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

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2024

OR

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

COMMISSION FILE NUMBER 001-36279

CARA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**75-3175693**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
400 Atlantic Street Suite 500 Stamford, Connecticut	**06901**
(Address of registrant's principal executive offices)	**(Zip Code)**

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

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value $0.001 per share	CARA	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. ☒ Yes ☐ No.

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). ☒ Yes ☐ No.

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

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

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

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

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of August 9, 2024 was: 54,846,639.

CARA THERAPEUTICS, INC.

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FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2024

PART I –FINANCIAL INFORMATION

PART I
FINANCIAL INFORMATION

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

CARA THERAPEUTICS, INC.

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

	June 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 49,239	$ 51,775
Marketable securities	7,379	48,983
Accounts receivable, net - related party	359	2,765
Inventory, net	1,644	2,821
Income tax receivable	697	697
Other receivables	764	555
Prepaid expenses	3,777	8,154
Restricted cash	—	408
Total current assets	63,859	116,158
Operating lease right-of-use assets	3,646	4,864
Property and equipment, net	3,490	3,322
Restricted cash, non-current	1,500	1,500
Total assets	$ 72,495	$ 125,844
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	$ 13,733	$ 25,592
Operating lease liability, current	168	—
Total current liabilities	13,901	25,592
Liability related to sales of future royalties and milestones, net	39,676	37,079
Operating lease liability, non-current	7,320	6,088
Total liabilities	60,897	68,759
Commitments and contingencies (Note 17)	—	—
Stockholders' equity:		
Preferred stock; $0.001 par value; 5,000,000 shares authorized at June 30, 2024 and December 31, 2023, zero shares issued and outstanding at June 30, 2024 and December 31, 2023	—	—
Common stock; $0.001 par value; 200,000,000 shares and 100,000,000 shares authorized at June 30, 2024 and December 31, 2023, respectively, 54,837,764 shares and 54,480,704 shares issued and outstanding at June 30, 2024 and December 31, 2023, respectively	54	54
Additional paid-in capital	747,122	742,036
Accumulated deficit	(735,457)	(684,745)
Accumulated other comprehensive loss	(121)	(260)
Total stockholders' equity	11,598	57,085
Total liabilities and stockholders' equity	$ 72,495	$ 125,844

See Notes to Condensed Consolidated Financial Statements.

CARA THERAPEUTICS, INC.

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

	Three Months Ended		Six Months Ended	
	June 30, 2024	June 30, 2023	June 30, 2024	June 30, 2023
Revenue:				
Collaborative revenue	$ —	$ 5,410	$ 788	$ 8,160
Commercial supply revenue	—	1,400	640	4,591
Royalty revenue	—	123	—	248
Clinical compound revenue	—	—	84	99
Other revenue	991	—	1,614	—
Total revenue	991	6,933	3,126	13,098
Operating expenses:				
Cost of goods sold	—	1,418	620	4,008
Research and development	9,308	30,310	31,272	54,644
General and administrative	6,408	7,545	13,224	14,436
Restructuring	2,581	—	4,982	—
Total operating expenses	18,297	39,273	50,098	73,088
Operating loss	(17,306)	(32,340)	(46,972)	(59,990)
Other income, net	689	861	1,641	1,846
Loss on inventory write-down	(1,489)	—	(1,489)	—
Non-cash interest expense on liability related to sales of future royalties and milestones	(1,910)	—	(3,892)	—
Net loss	$ (20,016)	$ (31,479)	$ (50,712)	$ (58,144)
Net loss per share:				
Basic and Diluted	$ (0.37)	$ (0.58)	$ (0.93)	$ (1.08)
Weighted average shares:				
Basic and Diluted	54,724,692	54,002,988	54,656,391	53,937,875
Other comprehensive income, net of tax of $0:				
Change in unrealized gains on available-for-sale marketable securities	70	371	139	942
Total comprehensive loss	$ (19,946)	$ (31,108)	$ (50,573)	$ (57,202)

See Notes to Condensed Consolidated Financial Statements.

CARA THERAPEUTICS, INC.

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

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Loss	Equity
Balance at December 31, 2023	54,480,704	$ 54	$ 742,036	$ (684,745)	$ (260)	$ 57,085
Stock-based compensation expense	—	—	1,660	—	—	1,660
Shares issued upon vesting of restricted stock units	186,375	—	1,685	—	—	1,685
Net loss	—	—	—	(30,696)	—	(30,696)
Other comprehensive income	—	—	—	—	69	69
Balance at March 31, 2024	54,667,079	$ 54	$ 745,381	$ (715,441)	$ (191)	$ 29,803
Stock-based compensation expense	—	—	1,507	—	—	1,507
Shares issued upon vesting of restricted stock units	170,685	—	234	—	—	234
Net loss	—	—	—	(20,016)	—	(20,016)
Other comprehensive income	—	—	—	—	70	70
Balance at June 30, 2024	54,837,764	$ 54	$ 747,122	$ (735,457)	$ (121)	$ 11,598

	Common Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Capital	Deficit	Loss	Equity
Balance at December 31, 2022	53,797,341	$ 53	$ 726,630	$ (566,232)	$ (1,672)	$ 158,779
Stock-based compensation expense	—	—	2,972	—	—	2,972
Shares issued upon exercise of stock options	93,218	1	559	—	—	560
Shares issued upon vesting of restricted stock units	83,793	—	381	—	—	381
Net loss	—	—	—	(26,665)	—	(26,665)
Other comprehensive income	—	—	—	—	571	571
Balance at March 31, 2023	53,974,352	$ 54	$ 730,542	$ (592,897)	$ (1,101)	$ 136,598
Stock-based compensation expense	—	—	3,116	—	—	3,116
Shares issued upon vesting of restricted stock units	94,454	—	326	—	—	326
Net loss	—	—	—	(31,479)	—	(31,479)
Other comprehensive income	—	—	—	—	371	371
Balance at June 30, 2023	54,068,806	$ 54	$ 733,984	$ (624,376)	$ (730)	$ 108,932

See Notes to Condensed Consolidated Financial Statements.

CARA THERAPEUTICS, INC.

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

	Six Months Ended,	
	June 30, 2024	**June 30, 2023**
Operating activities		
Net loss	$ (50,712)	$ (58,144)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	5,086	6,795
Non-cash interest expense on liability related to sales of future royalties and milestones, net of issuance costs accretion	3,892	—
Loss on inventory write-down	1,489	—
Depreciation and amortization	119	118
Noncash lease expense	525	759
Accretion of available-for-sale marketable securities, net	(543)	(56)
Changes in operating assets and liabilities:		
Accounts receivable, net - related party	2,406	(6,864)
Inventory	(312)	(1,037)
Other receivables	(209)	76
Prepaid expenses	4,377	1,291
Accounts payable and accrued expenses	(11,102)	2,935
Operating lease liability	—	(936)
Reimbursement of lease incentive	2,094	—
Net cash used in operating activities	(42,890)	(55,063)
Investing activities		
Proceeds from maturities of available-for-sale marketable securities	74,500	72,265
Proceeds from redemptions of available-for-sale marketable securities, at par	—	4,000
Purchases of available-for-sale marketable securities	(32,213)	(25,754)
Purchases of property and equipment	(1,046)	—
Net cash provided by investing activities	41,241	50,511
Financing activities		
Payments to royalty purchase and sale agreement	(1,295)	—
Proceeds from the exercise of stock options	—	560
Net cash (used in) provided by financing activities	(1,295)	560
Net decrease in cash, cash equivalents and restricted cash	(2,944)	(3,992)
Cash, cash equivalents and restricted cash at beginning of period	53,683	64,149
Cash, cash equivalents and restricted cash at end of period	$ 50,739	$ 60,157
Noncash investing and financing activities		
Accrual for leasehold improvements	$ 19	$ —

See Notes to Condensed Consolidated Financial Statements.

CARA THERAPEUTICS, INC.

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

1. Business

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

On June 14, 2024, the Board of Directors of the Company approved a streamlined operating plan exploring strategic alternatives focused on maximizing shareholder value after the Company announced its decision to discontinue the clinical program in notalgia paresthetica, or NP, on June 12, 2024. The Company's decision to discontinue the clinical program in NP followed the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. The Company's decision was not related to any safety or medical issues, or negative regulatory feedback related to the Company's NP program. In connection with the streamlined operating plan, the Board of Directors also approved a second reduction in the Company's workforce by approximately 70%, which the Company substantially completed by June 30, 2024 (see Note 17, *Commitments and Contingencies – Restructuring Actions*).

In August 2021, the Company received U.S. Food and Drug Administration, or FDA, approval for KORSUVA® (difelikefalin) injection, or KORSUVA injection, for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis. Commercial launch of KORSUVA injection began in the United States in April 2022 and the Company began recording the associated profit-sharing revenues in the second quarter of 2022.

In April 2022, the European Commission granted marketing authorization to difelikefalin injection under the brand name Kapruvia® (difelikefalin), or Kapruvia, for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adult hemodialysis patients. The marketing authorization approved Kapruvia for use in all member states of the European Union, or EU, as well as Iceland, Liechtenstein, and Norway. Kapruvia was also approved in the United Kingdom in April 2022. Commercial launches in Austria, Germany, Sweden, France, the Netherlands, Finland, and Norway have commenced. In August 2022, as part of the Access Consortium, difelikefalin injection was approved in Switzerland under the brand name Kapruvia, as well as Singapore and Canada under the brand name KORSUVA. Commercial launch in Switzerland has also commenced. In November 2022, difelikefalin injection was approved in the last Access Consortium country, Australia, under the brand name KORSUVA. Difelikefalin injection was also approved in the United Arab Emirates, Kuwait, Israel, Japan, and Saudi Arabia under the brand name KORSUVA in January 2023, May 2023, June 2023, September 2023, and January 2024, respectively. The Company expects additional approvals and commercial launches over the next 12-18 months. On November 1, 2023, the Company entered into a Purchase and Sale Agreement, or the HCR Agreement, with HCRX Investments Holdco, L.P. and Healthcare Royalty Partners IV, L.P., or collectively HCR, pursuant to which HCR will receive current and future royalty and milestone payments for Kapruvia and KORSUVA (ex U.S. only) up to certain capped amounts in exchange for certain payments made to the Company (see Note 10, *Royalty Purchase and Sale Agreement)*.

In 2018, the Company entered into a license and collaboration agreement with a joint venture between Vifor Pharma Group and Fresenius Medical Care Renal Pharmaceutical Ltd., or Vifor Fresenius Medical Care Renal Pharma Ltd., that provides full commercialization rights of Kapruvia, and where applicable KORSUVA, to Vifor Fresenius Medical Care Renal Pharma Ltd. worldwide (excluding the United States, Japan and South Korea). In 2020, the Company entered into a second licensing and collaboration agreement, along with stock purchase agreements, with Vifor (International) Ltd., or Vifor International, that provides full commercialization rights of KORSUVA injection to Vifor International in

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dialysis clinics in the United States under a profit-sharing arrangement (see Note 12, *Collaboration and Licensing Agreements)*.

In May 2022, Vifor International assigned its rights and obligations under the license agreement and a supply agreement, as permitted under the agreements, to Vifor Fresenius Medical Care Renal Pharma Ltd. The Company's rights and obligations under these agreements were unaffected by this assignment and the assignment did not affect the Company's economic rights under the agreements with Vifor International.

In August 2022, Vifor Pharma Group (which includes Vifor International) was acquired by CSL Limited and subsequently renamed CSL Vifor as part of the acquisition. The acquisition of Vifor Pharma Group did not affect any of the Company's rights and obligations pursuant to these agreements.

The Company also has a license agreement with Maruishi Pharmaceutical Co. Ltd., or Maruishi, under which the Company granted Maruishi an exclusive license to develop, manufacture, and commercialize drug products containing difelikefalin for acute pain and/or uremic pruritus in Japan. In September 2023, Maruishi received manufacturing and marketing approval from Japan's Ministry of Health, Labour and Welfare for KORSUVA IV Injection Syringe for the treatment of pruritus in hemodialysis patients (see Note 12, *Collaboration and Licensing Agreements)*. In the fourth quarter of 2023, the Company entered into the HCR Agreement pursuant to which HCR will receive current and future royalty and milestone payments for KORSUVA (Japan) up to certain capped amounts in exchange for certain payments to the Company (see Note 10, *Royalty Purchase and Sale Agreement)*.

As of June 30, 2024, the Company has raised aggregate net proceeds of approximately $520,700 from several rounds of equity financing, including its initial public offering, or IPO, which closed in February 2014 and four follow-on public offerings of common stock, which closed in July 2019, July 2018, April 2017 and August 2015, respectively, the issuance of common stock pursuant to its open market sales agreement with Jefferies LLC as sales agent in 2023, and the issuance of convertible preferred stock and debt prior to the IPO. The Company has also earned approximately $288,600 under its license and supply agreements for difelikefalin, primarily with CSL Vifor, Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, and an earlier product candidate for which development efforts ceased in 2007. Under the terms of the HCR Agreement, the Company received net proceeds of $36,474 for the sale of future ex-U.S. royalties and milestones under Vifor Agreement No. 2 (as defined below) and the Maruishi Agreement in November and December 2023. The Company has also received aggregate net proceeds of approximately $98,000 from the issuance and sale of the Company's common stock to Vifor International in connection with the Company's license agreement with CSL Vifor (see Note 12, *Collaboration and Licensing Agreements*).

