Cara Therapeutics, Inc.
Form 10-Q
August 07, 2018

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 (State or other jurisdiction of incorporation or organization)	75-3175693 (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

PART I –FINANCIAL INFORMATION

PART I

FINANCIAL INFORMATION

Item 1. Financial Statements.

CARA THERAPEUTICS, INC.

CONDENSED BALANCE SHEETS

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

(unaudited)

	June 30, 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,	34	33

respectively		
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 Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' 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 Shares	Amount	Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
Balance at December 31, 2017	32,662,255	$ 33	$ 307,158	$ (220,341)	$ (70)	$ 86,780
Sale of common stock under	1,174,827	1	14,555	—	—	14,556

license agreement						
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.

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CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

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

(unaudited)

1. Business

Cara Therapeutics, Inc., or the Company, is a clinical-stage biopharmaceutical corporation formed on July 2, 2004. The Company is focused on developing and commercializing new chemical entities designed to alleviate pruritus 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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

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

(unaudited)

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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

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

(unaudited)

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).

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

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

(unaudited)

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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

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

(unaudited)

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.

	As of June 30, 2018		As of December 31, 2017	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	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.

CARA THERAPEUTICS, INC.

NOTES TO CONDENSED FINANCIAL STATEMENTS

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

(unaudited)

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.

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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:

	Affected Line

Component of AOCI	Three Months Ended June 30, 2018	2017	Six Months Ended June 30, 2018	2017	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.

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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	$ —

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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

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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.

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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.

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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.

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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.

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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.

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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).

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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.

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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.

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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.

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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).

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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.

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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

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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.

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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," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," "will," or "would," and or the negative of t 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	Cara (Worldwide, other than South Korea); CKDP (South Korea)

		completed and data reported	
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 (>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			Six Months Ended		
	June 30,			June 30,		
Dollar amounts in	2018	2017	% change	2018	2017	% change

	thousands			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		