk

Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Nonetheless, deterioration of the credit quality of an investment security subsequent to purchase may subject us to the risk of not being able to recover the full principal value of the security.

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

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of June 30, 2018. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2018, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC, and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosures.

Changes in Internal Control Over Financial Reporting

Beginning January 1, 2018, we implemented ASC 606, *Revenue from Contracts with Customers*. Although the new revenue standard had no impact on our results of operations, financial position or cash flows for any historical period presented from our revenue-related contracts, we did implement changes to our processes related to revenue recognition and the control activities within them during the six months ended June 30, 2018. These included the development of new policies based on the five-step model provided in the new revenue standard, ongoing contract review requirements, and gathering of information provided for disclosures.

There was no other change in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended June 30, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Controls and Procedures

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

PART II

OTHER INFORMATION

Item 1. ***Legal Proceedings***

From time to time, we are subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings and we are not aware of any pending or threatened legal proceedings against us that we believe could have a material adverse effect on our business, operating results or financial condition.

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

Please refer to *Item 1A. Risk Factors* in our Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC on March 15, 2018, for a description of certain significant risks and uncertainties to which our business, operations and financial condition are subject. During the six months ended June 30, 2018, we did not identify any additional risk factors or any material changes to the risk factors discussed in the Annual Report on Form 10-K for the year ended December 31, 2017.

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
3.1	Amended and Restated Certificate of Incorporation (1)
3.2	Amended and Restated Bylaws (2)
10.1 †#	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 Chief Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.
32.1 †*	Certifications of Chief Executive Officer and Chief Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101 †	Interactive Data File
101.CAL †	XBRL Taxonomy Extension Calculation Linkbase.
101.INS †	XBRL Instance Document.
101.LAB †	XBRL Taxonomy Extension Label Linkbase.
101.PRE †	XBRL Taxonomy Extension Presentation Linkbase.
101.SCH †	XBRL Taxonomy Extension Schema Linkbase.
101.DEF †	XBRL Definition Linkbase Document.

(1) Filed as exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-36279) filed with the Securities and Exchange Commission on February 7, 2014 and incorporated herein by reference.

(2) Filed as exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-36279) filed with the Securities and Exchange Commission on February 7, 2014 and incorporated herein by reference.

† Filed herewith.

Confidential treatment has been requested for certain portions of this exhibit.

* These certifications are being furnished solely to accompany this quarterly report pursuant to 18 U.S.C. Section 1350 and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

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

CARA THERAPEUTICS, INC.

Date: August 7, 2018

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

Date: August 7, 2018

By /s/ MANI MOHINDRU
Mani Mohindru, Ph.D.
Chief Financial Officer
(Principal Financial and Accounting Officer)

EXHIBIT 10.1

[***] Text Omitted and Filed Separately with the Securities and Exchange Commission. Confidential Treatment Requested Under 17 C.F.R. Sections 200.80(b)(4) and 240.24b-2

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
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

1.71 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	[***]

Milestone Event	Milestone Payment
(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) [***] 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
with a copy to:	Vifor Pharma Management Ltd 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

[***] Confidential Treatment Requested

Exhibit 1.18

[***]

[***] Confidential Treatment Requested

Exhibit 1.34

Excluded Clinics and Programs

[***]

[***] Confidential Treatment Requested

Exhibit 1.62

Product Trademark

KORSUVA

[***] Confidential Treatment Requested

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, Derek Chalmers, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 7, 2018

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

EXHIBIT 31.2

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

I, Mani Mohindru, 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 7, 2018

By: /s/ Mani Mohindru
MANI MOHINDRU, Ph.D.
CHIEF FINANCIAL OFFICER

EXHIBIT 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended June 30, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Derek Chalmers, Ph.D., D.Sc., as Chief Executive Officer of the Company, and Mani Mohindru, Ph.D., as Chief Financial Officer of the Company, each hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of his or her knowledge, based upon a review of the Report:

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

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

/s/ DEREK CHALMERS
Name: Derek Chalmers, Ph.D., D.Sc.
Title: Chief Executive Officer
Date: August 7, 2018

/s/ MANI MOHINDRU
Name: Mani Mohindru, Ph.D.
Title: Chief Financial Officer
Date: August 7, 2018