As of June 30, 2024, the Company had unrestricted cash and cash equivalents and marketable securities of $56,618 and an accumulated deficit of $735,457. 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 $20,016 and $31,479 for the three months ended June 30, 2024 and 2023, respectively, and $50,712 and $58,144 for the six months ended June 30, 2024 and 2023, respectively, and had net cash used in operating activities of $42,890 and $55,063 for the six months ended June 30, 2024 and 2023, respectively.

The Company is subject to risks and uncertainties including, should it resume development of its product candidate or future product candidates, risks and uncertainties common to other life science companies including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, product liability, protection of proprietary technology, ability to raise additional financing, and compliance with FDA and other government regulations. Should the Company resume development of its product candidate or any future product

CARA THERAPEUTICS, INC.

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

candidate, even if the Company's development efforts are successful, it is uncertain when, if ever, the Company would generate additional recurring product revenue or achieve profitability.

2. Basis of Presentation

The Company's condensed consolidated financial statements include the results of the financial operations of Cara Therapeutics, Inc. and its wholly-owned subsidiary, Cara Royalty Sub, LLC, or Cara Royalty Sub, a Delaware limited liability company which was formed in November 2023 for the purpose of the transactions contemplated by the HCR Agreement described in Note 10, *Royalty Purchase and Sale Agreement*. All intercompany balances and transactions have been eliminated.

The unaudited interim condensed consolidated 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 condensed consolidated financial statements reflect all adjustments, consisting primarily of normal recurring accruals, necessary for a fair presentation of results for the periods presented. The results of operations for interim periods are not necessarily indicative of the results for the full year. Certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been condensed or omitted from this report, as is permitted by SEC rules and regulations; however, the Company believes that the disclosures are adequate to make the information presented not misleading. The condensed consolidated balance sheet data as of December 31, 2023 were derived from audited financial statements, but do not include all disclosures required by GAAP. These unaudited interim condensed consolidated 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, 2023.

Use of Estimates

The preparation of condensed consolidated 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 condensed consolidated financial statements as well as the reported amounts of revenues and expenses during the reporting period. The more significant estimates include the fair value of marketable securities that are classified as Level 2 of the fair value hierarchy, the amount and periods over which certain revenues will be recognized, including licensing and collaborative revenue recognized from non-refundable up-front and milestone payments and future ex-U.S. royalties and milestones projected in relation to the HCR Agreement, related party accounts receivable reserve, as applicable, inventory valuation and related reserves, research and development, or R&D, clinical costs and accrued research projects included in prepaid expenses and accounts payable and accrued expenses, the amount of non-cash compensation costs related to share-based payments to employees and non-employees, restructuring costs, the amount of lease incentives, as applicable, and the incremental borrowing rate used in lease calculations, and the likelihood of realization of deferred tax assets.

The impact from global economic conditions and potential and continuing disruptions to and volatility in the credit and equity markets in the United States and worldwide are highly uncertain and cannot be predicted, including impacts from global health crises, geopolitical tensions, such as the ongoing conflicts between Russia and Ukraine, conflict in the Middle East, and increasing tensions between China and Taiwan, and government actions implemented as a result of the foregoing, fluctuations in inflation, rising interest rates, uncertainty and liquidity concerns in the broader financial services industry, and a potential recession in the United States. Estimates and assumptions about future events and their effects cannot be determined with certainty and therefore require the exercise of judgment. As of the date of issuance of

CARA THERAPEUTICS, INC.

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

these condensed consolidated financial statements, the Company is not aware of any specific event or circumstance that would require the Company to update its estimates, assumptions and judgments or revise the reported amounts of assets and liabilities or the disclosure of contingent assets and liabilities. These estimates, however, may change as new events occur and additional information is obtained, and are recognized in the condensed consolidated financial statements as soon as they become known.

Actual results could differ materially from the Company's estimates and assumptions.

Significant Accounting Policies

There have been no material changes to the significant accounting policies previously disclosed in Note 2 to the Consolidated Financial Statements in the Company's Annual Report on Form 10-K for the year ended December 31, 2023.

Accounting Pronouncements Recently Adopted

In November 2023, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, or ASU 2023-07, which expanded the disclosures for reportable segments made by public entities. These amendments within ASU 2023-07 retained the existing disclosure requirements in ASC 280 and expanded upon them to require public entities to disclose significant expenses for reportable segments in both interim and annual reporting periods, as well as items that were previously disclosed only annually on an interim basis, including disclosures related to a reportable segment's profit or loss and assets. In addition, entities with a single reportable segment must provide all segment disclosures required in ASC 280, including the new disclosures for reportable segments under the amendments in ASU 2023-07. The amendments did not change the existing guidance on how a public entity identified and determined its reportable segments. A public entity should apply the amendments in ASU 2023-07 retrospectively to all prior periods presented in the financial statements. Upon transition, the segment expense categories and amounts disclosed in the prior periods should be based on the significant segment expense categories identified and disclosed in the period of adoption. The amendments in ASU 2023-07 are effective for annual periods for all public entities in fiscal years beginning after December 15, 2023, and in interim periods within fiscal years beginning after December 15, 2024. The Company adopted ASU 2023-07 on January 1, 2024, and expects to comply with any new applicable disclosures in its Annual Report on Form 10-K for the year ended December 31, 2024. The Company does not expect the adoption to have a material effect on its results of operations, financial position, and cash flows.

Accounting Pronouncements Not Yet Adopted

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*, or ASU 2023-09, which applies to all entities subject to income taxes. ASU 2023-09 requires disaggregated information about a reporting entity's effective tax rate reconciliation as well as information on income taxes paid. ASU 2023-09 is intended to provide more detailed income tax disclosures. For public business entities (PBEs), the new requirements will be effective for annual periods beginning after December 15, 2024. ASU 2023-09 will be applied on a prospective basis with the option to apply the standard retrospectively. The Company expects to adopt ASU 2023-09 on January 1, 2025, and it does not expect the adoption to have a material effect on its results of operations, financial position, and cash flows.

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, 2024, the Company's available-for-sale marketable securities consisted of debt securities issued by U.S. government-sponsored entities. As of December 31, 2023, the Company's available-for-sale marketable securities consisted of debt securities issued by the U.S. Treasury, U.S. government-sponsored entities and investment grade institutions (corporate bonds).

The following tables summarize the Company's available-for-sale marketable securities by major type of security as of June 30, 2024 and December 31, 2023:

As of June 30, 2024

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. government agency obligations	$ 7,500	$ —	$ (121)	$ 7,379
Total available-for-sale marketable securities	$ 7,500	$ —	$ (121)	$ 7,379

As of December 31, 2023

Type of Security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$ 37,243	$ 3	$ —	$ 37,246
U.S. government agency obligations	7,500	—	(262)	7,238
Corporate bonds	4,500	—	(1)	4,499
Total available-for-sale marketable securities	$ 49,243	$ 3	$ (263)	$ 48,983

The following tables summarize the fair value and gross unrealized losses of the Company's available-for-sale marketable securities by investment category and disaggregated by the length of time that individual debt securities have been in a continuous unrealized loss position as of June 30, 2024 and December 31, 2023:

As of June 30, 2024

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
U.S. government agency obligations	$ —	$ —	$ 7,379	$ (121)	$ 7,379	$ (121)
Total	$ —	$ —	$ 7,379	$ (121)	$ 7,379	$ (121)

As of December 31, 2023

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses	Fair Value	Gross Unrealized Losses
U.S. government agency obligations	$ —	$ —	$ 7,238	$ (262)	$ 7,238	$ (262)
Corporate bonds	—	—	2,000	(1)	2,000	(1)
Total	$ —	$ —	$ 9,238	$ (263)	$ 9,238	$ (263)

CARA THERAPEUTICS, INC.

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

As of June 30, 2024 and December 31, 2023, no allowance for credit losses were recognized on the Company's available-for-sale debt securities as no portion of the unrealized losses associated with those securities were due to credit losses. The information that the Company considered in reaching the conclusion that an allowance for credit losses was not necessary is as follows:

As of June 30, 2024 and December 31, 2023, the Company held a total of 2 out of 2 positions and 3 out of 9 positions, respectively, that were in an unrealized loss position, 2 of which had been in an unrealized loss position for 12 months or greater as of June 30, 2024. Unrealized losses individually and in aggregate, including any in an unrealized loss position for 12 months or greater, were not considered to be material for each respective period. Based on the Company's review of these securities, the Company believes that the cost basis of its available-for-sale marketable securities is recoverable.

U.S. government agency obligations. The unrealized losses on the Company's investments in direct obligations of U.S. government agencies were due to changes in interest rates and non-credit related factors. The credit ratings of these investments in the Company's portfolio have not been downgraded below investment grade status. The contractual terms of these investments do not permit the issuer to repay principal at a price less than the amortized cost bases of the investments, which is equivalent to the par value on the maturity date. The Company expects to recover the entire amortized cost bases of these securities on the maturity date. The Company does not intend to sell these investments, and it is not "more likely than not" that the Company will be required to sell these investments before recovery of their amortized cost bases. The Company held 2 out of 2 positions for its U.S. government agency obligations that were in unrealized loss positions as of June 30, 2024.

The Company classifies its marketable debt securities based on their contractual maturity dates. As of June 30, 2024, the Company's marketable debt securities mature at various dates through November 2024. The amortized cost and fair values of marketable debt securities by contractual maturity were as follows:

	As of June 30, 2024		As of December 31, 2023	
Contractual maturity	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Less than one year	$ 7,500	$ 7,379	$ 49,243	$ 48,983
More than one year	—	—	—	—
Total	$ 7,500	$ 7,379	$ 49,243	$ 48,983

All available-for-sale marketable securities are classified as marketable securities, current or marketable securities, non-current depending on the contractual maturity date of the individual available-for-sale security. Other income, net includes interest and dividends, accretion/amortization of discounts/premiums, realized gains and losses on sales of securities and credit loss expense due to declines in the fair value of securities, if any. The cost of securities sold is based on the specific identification method.

There were no sales of available-for-sale marketable securities during each of the three and six months ended June 30, 2024 and 2023.

As of June 30, 2024 and December 31, 2023, accrued interest receivables on the Company's available-for-sale debt securities were $119 and $139, respectively, and were included within other receivables.

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4. Accumulated Other Comprehensive Loss

The following table summarizes the changes in accumulated other comprehensive loss, net of tax, from unrealized gains on available-for-sale marketable securities, the Company's only component of accumulated other comprehensive loss, for the six months ended June 30, 2024 and 2023, respectively.

	Total Accumulated Other Comprehensive Loss
Balance, December 31, 2023	$ (260)
Other comprehensive income before reclassifications	139
Amount reclassified from accumulated other comprehensive loss	—
Net current period other comprehensive income	139
Balance, June 30, 2024	$ (121)
Balance, December 31, 2022	$ (1,672)
Other comprehensive income before reclassifications	942
Amount reclassified from accumulated other comprehensive loss	—
Net current period other comprehensive income	942
Balance, June 30, 2023	$ (730)

Amounts reclassified out of accumulated other comprehensive loss into net loss are determined by specific identification. There were no reclassifications out of accumulated other comprehensive loss and into net loss for each of the three and six months ended June 30, 2024 and 2023.

5. Fair Value Measurements

As of June 30, 2024 and December 31, 2023, the Company's financial instruments consisted of cash, cash equivalents, available-for-sale marketable securities, accounts receivable, net – related party, prepaid expenses, restricted cash, accounts payable and accrued liabilities, and liability related to the sales of future royalties and milestones. The fair values of cash, cash equivalents, accounts receivable, net – related party, prepaid expenses, restricted cash, accounts payable and accrued liabilities approximate their carrying values due to the short-term nature of these financial instruments. The fair value of the liability related to the sales of future royalties and milestones also approximates the carrying value. Available-for-sale marketable securities are reported at their fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services.

The Company validates the prices provided by its third-party pricing services by reviewing their pricing methods, obtaining market values from other pricing sources, and comparing them to the share prices presented by the third-party pricing services. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by its third-party pricing services as of June 30, 2024 or December 31, 2023.

The following tables summarize the Company's financial assets measured at fair value on a recurring basis as of June 30, 2024 and December 31, 2023.

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Fair value measurement as of June 30, 2024:

Financial assets Type of Instrument	Total	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Cash and cash equivalents:				
Money market funds and checking accounts	$ 49,239	$ 49,239	$ —	$ —
Available-for-sale marketable securities:				
U.S. government agency obligations	7,379	—	7,379	—
Restricted cash:				
Commercial money market account	1,500	1,500	—	—
Total financial assets	$ 58,118	$ 50,739	$ 7,379	$ —

Fair value measurement as of December 31, 2023:

Financial assets Type of Instrument	Total	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Cash and cash equivalents:				
Money market funds and checking accounts	$ 51,775	$ 51,775	$ —	$ —
Available-for-sale marketable securities:				
U.S. Treasury securities	37,246	—	37,246	—
U.S. government agency obligations	7,238	—	7,238	—
Corporate bonds	4,499	—	4,499	—
Restricted cash:				
Commercial money market account	1,908	1,908	—	—
Total financial assets	$ 102,666	$ 53,683	$ 48,983	$ —

There were no purchases, sales or maturities of Level 3 financial assets and no unrealized gains or losses related to Level 3 available-for-sale marketable securities during each of the three and six months ended June 30, 2024 and 2023. There were no transfers of financial assets into or out of Level 3 classification during each the three and six months ended June 30, 2024 and 2023.

6. Restricted Cash

In May 2023, the Company entered into a lease agreement with 400 Atlantic Joint Venture LLC and SLJ Atlantic Stamford LLC (tenants-in-common), or the Landlord, for the lease of 26,374 square feet of office space located at 400 Atlantic Street, Stamford, Connecticut 06901 for its new principal executive offices, or the New Lease. The Company is required to maintain a stand-by letter of credit as a security deposit under the New Lease for its office space in Stamford, Connecticut (refer to Note 17, *Commitments and Contingencies: Leases*). The fair value of the letter of credit approximates its contract value. The Company's bank requires the Company to maintain a restricted cash balance to serve as collateral for the letter of credit issued to the landlords by the bank. As of June 30, 2024, the restricted cash balance for the New Lease was invested in a commercial money market account.

As of June 30, 2024, the Company had $1,500 of restricted cash related to the New Lease in long-term assets. After the first and second anniversaries of the rent commencement date, the face amount of the letter of credit relating to the New Lease can be reduced by $500 each period if the Company is not in default of its lease obligations. As of December

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31, 2023, the Company had $408 of restricted cash related to its previous lease (which was terminated in December 2023 and became unrestricted in January 2024) in current assets and $1,500 of restricted cash related to the New Lease in long-term assets.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the Condensed Consolidated Balance Sheets that sum to the total of the same such amounts shown in the Condensed Consolidated Statements of Cash Flows.

	June 30, 2024	December 31, 2023
Cash and cash equivalents	$ 49,239	$ 51,775
Restricted cash, current assets	—	408
Restricted cash, long-term assets	1,500	1,500
Total cash, cash equivalents, and restricted cash shown in the Condensed Consolidated Statements of Cash Flows	$ 50,739	$ 53,683

7. Inventory, net

Inventory, net consists of the following:

	June 30, 2024	December 31, 2023
Raw materials	$ 2,124	$ 2,639
Work-in-process	1,009	708
	3,133	3,347
Less Inventory Reserve for Obsolescence	(1,489)	(526)
Total	$ 1,644	$ 2,821

As of June 30, 2024 and December 31, 2023, inventory balances include inventory costs subsequent to regulatory approval of KORSUVA injection on August 23, 2021. During the three and six months ended June 30, 2024, the Company wrote down $1,489 of commercial supply inventory due to obsolescence.

8. Prepaid expenses

As of June 30, 2024, prepaid expenses were $3,777, consisting of $2,458 of prepaid R&D clinical costs, $1,021 of prepaid insurance and $298 of other prepaid costs. As of December 31, 2023, prepaid expenses were $8,154, consisting of $7,245 of prepaid R&D clinical costs, $492 of prepaid insurance, and $417 of other prepaid costs.

9. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following:

	June 30, 2024	December 31, 2023
Accounts payable	$ 6,755	$ 11,583
Accrued research projects	1,010	4,343
Accrued compensation and benefits	1,214	6,519
Accrued professional fees and other	4,754	3,147
Total	$ 13,733	$ 25,592

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10. Royalty Purchase and Sale Agreement

During the fourth quarter of 2023, the Company, through its wholly-owned subsidiary Cara Royalty Sub, entered into the HCR Agreement with HCR, pursuant to which Cara Royalty Sub sold, or agreed to sell, to HCR certain of its rights to receive royalty payments, or the Royalties, due and payable to Cara Royalty Sub (as assignee of the Company) under the Maruishi Agreement and Vifor Agreement No. 2. (as defined below), collectively the Covered License Agreements, in exchange for up to $40,000. The Company has retained all of its rights, title and interest in, to and under the Covered License Agreements that relate to any non-intravenous formulation of difelikefalin.

Under the terms of the HCR Agreement, Cara Royalty Sub received an upfront payment of $16,915 in November 2023, representing the $17,500 to which the Company was initially entitled, net of advisory fees and certain of HCR's transaction-related expenses which the Company agreed to reimburse. In December 2023, Cara Royalty Sub received an additional payment of $19,770, representing the $20,000 milestone it achieved for Kapruvia (difelikefalin) pricing in Germany being approved above a certain threshold amount per dose, net of advisory fees. There were additional issuance costs of $211 related to the HCR Agreement resulting in aggregate net proceeds of $36,474. An additional $2,500 milestone payment is due to Cara Royalty Sub upon achievement of a 2024 sales milestone of KORSUVA in Japan.

The HCR Agreement will automatically expire, and the payment of Royalties to HCR will cease, when HCR has received payments of Royalties equal to two times the aggregate amount of payments made by HCR under the HCR Agreement if achieved on or prior to December 31, 2029, or 2.8 times the aggregate amount of payments made by HCR under the HCR Agreement, if not achieved on or prior to December 31, 2029. After the HCR Agreement expires, all rights to receive the Royalties return to Cara Royalty Sub.

Issuance costs pursuant to the HCR Agreement consisting primarily of advisory and legal fees totaled $1,025 including the amount of HCR's transaction-related expenses that the Company reimbursed. The effective interest rate includes cash flow projections for future royalty and milestone payments, which are sensitive to certain assumptions, including market size, market penetration and sales price, that are forward looking and could be affected by future market conditions. During the three and six months ended June 30, 2024, $610 and $1,295, respectively, were repaid to HCR under the HCR Agreement.

The following table summarizes the activity of the HCR Agreement (in thousands):

Royalty purchase and sale agreement balance at December 31, 2023	$	37,079
Payments		(1,295)
Non-cash interest expense		3,892
Balance at June 30, 2024	$	39,676
Effective interest rate		20.95 %

11. Stockholders' Equity

On June 7, 2024, the Company filed a Certificate of Amendment to its Certificate of Incorporation, or the Certificate, with the Secretary of State of the State of Delaware, which the Company's stockholders approved at the Company's Annual Meeting of Stockholders on June 4, 2024. The Certificate increased the authorized number of shares of common stock of the Company from 100,000,000 shares to 200,000,000 shares. The additional shares of common stock authorized by the Certificate have rights identical to the currently outstanding common stock of the Company and any issuance of common stock authorized by the Certificate would not affect the rights of the holders of currently

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outstanding common stock of the Company, except for effects incidental to increasing the number of shares of the Company's common stock outstanding, such as dilution of the earnings per share and voting rights of current holders of common stock. As of June 30, 2024, there were 54,837,764 shares of common stock and no shares of preferred stock issued and outstanding.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to dividends when and if declared by the Board of Directors, subject to the preferential rights of the holders of preferred stock, if any.

During the three months ended June 30, 2024, an aggregate of 170,685 time-based restricted stock units of certain employees and the Board of Directors vested and were settled in shares of the Company's common stock. During the six months ended June 30, 2024, an aggregate of 216,560 time-based restricted stock units of certain employees and the Board of Directors vested and were settled in shares of the Company's common stock (See Note 15, *Stock-Based Compensation*).

During the three months ended June 30, 2024, no performance-based restricted stock units vested or were settled in shares of the Company's common stock. During the six months ended June 30, 2024, an aggregate of 140,500 performance-based restricted stock units of certain employees vested and were settled in shares of the Company's common stock (See Note 15, *Stock-Based Compensation*).

During the three months ended June 30, 2023, an aggregate of 94,454 time-based restricted stock units of certain employees and the Board of Directors vested and were settled in shares of the Company's common stock. During the six months ended June 30, 2023, an aggregate of 178,247 time-based restricted stock units of certain employees and the Board of Directors were settled in shares of the Company's common stock (see Note 15, *Stock-Based Compensation*).

During the three and six months ended June 30, 2023, no performance-based restricted stock units vested or were settled in shares of the Company's common stock.

12. Collaboration and Licensing Agreements

Vifor (International) Ltd. (Vifor International)

In October 2020, the Company entered into a license agreement with Vifor International, or Vifor Agreement No. 1, under which the Company granted Vifor International an exclusive license solely in the United States to use, distribute, offer for sale, promote, sell and otherwise commercialize difelikefalin injection for all therapeutic uses relating to the inhibition, prevention or treatment of itch associated with pruritus in hemodialysis and peritoneal dialysis patients in the United States. Under Vifor Agreement No. 1, the Company retains all rights with respect to the clinical development of, and activities to gain regulatory approvals of, difelikefalin injection in the United States.

After the assignment of rights of Vifor Agreement No. 1 from Vifor International to Vifor Fresenius Medical Care Renal Pharma Ltd. in May 2022, Vifor Agreement No. 1 provides full commercialization rights in dialysis clinics to CSL Vifor in the United States under a profit-sharing arrangement. Pursuant to the profit-sharing arrangement, the Company is generally entitled to 60% of the net profits (as defined in Vifor Agreement No. 1) from sales of difelikefalin injection in the United States and CSL Vifor is entitled to 40% of such net profits (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by Vifor Agreement No. 2, as defined below), subject to potential temporary adjustment in future years based on certain conditions. Under Vifor Agreement No. 1, in consideration of CSL Vifor's conduct of the marketing, promotion, selling and distribution of difelikefalin injection in the United States, the Company pays a marketing and distribution fee to CSL Vifor based on the level of annual net

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sales. This fee as well as CSL Vifor's cost of goods sold, or COGS, are deducted from net sales in calculating the net profits that are subject to the profit-sharing arrangement under Vifor Agreement No. 1.

In addition, pursuant to Vifor Agreement No. 1, the Company is eligible to receive payments of up to $240,000 upon the achievement of certain sales-based milestones.

The Company retains the rights to make and have made difelikefalin injection, or the Licensed Product, on a non-exclusive basis, in the United States for commercial sale of the Licensed Product for use in all therapeutic areas to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients, or the Field, anywhere in the world and for supply of Licensed Product to CSL Vifor under the terms of a supply agreement, or the Vifor International Supply Agreement, which was executed in September 2021. The supply price is the Company's COGS, as calculated under GAAP, plus an agreed upon margin. The Vifor International Supply Agreement will co-terminate with Vifor Agreement No. 1. The Company also retains the rights to import, distribute, promote, sell and otherwise commercialize the Licensed Product on an exclusive basis outside of the Field either in or outside of the United States.

The Vifor International Supply Agreement is accounted for as a customer option that is not a material right because the selling price of the Licensed Product under the Vifor International Supply Agreement is the Company's COGS plus an agreed upon margin, which is commensurate with the "COGS plus" model that the Company would charge other parties under similar agreements (the standalone selling price) and not at a discount. Therefore, the sale of commercial supply to CSL Vifor is not a performance obligation under Vifor Agreement No. 1 but rather the Vifor International Supply Agreement is a separate agreement from Vifor Agreement No. 1. The only performance obligation under the Vifor International Supply Agreement is the delivery of the Licensed Product to CSL Vifor for commercialization.

Vifor Fresenius Medical Care Renal Pharma Ltd.

In May 2018, the Company entered into a license agreement with Vifor Fresenius Medical Care Renal Pharma Ltd., or Vifor Agreement No. 2, under which the Company granted Vifor Fresenius Medical Care Renal Pharma Ltd. an exclusive, royalty-bearing license, or the Vifor License, to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize the Licensed Product in the Field worldwide (excluding the United States, Japan and South Korea), or the Territory.

The Company is eligible to receive from Vifor Fresenius Medical Care Renal Pharma Ltd. additional commercial milestone payments in the aggregate of up to $440,000, all of which are sales related. The Company is also eligible to receive tiered double-digit royalty payments based on annual net sales, as defined in Vifor Agreement No. 2, of difelikefalin injection in the licensed territories. The Company retained full commercialization rights for difelikefalin injection for the treatment of chronic kidney disease associated pruritus in the United States except in the dialysis clinics of FMCNA, where Vifor Fresenius Medical Care Renal Pharma Ltd. will promote difelikefalin injection under a profit-sharing arrangement (as defined in Vifor Agreement No. 2), based on net FMCNA clinic sales (as defined in Vifor Agreement No. 2) and the Company and Vifor Fresenius Medical Care Renal Pharma Ltd. are each entitled to 50% of such net profits, subject to potential adjustments in a calendar year based on certain conditions.

The Company retains the rights to make and have made the Licensed Product in the Territory for commercial sale by Vifor Fresenius Medical Care Renal Pharma Ltd. in the Field in or outside the Territory and for supply of Licensed Product to Vifor Fresenius Medical Care Renal Pharma Ltd. under the terms of a supply agreement, or the Vifor Supply Agreement, which was executed in May 2020. The supply price is the Company's COGS, as calculated under GAAP, plus an agreed upon margin. The Vifor Supply Agreement will co-terminate with Vifor Agreement No. 2.

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The Vifor Supply Agreement is accounted for as a customer option that is not a material right because the selling price of the Licensed Product under the Vifor Supply Agreement is the Company's COGS plus an agreed upon margin, which is commensurate with the "COGS plus" model that the Company would charge other parties under similar agreements (the standalone selling price) and not at a discount. Therefore, the sale of compound to Vifor Fresenius Medical Care Renal Pharma Ltd. is not a performance obligation under Vifor Agreement No. 2 but rather the Vifor Supply Agreement is a separate agreement from Vifor Agreement No. 2. The only performance obligation under the Vifor Supply Agreement is the delivery of the Licensed Product to Vifor Fresenius Medical Care Renal Pharma Ltd. for commercialization.

Maruishi Pharmaceutical Co., Ltd. (Maruishi)

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

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

In September 2022, Maruishi submitted a New Drug Application in Japan for approval of difelikefalin injection for the treatment of pruritus in hemodialysis patients. In September 2023, Maruishi received manufacturing and marketing approval from Japan's Ministry of Health, Labour and Welfare for KORSUVA IV Injection Syringe for the treatment of pruritus in hemodialysis patients. In November 2023, the Company entered into an API supply agreement with Maruishi for difelikefalin.

Chong Kun Dang Pharmaceutical Corporation (CKDP)

In April 2012, the Company entered into a license agreement with CKDP, or the CKDP Agreement, in South Korea, under which the Company granted CKDP an exclusive license to develop, manufacture and commercialize drug products containing difelikefalin in South Korea. The Company and CKDP are each required to use commercially reasonable efforts, at their respective expense, to develop, obtain regulatory approval for and commercialize difelikefalin in the United States and South Korea, respectively.

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

13. Revenue Recognition

The Company has recognized revenue under its license and collaboration agreements from (1) its share of the profit generated by KORSUVA injection sales in the United States during the six months ended June 30, 2024 and the three and six months ended June 30, 2023; (2) commercial supply revenue from the Company's sales of commercial product

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to CSL Vifor during the six months ended June 30, 2024 and the three and six months ended June 30, 2023; (3) royalty revenue from net sales of Kapruvia in Europe during each of the three and six months ended June 30, 2023; (4) clinical compound sales from certain license agreements during each of the six months ended June 30, 2024 and 2023; and (5) other revenue which represents royalty payments earned by the Company under Vifor Agreement No. 2 and the Maruishi Agreement under the HCR Agreement during the three and six months ended June 30, 2024. As of June 30, 2024, the Company has not earned any sales-based milestones under its collaboration agreements.

As of June 30, 2024, the Company had license and collaboration agreements with CSL Vifor, Maruishi and CKDP. The following table provides amounts included in the Company's Condensed Consolidated Statements of Comprehensive Loss as revenue for each of the three and six months ended June 30, 2024 and 2023, respectively:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	2023	2024	2023
Collaborative revenue				
CSL Vifor (KORSUVA injection profit sharing)	$ —	$ 5,410	$ 788	$ 8,160
Total collaborative revenue	$ —	$ 5,410	$ 788	$ 8,160
Commercial supply revenue				
CSL Vifor (KORSUVA injection)	$ —	$ 1,400	$ 640	$ 4,591
Total commercial supply revenue	$ —	$ 1,400	$ 640	$ 4,591
Royalty revenue				
CSL Vifor (Kapruvia ex-U.S.)	$ —	$ 123	$ —	$ 248
Total royalty revenue	$ —	$ 123	$ —	$ 248
Clinical compound revenue				
Maruishi	$ —	$ —	$ 84	$ 99
Total clinical compound revenue	$ —	$ —	$ 84	$ 99
Other revenue (non-cash)				
CSL Vifor (Kapruvia ex-U.S.)	$ 359	$ —	$ 649	$ —
Maruishi	632	—	965	—
Total other revenue	$ 991	$ —	$ 1,614	$ —

Collaborative revenue

Beginning in April 2022, the Company began recording its share of the profit generated by KORSUVA injection sales by CSL Vifor to third parties in the United States. Under the license agreements with CSL Vifor, KORSUVA injection net sales are calculated by CSL Vifor which are net of discounts, rebates, and allowances. These amounts include the use of estimates and judgments, which could be adjusted based on actual results in the future. The Company records its share of the net profits from the sales of KORSUVA injection in the United States on a net basis (since the Company is not the primary obligor and does not retain inventory risk) and presents the revenue earned each period as collaborative revenue.

For the three months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $2,664, which resulted in the Company's profit share amount of negative $1,447. For the three months ended June 30, 2023, CSL Vifor recorded net sales of $11,467, which resulted in the Company's profit share amount of $5,410. The negative net sales reported by CSL Vifor was primarily due to higher rebates and chargebacks due to price decreases on KORSUVA injection related to the expiration of Transition Drug Add-on Payment Adjustment in April 2024. Based on the terms of the agreement, the negative profit will be offset against net

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profits in future periods. However, the Company has recorded a liability in accrued professional fees and other within accounts payable and accrued expenses for $1,447 and a corresponding expense in other general and administrative, or G&A, expense as a result of the negative profit share amount in the second quarter of 2024. For the six months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $858. For the six months ended June 30, 2023, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately $17,141. For the six months ended June 30, 2024 and 2023, the Company recorded associated collaborative revenue of $788 and $8,160, respectively.

Commercial supply revenue

Under the Vifor International Supply Agreement, the Company's only performance obligation is the delivery of KORSUVA injection to CSL Vifor in accordance with the receipt of purchase orders. Revenue from the sale of commercial supply product to CSL Vifor is recognized as delivery of the product occurs. There was no commercial supply revenue for the three months ended June 30, 2024. The Company had commercial supply revenue of $1,400 for the three months ended June 30, 2023, with associated COGS of $1,418, and $640 and $4,591 for the six months ended June 30, 2024 and 2023, respectively, with associated COGS of $620 and $4,008, respectively.

Royalty revenue

Royalty revenue includes amounts related to the Company's royalties earned from CSL Vifor on the net sales of Kapruvia in Europe, based on the amount of net sales in a licensed territory during a calendar year. Sales-based royalty payments related to a license of IP are recognized as revenue when the respective sales occur, and the net sales tier is achieved. The Company recognized royalty revenue of approximately $123 and $248 for the three and six months ended June 30, 2023, respectively, which were related to the Company's royalties on the net sales of Kapruvia in Europe. Beginning on October 1, 2023, royalty revenue is no longer recognized until the Company has fulfilled its obligations under the HCR Agreement (see Note 10, *Royalty Purchase and Sale Agreement*).

Clinical compound revenue

The Company's only performance obligation under the supply agreement with Maruishi is to deliver clinical compound to Maruishi in accordance with the receipt of purchase orders. There was no clinical compound revenue for the three months ended June 30, 2024 and 2023. During the six months ended June 30, 2024 and 2023, the Company recognized clinical compound revenue of $84 and $99, respectively, from the sale of clinical compound to Maruishi.

Other revenue

The Company recorded other non-cash revenue of $991 and $1,614 which represents the royalty payments earned by the Company under Vifor Agreement No. 2 and the Maruishi Agreement during the three and six months ended June 30, 2024, respectively, in conjunction with ex-U.S. sales of KORSUVA/Kapruvia, which will be remitted to HCR under the terms of the HCR Agreement. This non-cash revenue will continue to be recorded until the Company has fulfilled its obligations under the HCR Agreement. There was no other revenue recorded for the three and six months ended June 30, 2023 as the HCR Agreement went into effect during the fourth quarter of 2023 (see Note 10, *Royalty Purchase and Sale Agreement*).

Contract balances

As of June 30, 2024 and December 31, 2023, the Company recorded accounts receivable, net – related party of $359 and $2,765, respectively, which primarily related to royalty payments from CSL Vifor in the current period and its

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profit-sharing revenue from sales of KORSUVA injection in the United States by CSL Vifor, its commercial supply of KORSUVA injection to CSL Vifor, and royalty payments from CSL Vifor in the prior period. The Company also recorded $645 and $415 within other receivables which primarily related to royalty payments from Maruishi as of June 30, 2024 and December 31, 2023, respectively. There were no other contract assets or contract liabilities related to the CSL Vifor, Maruishi and CKDP agreements as of June 30, 2024 and December 31, 2023.

The Company routinely assesses the creditworthiness of its license and collaboration partners. The Company has not experienced any losses related to receivables from its license and collaboration partners as of June 30, 2024 and December 31, 2023.

14. Net Loss Per Share

The Company computes basic net loss per share by dividing net loss by the weighted-average number of shares of common stock outstanding. Diluted net loss per share includes the potential dilutive effect of common stock equivalents as if such securities were exercised during the period, when the effect is dilutive. Common stock equivalents may include outstanding stock options or restricted stock units, which are included using the treasury stock method when dilutive. For each of the three and six months ended June 30, 2024 and 2023, 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,	
	2024	2023	2024	2023
Basic:				
Weighted average common shares outstanding	54,724,692	54,002,988	54,656,391	53,937,875
Diluted:				
Weighted average common shares outstanding - Basic	54,724,692	54,002,988	54,656,391	53,937,875
Common stock equivalents*	—	—	—	—
Denominator for diluted net loss per share	54,724,692	54,002,988	54,656,391	53,937,875

* 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,	
	2024	2023	2024	2023
Net loss - basic and diluted	$ (20,016)	$ (31,479)	$ (50,712)	$ (58,144)
Weighted-average common shares outstanding:				
Basic and diluted	54,724,692	54,002,988	54,656,391	53,937,875
Net loss per share, basic and diluted:	$ (0.37)	$ (0.58)	$ (0.93)	$ (1.08)

As of June 30, 2024, 6,067,881 stock options and 976,799 restricted stock units were outstanding, which could potentially dilute basic earnings per share in the future, but were not included in the computation of diluted net loss per share because to do so would have been anti-dilutive as a result of the net loss for the period.

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As of June 30, 2023, 8,134,597 stock options and 791,853 restricted stock units were outstanding, which could potentially dilute basic earnings per share in the future, but were not included in the computation of diluted net loss per share because to do so would have been anti-dilutive as a result of the net loss for the period.

15. Stock-Based Compensation

2019 Inducement Plan

In October 2019, the Company's Board of Directors adopted the 2019 Inducement Plan, or the 2019 Plan, which is a non-stockholder approved stock plan adopted pursuant to the "inducement exception" provided under Nasdaq Listing Rule 5635(c)(4), or Rule 5635, for the purpose of awarding (i) non-statutory stock options, (ii) restricted stock awards, (iii) restricted stock unit awards, (iv) other stock awards (collectively, the Inducement Awards) to new employees of the Company, as inducement material to such new employees entering into employment with the Company. In November 2019, the Company filed a Registration Statement on Form S-8 with the SEC covering the offering of up to 300,000 shares of its common stock, par value $0.001, pursuant to the Company's 2019 Plan. Initial grants of Inducement Awards made to employees vest as to 25% on the first anniversary of the date of grant and the balance ratably over the next 36 months and subsequent grants vest monthly over a period of four years from the grant date.

2014 Equity Incentive Plan

The Company's 2014 Equity Incentive Plan, or the 2014 Plan, is administered by the Company's Board of Directors or a duly authorized committee thereof, referred to as the Plan administrator. The 2014 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock unit awards, stock appreciation rights, performance stock awards and other forms of equity compensation, collectively referred to as Stock Awards. Additionally, the 2014 Plan provides for the grant of performance cash awards. Incentive stock options may be granted only to employees. All other awards may be granted to employees, including officers, non-employee directors, and consultants. No incentive stock options may be granted under the 2014 Plan after the tenth anniversary of the effective date of the 2014 Plan. Stock Awards granted under the 2014 Plan vest at the rate specified by the Plan administrator. Initial grants of Stock Awards made to employees and non-employee consultants generally vest as to 25% on the first anniversary of the date of grant and the balance ratably over the next 36 months and subsequent grants generally vest monthly over a period of four years from the grant date, or upon the probable achievement of corporate goals. Stock options initially granted to members of the Company's Board of Directors generally vest over a period of three years in equal quarterly installments from the date of the grant, subject to the option holder's continued service as a director through such date. Subsequent grants to directors that are made automatically at Annual Meetings of Stockholders vest fully on the earlier of the first anniversary of the date of grant and the next Annual Meeting of Stockholders. The Plan administrator determines the term of Stock Awards granted under the 2014 Plan up to a maximum of ten years.

The aggregate number of shares of the Company's common stock reserved for issuance under the 2014 Plan has automatically increased on January 1 of each year, beginning on January 1, 2015 and continued 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, 2024, the aggregate number of shares of common stock that may be issued pursuant to Stock Awards under the 2014 Plan automatically increased from 12,203,023 to 13,837,444. 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.

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Restricted Stock Units

Under the 2014 Plan, there were 903,883 restricted stock units granted during each of the three and six months ended June 30, 2024. During the three and six months ended June 30, 2023, the Company granted 194,172 and 601,172 restricted stock units, respectively. No restricted stock units were granted under the 2019 Inducement Plan during the three and six months ended June 30, 2024 and 2023.

The weighted-average grant date fair value per share of restricted stock units granted to non-employee members of the Company's Board of Directors during each of the three and six months ended June 30, 2024 was $0.66. The weighted-average grant date fair value per share of restricted stock units granted to employees and non-employee members of the Company's Board of Directors during the three and six months ended June 30, 2023 was $3.09 and $7.81, respectively.

As of June 30, 2024, the Company's restricted stock units consist of time-based restricted stock units. All remaining performance-based restricted stock units either vested or were forfeited in the first quarter of 2024. For time-based restricted stock units, the Company recognizes compensation expense associated with these restricted stock units ratably over the award's vesting period following the grant date. For performance-based restricted stock units, vesting was contingent on the achievement of certain performance targets, subject to the recipient's continuous service through each performance target. Recognition of compensation expense associated with these performance-based awards began when, and to the extent, the performance criteria were probable of achievement and the employee had met the service conditions.

During the three and six months ended June 30, 2024 and 2023, the Company recognized compensation expense relating to restricted stock units as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	2023	2024	2023
Research and development	$ (6)	$ 116	$ 249	$ 295
General and administrative	327	445	1,684	898
Total restricted stock unit expense	$ 321	$ 561	$ 1,933	$ 1,193

A summary of restricted stock unit activity related to employees and non-employee members of the Company's Board of Directors as of and for the six months ended June 30, 2024 is presented below:

	Number of Units	Weighted Average Grant Date Fair Value
Outstanding, December 31, 2023	566,324	$ 9.27
Awarded	903,883	0.66
Vested and released	(357,060)	7.58
Forfeited	(136,348)	10.57
Outstanding, June 30, 2024	976,799	$ 1.74
Restricted stock units exercisable (vested and deferred), June 30, 2024	—	

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Stock Options

Under the 2014 Plan, the Company granted 1,170,000 and 349,767 stock options during the three months ended June 30, 2024 and 2023, respectively, and 3,045,125 and 1,798,921 stock options during the six months ended June 30, 2024 and 2023, respectively. No stock options were granted under the 2019 Inducement Plan during the three and six months ended June 30, 2024 and 2023. The fair values of stock options granted during the three and six months ended June 30, 2024 and 2023 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,	
	2024	2023	2024	2023
Risk-free interest rate	4.34%	3.38% - 3.89%	4.12% - 4.34%	3.38% - 4.22%
Expected volatility	89.8%	80.3% - 81.3%	89.6% - 89.8%	76.3% - 81.3%
Expected dividend yield	0%	0%	0%	0%
Expected life of employee and Board options (in years)	6.25	6.25	6.25	6.25

The weighted-average grant date fair value per share of options granted to employees and non-employee members of the Company's Board of Directors for their Board service during the three months ended June 30, 2024 and 2023 was $0.66 and $2.43, respectively, and during the six months ended June 30, 2024 and 2023 was $0.86 and $6.18, respectively. No options were granted to non-employee consultants during the three and six months ended June 30, 2024 and 2023.

During the three and six months ended June 30, 2024 and 2023, the Company recognized compensation expense relating to stock options as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	2023	2024	2023
Research and development	$ 275	$ 1,447	$ 779	$ 2,927
General and administrative	1,145	1,434	2,374	2,675
Total stock option expense	$ 1,420	$ 2,881	$ 3,153	$ 5,602

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, 2024 is presented below:

	Number of Shares	Weighted Average Exercise Price
Outstanding, December 31, 2023	7,897,647	$ 12.99
Granted	3,045,125	0.86
Exercised	—	—
Forfeited	(3,139,154)	4.81
Expired	(1,735,737)	14.15
Outstanding, June 30, 2024	6,067,881	$ 10.80
Options exercisable, June 30, 2024	3,797,495	

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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 each of the three and six months ended June 30, 2024 and 2023.

16. Income Taxes

The Company has recognized a full tax valuation allowance against its deferred tax assets as of June 30, 2024 and December 31, 2023. The tax benefit related to the exercise of stock options is recognized as a deferred tax asset that is offset by a corresponding valuation allowance. As such, the Company's effective tax rate is zero for each of the three and six months ended June 30, 2024 and 2023.

Historically, the Company's benefit from income taxes related to state R&D tax credits exchanged for cash pursuant to the Connecticut R&D Tax Credit Exchange Program, which permits qualified small businesses engaged in R&D activities within Connecticut to exchange their unused R&D tax credits for a cash amount equal to 65% of the value of the exchanged credits. The Company has not exchanged its R&D tax credit for cash during the three and six months ended June 30, 2024, and it was not eligible to exchange its R&D tax credit for cash during the three and six months ended June 30, 2023. Therefore, there was no benefit from income taxes for either of the three and six months ended June 30, 2024 and 2023. As of June 30, 2024, the Company recorded $697 within income tax receivable which related to the 2020 R&D credit.

The Inflation Reduction Act of 2022 included tax legislation that became effective early in 2023. Significant legislation for corporate taxpayers includes a corporate alternative minimum tax of 15.0% for companies with $1,000,000 or more in average net financial statement profits over the three previous years, as well as a 1.0% indirect excise tax on the repurchase of shares by a publicly traded company. The Company does not expect this legislation to have an effect on its tax provision as of June 30, 2024; however, the Company will continue to evaluate the effect on the tax provision each reporting period.

17. Commitments and Contingencies

License Agreement with Enteris Biopharma, Inc.

In August 2019, the Company entered into a non-exclusive license agreement, or the Enteris License Agreement, with Enteris Biopharma, Inc., or Enteris, pursuant to which Enteris granted to the Company a non-exclusive, royalty-bearing license, including the right to grant sublicenses, under certain proprietary technology and patent rights related to or covering formulations for oral delivery of peptide active pharmaceutical ingredients with functional excipients to enhance permeability and/or solubility, known as Enteris's Peptelligence® technology, to develop, manufacture and commercialize products using such technology worldwide, excluding Japan and South Korea.

The Company is also obligated, pursuant to the Enteris License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. During the three and six months ended June 30, 2024 and 2023, no milestone payments or royalties were paid to Enteris by the Company in relation to the Enteris License Agreement.

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Manufacturing Agreements

In July 2021, the Company entered into an API Commercial Supply Agreement with Polypeptide Laboratories S.A., or PPL, that defines each party's responsibilities with respect to PPL's manufacture and supply of the active pharmaceutical ingredient difelikefalin, or API, for the difelikefalin injection product candidate. Under the API Commercial Supply Agreement, PPL shall manufacture API at its facility for sale and supply to the Company, in the amounts as set forth in purchase orders to be provided by the Company. The Company will be required to purchase its requirements of API for each year of the term of the agreement, based on internal forecasts.

The API Commercial Supply Agreement will continue until the fifth anniversary of the approval by the FDA of the new drug application for KORSUVA injection, unless the API Commercial Supply Agreement is earlier terminated, and will automatically be extended for successive five-year periods unless either party gives notice to the other party of its intention to terminate.

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

In July 2019, the Company entered into two related Product Agreements under the MSA, one with each of Patheon and Patheon Manufacturing Services LLC, or Patheon Greenville, to govern the terms and conditions of the manufacture of commercial supplies of difelikefalin injection, the Company's lead product candidate. Pursuant to the Product Agreements, Patheon and Patheon Greenville will manufacture commercial supplies of difelikefalin injection at the Monza, Italy and Greenville, North Carolina manufacturing sites, respectively, from active pharmaceutical ingredient supplied by the Company. Patheon and Patheon Greenville will be responsible for supplying the other required raw materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

In December 2023, the Company entered into an agreement with Patheon to reimburse Patheon approximately $1,700 for forecasted manufacturing commitments that are no longer needed due to the reduced demand expectations of KORSUVA in the United States. As of June 30, 2024, $246 remained within accounts payable and accrued expenses on its Condensed Consolidated Balance Sheet. In connection with the agreement with Patheon, the Company agreed to schedule additional manufacturing commitments in 2024.

Restructuring Actions

In January 2024, the Company announced a workforce reduction of up to 50% of its employees in order to reduce its operating expenses and focus its efforts on development of oral difelikefalin in chronic pruritus associated with NP. As a result, the Company made estimates and judgements regarding its future plans, including future employee termination costs to be incurred in conjunction with involuntary separations when such separations are probable and estimable. In the first quarter of 2024, the Company recorded a pre-tax severance expense of $2,401, which was included within restructuring expenses on the Condensed Consolidated Statements of Comprehensive Loss for the six months ended June 30, 2024. The remaining amounts to be paid as of June 30, 2024 are included within accounts payable and accrued expenses on the Condensed Consolidated Balance Sheet.

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In connection with the streamlined operating plan approved by the Board of Directors in June 2024 (see Note 1, *Business*), the Board of Directors also approved a second reduction in the Company's workforce by approximately 70%, which the Company substantially completed by June 30, 2024. As a result, the Company made additional estimates and judgments regarding its future plans, including future employee termination costs to be incurred in conjunction with involuntary separations when such separations are probable and estimable. During the three months ended June 30, 2024, the Company recorded a pre-tax severance expense of $2,581, which was included within restructuring expenses on the Condensed Consolidated Statements of Comprehensive Loss for each of the three and six months ended June 30, 2024. The remaining amounts to be paid as of June 30, 2024 are included within accounts payable and accrued expenses on the Condensed Consolidated Balance Sheet.

The detail of activity related to the Company's restructuring action is as follows:

Total expense recorded in the three months ended March 31, 2024	$	2,401
Payments made in the three months ended March 31, 2024		(1,702)
Remaining amounts to be paid as of March 31, 2024		699
Total expense recorded in the three months ended June 30, 2024		2,581
Payments made in the three months ended June 30, 2024		(301)
Remaining amounts to be paid as of June 30, 2024	$	2,979

Leases (Original Corporate Headquarters in 2015 & Amendment for Additional Space in 2020)

Lease expense was recognized on a straight-line basis over the lease term of the Company's previous lease agreements for its original headquarters, and additional office space, in Stamford, Connecticut. As a result, $406 and $813 of operating lease cost, or lease expense, was recognized for the three and six months ended June 30, 2023, respectively, consisting of $284 relating to R&D lease expense and $122 relating to G&A lease expense for the three months ended June 30, 2023, and $569 relating to R&D lease expense and $244 relating to G&A lease expense for the six months ended June 30, 2023. There was no lease expense recognized on these former lease agreements for the three and six months ended June 30, 2024 since these agreements terminated in December 2023.

Lease (*New Corporate Headquarters in May 2023*)

On May 11, 2023, the Company entered into the New Lease for the Company's new principal executive offices. The initial term of the New Lease commenced on November 1, 2023, or the Commencement Date, and will expire on the last day of the calendar month in which occurs the tenth anniversary of the Rent Commencement Date, as defined below, or the Term.

In connection with the signing of the New Lease, the Company entered into a standby letter of credit agreement for $1,500 which serves as a security deposit for the leased office space. This standby letter of credit is secured with restricted cash in a money market account and is included within long-term assets as of June 30, 2024 (refer to Note 6, *Restricted Cash*).

The annual fixed rent rate under the New Lease is initially $1.3 million (considered by the Company to be at market rate as of the signing of the New Lease), which will commence on November 1, 2024, or the Rent Commencement Date, and will increase 2.5% annually thereafter. The Company expects to begin paying rent in November 2024.

The Company is also responsible for the payment of Additional Rent, as defined in the New Lease, including its share of the operating and tax expenses for the building. As a result, the New Lease contains both a lease (the right to use

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the asset) and a non-lease component (common area maintenance services) which are accounted for separately. The Company allocates the consideration to the lease and non-lease component on a relative standalone price basis.

The Company has the option to extend the Term under the New Lease for an additional five years on the same terms and conditions (other than with respect to the annual fixed rent at the annual fair market rental rate, as defined in the New Lease) as set forth in the New Lease. This renewable term is not included as part of the lease term as defined in ASC 842 since it is not reasonably certain that the Company will exercise that option on the Commencement Date.

Since the New Lease does not provide an implicit interest rate, the Company used an incremental borrowing rate equal to the 3-month Secured Overnight Financing Rate, or SOFR, plus 7.75% per annum subject to a 3-month SOFR floor of 2.75%, which is based on the rate that the Company could obtain in the market for a fully collateralized loan equal to the term of the New Lease, or 12.83%.

On July 28, 2023, the Company recorded a lease liability and a right-of-use asset, or the ROU asset, for the New Lease since it obtained control of the premises to begin work on its leasehold improvements prior to the Commencement Date. The initial lease liability of $6,672 was recorded as the sum of the present value of the future minimum lease payments over the term of the lease. Lease incentives of $2,900 were not included within lease payments since the timing of these costs being incurred and reimbursed to the Company was uncertain, and they were neither paid nor payable as of July 28, 2023. These lease incentives reduced the lease liability and ROU asset by the costs incurred once the Company actually incurred the costs and the amounts qualified for reimbursement. The reduction to the lease liability was reversed once the Company was reimbursed for the qualified costs. The reduction to the ROU asset will be recognized prospectively over the remainder of the lease term. The ROU asset of $6,779 was initially recorded as the amount of the lease liability plus prepaid rent paid in May 2023. During the three and six months ended June 2024, the Company was reimbursed $368 and $2,094 of qualified reimbursable lease incentives. As a result, there were no lease incentives remaining to be reimbursed to the Company as of June 30, 2024.

Beginning on July 28, 2023 and during the entire term of the New Lease, interest expense is calculated using the effective interest method and the ROU asset (including prepaid rent) will be amortized on a straight-line basis over the lease term, and both will be recorded as lease expense. As a result, lease expense of $256 and $525 for the New Lease was recorded for the three and six months ended June 30, 2024, consisting of $195 relating to R&D lease expense and $61 relating to G&A lease expense for the three months ended June 30, 2024, and $368 relating to R&D expense and $157 relating to G&A expense for the six months ended June 30, 2024.

Other information related to the leases (both previous and new) was as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	2023	2024	2023
Cash paid for amounts included in the measurement of lease liabilities:				
Operating cash outflows relating to operating leases	$ —	$ 496	$ —	$ 990
ROU assets obtained in exchange for new operating lease liabilities	$ —	$ —	$ —	$ —
Remaining lease term - operating leases (years)	10.3	0.5	10.3	0.5
Discount rate - operating leases	12.8 %	7.0 %	12.8 %	7.0 %

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Future minimum lease payments under non-cancellable operating leases, as well as a reconciliation of these undiscounted cash flows to the operating lease liabilities as of June 30, 2024, were as follows:

Year Ending December 31,	
2024 (Excluding the six months ended June 30, 2024)	$ 108
2025	1,298
2026	1,330
2027	1,363
2028	1,398
Thereafter	8,874
Total future minimum lease payments, undiscounted	14,371
Less imputed interest	(6,883)
Total	$ 7,488
Operating lease liability reported as of June 30, 2024:	
Operating lease liability - current	$ 168
Operating lease liability - non-current	7,320
Total	$ 7,488

18. Related Party Transactions

As of June 30, 2024, Vifor International owned 7,396,770, or 13.5%, of the Company's common stock. CSL Vifor and its affiliates are considered related parties as of June 30, 2024 and December 31, 2023 (see Note 12, *Collaboration and Licensing Agreements*).

As of June 30, 2024 and December 31, 2023, amounts due from CSL Vifor of $359 and $2,765, respectively, primarily relating to royalty payments from CSL Vifor in the current period and the Company's share of the profit generated by sales of KORSUVA injection in the United States by CSL Vifor, its commercial supply of KORSUVA injection to CSL Vifor, and royalty payments from CSL Vifor in the prior period were included within accounts receivable, net – related party.

The Company's collaborative revenue of $788 and $8,160 from its share of the profit generated by sales of KORSUVA injection in the United States by CSL Vifor was included within collaborative revenue for the six months ended June 30, 2024 and 2023, respectively. The Company's collaborative revenue of $5,410 from its share of the profit generated by sales of KORSUVA injection in the United States by CSL Vifor was included within collaborative revenue for the three months ended June 30, 2023. The Company also recorded a liability in accrued professional fees and other within accounts payable and accrued expenses for $1,447 and a corresponding expense in other G&A expense as a result of the negative profit share amount in the second quarter of 2024.

Sales of KORSUVA injection to CSL Vifor of $640 and $4,591 were included within commercial supply revenue for the six months ended June 30, 2024 and 2023, respectively. Sales of KORSUVA injection to CSL Vifor of $1,400 were included within commercial supply revenue for the three months ended June 30, 2023.

The Company recorded $123 and $248 as royalty revenue based on net sales of Kapruvia outside of the United States during the three and six months ended June 30, 2023, respectively. There was no royalty revenue recorded during the three and six months ended June 30, 2024.

The Company recorded $359 and $649 as other revenue from its royalty payments from CSL Vifor for the three and six months ended June 30, 2024, respectively. There was no other revenue recorded for the three and six months ended June 30, 2023.

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

In this Quarterly Report on Form 10-Q, the terms "we," "us" and "our" refer to Cara Therapeutics, Inc. Also, in this Quarterly Report, unless the context otherwise requires, we use the term "CSL Vifor" to refer to CSL Vifor and its affiliated entities, including where applicable, the joint venture between CSL Vifor and Fresenius Medical Care with which we are a party to two collaborations for the commercialization of KORSUVA (difelikefalin) injection.

Cautionary Note Regarding Forward-Looking Statements

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

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

- substantial uncertainties regarding our exploration of strategic alternatives to maximize shareholder value, including whether we are able to identify and implement any potential strategic alternatives, in a timely manner or at all, whether we realize all or any of the anticipated benefits of any such transaction and whether any such transactions would generate value for stockholders;

- our plans to develop and commercialize our product candidate or any potential future product candidates, should we resume development activities in the future;

- our ability to execute on our strategic plans, including efforts to significantly reduce our operating expenses;

- should we resume development of our product candidate or any future product candidates, the timing of our clinical trials and reporting of our results from these trials;

- should we resume development of our product candidate or any future product candidates, the potential results of preclinical studies and clinical trials and future regulatory and development milestones for our future product candidates;

- the performance of third-party manufacturers, clinical research organizations, or CROs, should we resume development of our product candidate or any future product candidates, and other vendors;

- should we resume development of our product candidate or any future product candidates, the size and growth of the potential markets;

- should we resume development of our product candidate or any future product candidates, the rate and degree of market acceptance of any other future approved indications or products;

- should we resume development of our product candidate or any future product candidates, our ability to obtain and maintain additional regulatory approval of our future product candidate, and the labeling under any approval we may obtain;
- should we resume development of our product candidate or any future product candidates, our ability to establish additional collaborations for our future product candidates;
- the continued service of our key scientific personnel, should we resume development of our product candidate or any future product candidates, or management personnel;
- should we resume development of our product candidate or any future product candidates, our ability to establish commercialization and marketing capabilities for any future approved products;
- regulatory developments in the United States and foreign countries;
- should we resume development of our product candidate or any future product candidates, our ability to obtain and maintain coverage and adequate reimbursement from third-party payers and governments for any other future approved indications or products;
- our planned use of our cash and cash equivalents and marketable securities and, should we resume development of our product candidate or any future product candidates, 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;
- should we resume development of our product candidate or any future product candidates, our ability to obtain and maintain intellectual property protection for our product candidate or future product candidates and our ability to operate our business without infringing on the intellectual property rights of others;
- our ability to maintain proper and effective internal controls, especially due to our high dependence on CSL Vifor for timely and accurate information;
- should we resume development of our product candidate or any future product candidates, the success of competing drugs that are or may become available;
- the potential effects of any global health crises, geopolitical tensions and macroeconomic conditions on our business, operations and, should we resume development of any future product candidates, clinical development and regulatory timelines and plans; and
- the performance of our current and future collaborators and licensees, including CSL Vifor, Maruishi Pharmaceuticals Co. Ltd., or Maruishi, and Chong Kun Dang Pharmaceutical Corp., or CKDP, as well as sub-licensees, including Winhealth Pharma and Kissei Pharmaceutical Co. Ltd., or Kissei, and our ability to maintain such collaborations.

You should refer to the “Risk Factors” section of this Quarterly Report on Form 10-Q for a discussion of material factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Quarterly Report on Form 10-Q will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives

and plans in any specified time frame or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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

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

Overview

Introduction

We are a biopharmaceutical company that has been focused on leading a new treatment paradigm to improve the lives of patients suffering from chronic pruritus. On June 14, 2024, our Board of Directors approved a streamlined operating plan exploring strategic alternatives focused on maximizing shareholder value after we announced our decision to discontinue the clinical program in notalgia paresthetica, or NP, on June 12, 2024. Our decision to discontinue the clinical program in NP followed the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. The decision was not related to any safety or medical issues, or negative regulatory feedback related to our NP program. In connection with the streamlined operating plan, our Board of Directors also approved a second reduction in our workforce by approximately 70%, which was substantially completed by June 30, 2024 (see Note 17 of Notes to Condensed Consolidated Financial Statements, *Commitments and Contingencies – Restructuring Actions*, in this Quarterly Report on Form 10-Q).

We also developed an IV formulation of oral difelikefalin, which is approved for the treatment of moderate-to-severe pruritus associated with advanced chronic kidney disease in adults undergoing hemodialysis in the United States, the European Union, or EU, and multiple other countries. The IV formulation is out-licensed worldwide.

Corporate History

We were incorporated and commenced operations in 2004, and our primary activities to date have been organizing and staffing our company, developing our lead product and product candidates, including conducting preclinical studies and clinical trials of difelikefalin-based product candidates and raising capital. To date, we have financed our operations primarily through sales of our equity and debt securities, sales of our royalties from ex-U.S. sales of our commercial product, and payments from license agreements.

NASDAQ Notice/Other Matters

On February 1, 2024, we received a letter from The Nasdaq Stock Market, or Nasdaq, notifying us that, for the previous 30 consecutive business day periods prior to the date of the letter, the closing bid price for our common stock was below $1.00. In accordance with Nasdaq Listing Rule 5810(c)(3)(A), we were provided an initial period of 180 calendar days, or until July 30, 2024, to regain compliance with Nasdaq's bid price requirement. On July 31, 2024, we received a notice, or the Extension Notice, from the Listing Qualifications Department of Nasdaq informing us that Nasdaq granted us an additional 180 calendar days, or until January 27, 2025, to regain compliance with the minimum closing bid price requirement for continued listing on The Nasdaq Capital Market under Nasdaq Listing Rule 5550(a)(2), or the Rule. In connection with the Extension Notice, the listing of our common stock was transferred from the Nasdaq Global Market to the Nasdaq Capital Market, effective as of August 1, 2024. The Extension Notice has no other immediate effect on the listing of the Company's common stock.

If at any time before January 27, 2025, the closing bid price of our common stock is at least $1.00 per share for a minimum of 10 consecutive business days, Nasdaq will provide written confirmation that we have achieved compliance with the Rule.

We intend to continue actively monitor the bid price for our common stock between now and January 27, 2025, and will consider available options to resolve the deficiency and regain compliance with the Rule. These options include, but are not limited to, effecting a reverse stock split, if necessary, to attempt to regain compliance. If we do not regain compliance within the additional compliance period, Nasdaq will provide notice that our common stock will be subject to delisting. We would then be entitled to appeal that determination to a Nasdaq hearings panel. There is no assurance, however, that the Company will regain compliance with the Rule or that our common stock will not be delisted from Nasdaq.

Our stockholders approved, at our 2024 Annual Meeting of Stockholders on June 4, 2024, a series of alternate amendments to our Amended and Restated Certificate of Incorporation to effect a reverse stock split of our common stock and corresponding proportionate reduction in the total number of authorized shares of our common stock, where the Board of Directors will have the discretion to select the reverse stock split ratio from within a range between and including one-for-four and one-for-twelve. To date, we have not effected a reverse stock split and corresponding reduction in authorized shares. Any such reverse stock split and corresponding reduction in authorized shares of common stock, and the reverse stock split ratio, will be at the sole discretion of the Board of Directors at any time prior to our 2025 Annual Meeting of Stockholders, and the Board of Directors may elect never to do so.

On June 7, 2024, we filed the Certificate of Amendment to our Certificate of Incorporation, or the Certificate, with the Secretary of State of the State of Delaware which was approved by our stockholders at our Annual Meeting of Stockholders on June 4, 2024. The Certificate increased the authorized number of shares of our common stock from 100,000,000 shares to 200,000,000 shares. The additional shares of common stock authorized by the Certificate have rights identical to our currently outstanding common stock and any issuance of common stock pursuant to the Certificate would not affect the rights of the holders of our currently outstanding common stock, except for effects incidental to increasing the number of shares of our common stock outstanding, such as dilution of the earnings per share and voting rights of current holders of our common stock.

Our Product Portfolio

Product	Indication	Status	Next Milestone	Commercialization Rights
KORSUVA (difelikefalin) injection/Kapruvia	Pruritus CKD - Hemodialysis	Approved in the U.S. (08/2021) Approved in EU incl. UK (04/2022) Approved in Japan (09/2023) Other approvals: Switzerland, Canada, Singapore, Australia, Kuwait, Israel, UAE, Saudi Arabia		CSL Vifor (Worldwide excl. Japan and South Korea)*; Maruishi (Japan); CKDP (South Korea)

**We are party to two collaborations for the commercialization of KORSUVA (difelikefalin) injection/Kapruvia with a joint venture between CSL Vifor and Fresenius Medical Care. In this Quarterly Report, unless the context otherwise requires, "CSL Vifor" refers to CSL Vifor and its affiliated entities, including, where applicable, the joint venture.*

KORSUVA (difelikefalin) injection – Our Commercial Stage Product

Overview

We have out-licensed to CSL Vifor the commercialization of KORSUVA injection/Kapruvia in dialysis patients with moderate-to-severe pruritus associated with chronic kidney disease, or advanced CKD-aP, worldwide, excluding Japan (licensed to Maruishi/sub-licensee Kissei), and South Korea (licensed to CKDP).

On August 23, 2021, KORSUVA injection was approved by the U.S. Food and Drug Administration, or FDA, for the treatment of moderate-to-severe pruritus associated with advanced CKD in adults undergoing hemodialysis. In December 2021, Centers for Medicare & Medicaid Services, or CMS, granted Transition Drug Add-on Payment Adjustment, or TDAPA, to KORSUVA injection in the anti-pruritic functional category. TDAPA went into effect on April 1, 2022 for two years. The commercial launch of KORSUVA injection commenced in April 2022 and we began recording the associated profit-sharing revenues in the second quarter of 2022. On October 27, 2023, CMS published the final CY 2024 rule, which finalized the post-TDAPA add-on payment as proposed in the draft CY 2024 rule. Under the final rule, TDAPA drugs in existing functional categories will receive a post-TDAPA add-on payment set at 65 percent of the total trailing 12-months expenditure levels for the given renal dialysis drug or biological product. The post-TDAPA add-on payment will be applied to all End Stage Renal Disease, or ESRD, Prospective Payment System, or PPS, payments and paid for 3 years, adjusted annually. The add-on payments for KORSUVA injection commenced on April 1, 2024. The unfavorable CMS reimbursement codified in the final CY2024 rule has resulted in a lack of sequential revenues growth for KORSUVA injection since its launch.

For the three months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $2.7 million, which resulted in our profit share amount of negative $1.4 million. For the three months ended June 30, 2023, CSL Vifor recorded net sales of $11.4 million, which resulted in our profit share amount of $5.4 million. The negative net sales reported by CSL Vifor was primarily due to higher rebates and chargebacks due to price decreases on KORSUVA injection related to the expiration of TDAPA in April 2024. Based on the terms of the agreement, the negative profit will be offset against net profits in future periods. However, we have recorded a liability in accrued professional fees and other within accounts payable and accrued expenses for $1.4 million and a corresponding expense in other general and administrative, or G&A, expense as a result of the negative profit share amount in the second quarter of 2024. For the six months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $0.9 million. For the six months ended June 30, 2023, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately $17.1 million. For the six months ended June 30, 2024 and 2023, we recorded associated collaborative revenue of $0.8 million and $8.2 million, respectively. As a result of the final CY 2024 rule, we expect no meaningful revenue contribution from KORSUVA injection following the TDAPA period expiration.

In April 2022, the European Commission granted a marketing authorization to difelikefalin injection under the brand name Kapruvia for the treatment of moderate-to-severe pruritus associated with advanced CKD in adult hemodialysis patients. The marketing authorization approves Kapruvia for use in all member states of the EU, as well as Iceland, Liechtenstein, and Norway. Difelikefalin injection was also approved in the UK (04/2022) and Switzerland (08/2022) under the brand name Kapruvia as well as Singapore (08/2022), Canada (08/2022), Australia (11/2022), UAE (01/2023), Kuwait (05/2023), Israel (06/2023), Japan (09/2023), and Saudi Arabia (01/2024) under the brand name KORSUVA injection. For the three and six months ended June 30, 2023, we recorded royalty revenue of approximately $123,000 and $248,000, respectively, which represented our royalties on net sales of Kapruvia.

During the fourth quarter of 2023, we entered into a Purchase and Sale Agreement, or the HCR Agreement, with HCRX Investments Holdco, L.P. and Healthcare Royalty Partners IV, L.P., or collectively HCR, pursuant to which HCR will receive current and future royalty and milestone payments for Kapruvia and KORSUVA (ex-U.S. only) up to certain capped amounts in exchange for certain payments made to us. As a result, there was no royalty revenue recorded for the three and six months ended June 30, 2024. However, we recorded other revenue of approximately $1.0 million and $1.6 million for the three and six months ended June 30, 2024, respectively, of which approximately $0.4 million and $0.6 million, respectively, related to CSL Vifor royalties to be paid to HCR under this agreement (see “Royalty Purchase and Sale Agreement” below).

We have out-licensed to Maruishi and its sub-licensee Kissei the commercialization of KORSUVA injection in Japan. In September 2023, Maruishi received manufacturing and marketing approval from Japan’s Ministry of Health, Labour and Welfare for KORSUVA IV Injection Syringe for the treatment of pruritus in hemodialysis patients.

During the fourth quarter of 2023, we entered into the HCR Agreement where we sold our future royalties and milestones for KORSUVA in Japan to HCR. For the three and six months ended June 30, 2024, we recorded other revenue of approximately $1.0 million and $1.6 million, respectively, of which approximately $0.6 million and $1.0

million, respectively, related to Maruishi royalties to be paid to HCR under this agreement (see "Royalty Purchase and Sale Agreement" below). There was no other revenue recorded for the three and six months ended June 30, 2023 as the HCR Agreement was not entered into until the fourth quarter of 2023.

As a result of our sales of the royalties and milestones for KORSUVA/Kapruvia, we expect no meaningful revenue contribution from KORSUVA/Kapruvia royalties and milestones in the foreseeable future.

KORSUVA Injection U.S. Commercialization

In April 2022, our partner CSL Vifor initiated the commercialization of KORSUVA injection in the United States. The launch was initially driven by independent and mid-size dialysis organizations coupled with product stocking at the wholesaler level. In the third quarter of 2022, large dialysis organizations, or LDOs, came on-line driving a significant quarter-to-quarter increase in order volume from the wholesaler. This stocking at the clinic level, particularly from Fresenius Medical Care, or FMC, resulted in significant subsequent quarterly revenue fluctuations. In the third quarter of 2023, FMC decided to reallocate all remaining clinic level inventory within its network of clinics resulting in limited revenues in the fourth quarter of 2023 and during the three months ended March 31, 2024 and no revenue in the three months ended June 30, 2024.

KORSUVA Injection and Kapruvia Revenue and Other Metrics

We generate revenue from our commercial products KORSUVA injection and Kapruvia primarily through our collaboration agreements with CSL Vifor:

- Collaborative revenue from our share of the profit generated by KORSUVA injection sales in the United States. There was no collaborative revenue recorded during the three months ended June 30, 2024. For the three months ended June 30, 2023, we recorded collaborative revenue of $5.4 million. For the six months ended June 30, 2024 and 2023, we recorded collaborative revenue of $0.8 million and $8.2 million, respectively.

- Commercial supply revenue from our sales of commercial product to CSL Vifor, which is subsequently sold to wholesalers. There was no commercial supply revenue recorded during the three months ended June 30, 2024. For the three months ended June 30, 2023, we recorded commercial supply revenue of $1.4 million. For the six months ended June 30, 2024 and 2023, we recorded commercial supply revenue of $0.6 million and $4.6 million, respectively.

- Royalty revenue in conjunction with the launch of Kapruvia. For the three and six months ended June 30, 2023, we recorded royalty revenue of approximately $123,000 and $248,000, respectively, which represented royalty payments earned by us. We recorded no royalty revenue in connection with Kapruvia for the three and six months ended June 30, 2024 as a result of entering the HCR Agreement in the fourth quarter of 2023.

During the fourth quarter of 2023, we entered into the HCR Agreement where we sold our current and future royalties and milestone payments for Kapruvia and KORSUVA injection to HCR. For the three and six months ended June 30, 2024, we recorded other revenue of approximately $1.0 million and $1.6 million, respectively, of which approximately $0.4 million and $0.6 million, respectively, related to CSL Vifor royalties to be paid to HCR under this agreement and approximately $0.6 million and $1.0 million, respectively, related to Maruishi royalties to be paid to HCR under this agreement (see "Royalty Purchase and Sale Agreement" below).

We are also eligible for sales-based or regulatory milestone payments, which could be earned in the future in accordance with certain licensing agreements and would be subject to the HCR Agreement for ex-U.S. milestone payments. For the three and six months ended June 30, 2024 and 2023, we did not record any sales-based or regulatory milestone revenue.

Additional metrics that we have reported in the past:

- Net sales of KORSUVA injection in the United States. This amount is the net sales amount recorded by CSL Vifor to reflect shipments of KORSUVA injection vials from CSL Vifor to wholesalers. For the three months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $2.7 million. For the three months ended June 30, 2023, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately $11.4 million. For the six months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $0.9 million. For the six months ended June 30, 2023, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately $17.1 million.

- Shipments of KORSUVA injection vials from wholesalers in the United States to the dialysis clinics. 80,328 and 66,852 KORSUVA injection vials were shipped from wholesalers to the dialysis clinics for the three months ended June 30, 2024 and 2023, respectively, and 192,048 and 112,572 KORSUVA injection vials were shipped from wholesalers to the dialysis clinics for the six months ended June 30, 2024 and 2023, respectively. Of the vials shipped to the FMC dialysis centers for the three and six months ended June 30, 2024, a portion was reallocated product by FMC within its network of clinics.

Difelikefalin Development in Pruritus

Difelikefalin, our selective, predominantly peripherally acting, non-scheduled Kappa opioid receptor agonist, acts on the peripheral neurons responsible for sensing pruritus. Given this unique mechanism of action, difelikefalin is thought to work broadly independent of the origin of itch. To date, we have studied difelikefalin for pruritus associated with systemic, inflammatory, and neuropathic diseases. The IV formulation is approved in the United States, EU and other countries around the world for the treatment of advanced CKD-aP in adults undergoing hemodialysis. We studied the oral formulation at multiple dosage strengths in moderate-to-severe pruritus associated with NP with positive efficacy signals across all completed mono therapy studies. In our NP program, oral difelikefalin was generally well tolerated with all adverse events in difelikefalin-treated patients reported as mild or moderate in severity.

On June 12, 2024, we announced our decision to discontinue the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP. Oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. The decision was not related to any safety or medical issues, or negative regulatory feedback related to our NP program.

On June 14, 2024, our Board of Directors approved a streamlined operating plan exploring strategic alternatives focused on maximizing shareholder value based on the decision to discontinue the NP program.

Royalty Purchase and Sale Agreement

During the fourth quarter of 2023, we, through our wholly-owned subsidiary Cara Royalty Sub LLC, or Cara Royalty Sub, entered into the HCR Agreement, pursuant to which Cara Royalty Sub sold to HCR certain of its rights to receive future royalties and milestone payments, or the Royalties, due and payable to Cara Royalty Sub (as our assignee) under our agreements with Maruishi and CSL Vifor, collectively the Covered License Agreements, in exchange for up to $40.0 million. We have retained all of our rights, title and interest in, to and under the Covered License Agreements that relate to any non-intravenous formulation of difelikefalin.

Under the terms of the HCR Agreement, Cara received an initial payment of $17.5 million less certain transaction costs in November 2023. In December 2023, we received an additional $20.0 million less certain advisory fees, upon satisfying the milestone event for pricing of Kapruvia® (difelikefalin) in Germany being approved above a certain threshold amount per dose. The terms of the HCR Agreement also provide for an additional $2.5 million milestone payment to Cara Royalty Sub upon achievement of a 2024 sales milestone of KORSUVA in Japan.

The HCR Agreement will automatically expire, and the payment of Royalties to HCR will cease, when HCR has received payments of Royalties equal to two times the aggregate amount of payments made by HCR under the HCR Agreement if achieved on or prior to December 31, 2029, or 2.8 times the aggregate amount of payments made by HCR under the HCR Agreement, if not achieved on or prior to December 31, 2029. In the event of a change of control, Cara Royalty Sub will pay to HCR an amount equal to 2.8 times the aggregate amount of payments made by HCR less the total net amounts paid by Cara Royalty Sub to HCR as of the effective date of control. In certain situations, Cara Royalty Sub would not be obligated to pay the change of control payment to HCR. After the HCR Agreement expires, all rights to receive the Royalties return to Cara Royalty Sub. During the three and six months ended June 30, 2024, approximately $0.6 million and $1.3 million, respectively, was repaid to HCR under the HCR Agreement.

Collaboration and License Agreements

Agreements with CSL Vifor

We are party to two separate license agreements with CSL Vifor. In October 2020, we granted CSL Vifor an exclusive license solely in the United States to use, distribute, offer for sale, promote, sell, and otherwise commercialize KORSUVA (difelikefalin) injection for all therapeutic uses relating to the inhibition, prevention or treatment of itch associated with pruritus in hemodialysis and peritoneal dialysis patients in the United States.

We received an upfront payment of $100.0 million and an additional payment of $50.0 million for the purchase of an aggregate of 2,939,552 shares of our common stock at a price of $17.0094 per share, which represented a premium over a pre-determined average closing price of our common stock. The U.S. regulatory approval of KORSUVA injection in August 2021 triggered an additional $50.0 million equity purchase by CSL Vifor in October 2021, in which we sold an aggregate of 3,282,391 shares of our common stock at a price of $15.23 per share, which represented a 20% premium to the 30-day trailing average price of our common stock. In addition, pursuant to this agreement, we are eligible to receive payments of up to $240.0 million upon the achievement of certain sales-based milestones. However, based on the limited commercial success of KORSUVA injection, we do not expect to achieve these sales-based milestones.

Pursuant to the agreement for commercialization of KORSUVA in the United States, we are generally entitled to 60% of the net profits from sales of KORSUVA injection in the United States and CSL Vifor is entitled to 40% of such net profits (excluding sales to Fresenius Medical Center dialysis clinics, compensation for which is governed by a separate agreement), subject to potential temporary adjustment in future years based on certain conditions. Under this agreement, in consideration of CSL Vifor's conduct of the marketing, promotion, selling and distribution of KORSUVA injection in the United States, we pay a marketing and distribution fee to CSL Vifor based on the level of annual net sales. This fee as well as CSL Vifor's cost of goods sold, or COGS, are deducted from net sales in calculating the net profits that are subject to the profit-sharing arrangement under the agreement.

Under a separate agreement with CSL Vifor, in May 2018, we granted CSL Vifor a license to seek regulatory approval to commercialize, import, export, use, distribute, offer for sale, promote, sell and otherwise commercialize KORSUVA (difelikefalin) injection for all therapeutic uses to prevent, inhibit or treat itch associated with pruritus in hemodialysis and peritoneal-dialysis patients worldwide (excluding the United States, Japan and South Korea). Under the agreement, CSL Vifor also has the right to promote KORSUVA injection in the United States in the dialysis clinics of Fresenius Medical Care North America, or FMCNA, under a profit-sharing arrangement.

Upon entry into this agreement, we received a non-refundable, non-creditable $50.0 million upfront payment for the purchase of an aggregate of 1,174,827 shares of our common stock at a price of $17.024 per share, which represented a premium over a pre-determined average closing price of our common stock.

As a result of the European Commission's regulatory approval of Kapruvia in April 2022, we received a $15.0 million regulatory milestone payment from CSL Vifor. After U.S. regulatory approval of KORSUVA injection in August 2021, we received a $15.0 million regulatory milestone payment.

We are eligible to receive from CSL Vifor commercial milestone payments in the aggregate of up to $440.0 million, all of which milestones are sales related. We are also eligible to receive tiered double-digit royalty payments based on

annual net sales, as defined, of KORSUVA (difelikefalin) injection in the licensed territories. In the United States, CSL Vifor will promote KORSUVA (difelikefalin) injection in the dialysis clinics of FMCNA under a profit-sharing arrangement (subject to the terms and conditions of this agreement) based on net FMCNA clinic sales) and Vifor Fresenius Medical Care Renal Pharma Ltd. is entitled to 50% of such net profits, subject to potential adjustments in a calendar year based on certain conditions. During the fourth quarter of 2023, we entered into the HCR Agreement pursuant to which we sold our future royalties and milestone payments under this agreement to HCR (see "Royalty Purchase and Sale Agreement" above).

Maruishi Pharmaceutical Co., Ltd., or Maruishi

In April 2013, we entered into a license agreement with Maruishi, or the Maruishi Agreement, under which we granted Maruishi an exclusive license to develop, manufacture and commercialize drug products containing difelikefalin in Japan in the acute pain and uremic pruritus fields. Maruishi has a right of first negotiation for any other indications for which we develop difelikefalin and, under certain conditions, Maruishi may substitute another pruritus indication for the uremic pruritus indication originally included in its license from us. Maruishi's right of first negotiation has expired for the indication of chronic pruritus associated with NP. Maruishi is required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize difelikefalin in Japan. We are required to use commercially reasonable efforts, at our expense, to develop, obtain regulatory approval for and commercialize difelikefalin in the United States.

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

Under the terms of the Maruishi Agreement, we received a non-refundable and non-creditable upfront license fee of $15.0 million and are eligible to receive up to an aggregate of $10.5 million in clinical development and regulatory milestones (before contractual foreign currency exchange adjustments). In January 2021, we met the milestone criteria, as set forth in the Maruishi Agreement, for Maruishi's first initiation of a Phase 3 trial for uremic pruritus in Japan. As a result, we received the $2.0 million milestone payment ($1.9 million after contractual foreign currency exchange adjustments) in May 2021.

In September 2022, Maruishi submitted a New Drug Application in Japan for approval of difelikefalin injection for the treatment of pruritus in hemodialysis patients. In September 2023, Maruishi received manufacturing and marketing approval from Japan's Ministry of Health, Labour and Welfare for KORSUVA IV Injection Syringe for the treatment of pruritus in hemodialysis patients. In conjunction with the approval, we earned a $1.4 million milestone payment per the terms of the licensing agreement. In November 2023, we entered into an active pharmaceutical ingredient, or API, supply agreement with Maruishi for difelikefalin.

To date, we have received $6.5 million (before contractual foreign currency exchange adjustments) of clinical development and regulatory milestones from Maruishi. We are also eligible to receive a one-time sales milestone of one billion Yen when a certain sales level is attained. We also receive a mid-double-digit percentage of all non-royalty payments received by Maruishi from its sublicensees, if any, and tiered royalties based on net sales, if any, with minimum royalty rates in the low double digits and maximum royalty rates in the low twenties. Maruishi's obligation to pay us royalties continues, on a product-by-product basis, until the expiration of the last-to-expire licensed patent covering such product or the later expiration of any market exclusivity period. During the fourth quarter of 2023, we entered into the HCR Agreement pursuant to which we sold our future royalties and milestone payments under the Maruishi Agreement to HCR (see "Royalty Purchase and Sale Agreement" above).

Chong Kun Dang Pharmaceutical Corporation, or CKDP

In April 2012, we entered into a license agreement with CKDP, or the CKDP Agreement, under which we granted CKDP an exclusive license to develop, manufacture and commercialize drug products containing difelikefalin in South Korea. CKDP is required to use commercially reasonable efforts, at its expense, to develop, obtain regulatory approval for and commercialize difelikefalin in South Korea. We are required to use commercially reasonable efforts, at our expense, to develop, obtain regulatory approval for and commercialize difelikefalin in the United States.

Under the terms of the CKDP Agreement, we received a non-refundable and non-creditable $0.6 million upfront payment and are eligible to receive up to an aggregate of $3.8 million in development and regulatory milestones (before South Korean withholding taxes). To date, we have received $2.3 million (before South Korean withholding tax) of development and regulatory milestones. We are also eligible to receive a mid-double-digit percentage of all non-royalty payments received by CKDP from its sublicensees, if any, and tiered royalties ranging from the high single digits to the high teens based on net sales, if any. CKDP's obligation to pay us royalties continues, on a product-by-product basis, until the expiration of the last-to-expire licensed patent covering such product or the later expiration of any market exclusivity period.

The CKDP Agreement continues until CKDP no longer has any obligation to pay us royalties on any product. Either we or CKDP may terminate the CKDP Agreement for the other party's breach of the CKDP Agreement or bankruptcy. CKDP may terminate the CKDP Agreement if any of the licensed patent rights is invalid, unenforceable, is narrowed in scope or is deemed unpatentable, except as a result of a challenge by CKDP, or a third party commercializes a product containing a compound identical to difelikefalin without infringing any of the licensed patent rights in South Korea. We may terminate the CKDP Agreement if CKDP challenges the licensed patent rights or if a third party in South Korea owns an issued patent that claims difelikefalin and CKDP's sale of products would infringe that patent. In addition, in connection with the CKDP Agreement, CKDP made a $0.4 million equity investment in our company.

Manufacturing and License Agreements

Polypeptide Laboratories S.A., or PPL

In July 2021, we entered into an API Commercial Supply Agreement with Polypeptide Laboratories S.A., or PPL, that defines each party's responsibilities with respect to PPL's manufacture and supply of API for the difelikefalin injection product candidate. Under the API Commercial Supply Agreement, PPL shall manufacture API at its facility for sale and supply to us, in the amounts as set forth in purchase orders to be provided by us. We will be required to purchase our requirements of API for each year of the term of the agreement, based on internal forecasts.

The API Commercial Supply Agreement will continue until the fifth anniversary of the approval by the FDA of the New Drug Application for KORSUVA injection, unless the API Commercial Supply Agreement is earlier terminated, and will automatically be extended for successive five-year periods unless either party gives notice to the other party of its intention to terminate.

Enteris Biopharma, Inc., or Enteris

In August 2019, we entered into a non-exclusive license agreement with Enteris Biopharma, Inc. (Enteris), or the Enteris License Agreement. Pursuant to the Enteris License Agreement, Enteris granted to us a non-exclusive, royalty-bearing license, including the right to grant sublicenses, under certain proprietary technology and patent rights related to or covering formulations for oral delivery of peptide active pharmaceutical ingredients with functional excipients to enhance permeability and/or solubility, known as Enteris's Peptelligence® technology, to develop, manufacture and commercialize products using such technology worldwide, excluding Japan and South Korea.

As consideration for the licensed rights under the Enteris License Agreement, we paid an upfront fee equal to $8.0 million, consisting of $4.0 million in cash and $4.0 million in shares of our common stock.

We are also obligated, pursuant to the Enteris License Agreement, to pay Enteris (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. Until the second anniversary of the entry into the Enteris License Agreement, we had the right, but not the obligation, to terminate our obligation to pay any royalties under the Royalty Buyout. We did not exercise our Royalty Buyout right and such right expired in August 2021. During the three and six months ended June 30, 2024 and 2023, no milestone payments or royalties were paid to Enteris by us in relation to the Enteris License Agreement.

The Enteris License Agreement will expire on a country-by-country, licensed product-by-licensed product basis upon the later of (1) the expiration (or invalidation) of all valid claims in licensed patent rights that cover such product in such country, (2) the end of the calendar quarter in which generic competition (as defined in the Enteris License Agreement) occurs for such product in such country and (3) ten years from the first commercial sale of such product.

Either party may terminate the Enteris License Agreement upon written notice if the other party has failed to remedy a material breach within 60 days (or 30 days in the case of a material breach of a payment obligation). Enteris may terminate the Enteris License Agreement upon 30 days' written notice to us if we or any of our affiliates formally challenge the validity of any licensed patent rights or assists a third party in doing so. We may terminate the Enteris License Agreement for any reason or no reason (a) prior to receipt of first regulatory approval for a licensed product in the United States for any indication upon 30 days' prior written notice to Enteris or (b) on or after receipt of first regulatory approval for a licensed product in the United States for any indication upon 60 days' prior written notice to Enteris. In June 2024, we announced our decision to discontinue the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP.

Patheon UK Limited, or Patheon

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

The MSA has an initial term ending December 31, 2024, and will automatically renew after the initial term for successive terms of two years each if there is a Product Agreement in effect, unless either party gives notice of its intention to terminate the MSA at least 18 months prior to the end of the then current term.

Either party may terminate the MSA or a Product Agreement upon written notice if the other party (1) has failed to remedy a material breach within a specified time or (2) is declared insolvent or bankrupt, voluntarily files a petition of bankruptcy or assigns such agreement for the benefit of creditors. We may terminate a Product Agreement (a) upon 90 days' prior written notice if any governmental agency takes any action that prevents us from selling the relevant product in the relevant territory, (b) upon six months' prior written notice if we do not intend to order manufacturing services due to a product's discontinuance in the market, or (c) upon 90 days' prior written notice if we determine that the manufacture or supply of a product likely infringes third-party rights. Patheon may terminate the MSA or a Product Agreement (i) upon six months' prior written notice if we assign such agreement to an assignee that is unacceptable to Patheon for certain reasons, or (ii) upon 30 days' prior written notice if, after the first year of commercial sales, we forecast zero volume for 12 months.

The MSA contains, among other provisions, customary representations and warranties by the parties, a grant to Patheon of certain limited license rights to our intellectual property in connection with Patheon's performance of the services under the MSA, certain indemnification rights in favor of both parties, limitations of liability and customary confidentiality provisions.

Also in July 2019, we entered into two related Product Agreements under the MSA, one with each of Patheon and Patheon Manufacturing Services LLC, or Patheon Greenville, to govern the terms and conditions of the manufacture of commercial supplies of difelikefalin injection, our lead product candidate. Pursuant to the Product Agreements, Patheon and Patheon Greenville will manufacture commercial supplies of difelikefalin injection at the Monza, Italy and Greenville, North Carolina manufacturing sites, respectively, from API supplied by us. Patheon and Patheon Greenville will be responsible for supplying the other required raw materials and packaging components, and will also provide supportive manufacturing services such as quality control testing for raw materials, packaging components and finished product.

In December 2023, we entered into an agreement with Patheon to reimburse Patheon approximately $1.7 million for forecasted manufacturing commitments that are no longer needed due to the reduced demand expectations of KORSUVA in the United States. As of June 30, 2024, $0.2 million of the $1.7 million remained within accounts payable and accrued expenses on our Condensed Consolidated Balance Sheet. In connection with the agreement with Patheon, we agreed to schedule additional manufacturing commitments in 2024.

Components of Operating Results

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

Revenue

To date, we have generated revenue primarily from (1) collaborative revenue from our share of the profit generated by KORSUVA injection sales in the United States; (2) commercial supply revenue from our sales of commercial product to CSL Vifor, which is subsequently sold to wholesalers; (3) the receipt of upfront license fees and milestone payments; (4) royalty revenue in conjunction with sales of Kapruvia in Europe through September 30, 2023; and (5) clinical compound sales from certain license agreements. We are eligible to receive sales-based milestones in the future in accordance with certain licensing agreements.

Beginning in the fourth quarter of 2023, the revenue received under our agreements with CSL Vifor and Maruishi for royalty and sales-based milestone payments received in conjunction with ex-U.S. sales of KORSUVA/Kapruvia were recorded as other revenue and considered non-cash until we have fulfilled our obligations under HCR Agreement (see “Royalty Purchase and Sale Agreement” above).

To date, we have earned a total of $138.3 million in clinical development or regulatory milestone payments, clinical compound and commercial compound sales from certain license agreements, collaborative revenue from our share of the profit generated by KORSUVA injection sales, and royalty revenue (which ceased upon entry into the HCR Agreement during the fourth quarter of 2023).

Revenue from sales of KORSUVA injection in future periods is subject to uncertainties and will depend on several factors, including the success of our and our commercial partners’ commercialization efforts in the United States, the number of new patients adopting or switching to KORSUVA injection, patient retention and sustained demand, the number of physicians prescribing KORSUVA injection, the rate of monthly prescriptions, reimbursement from third-party payors including the U.S. government, and market trends. More specifically, in December 2021, CMS granted TDAPA to KORSUVA injection in the anti-pruritic functional category. TDAPA went into effect on April 1, 2022, for two years. On October 27, 2023, CMS published the final CY 2024 rule, which finalized the post-TDAPA add-on payment as proposed in the draft CY 2024 rule. Under the final rule, TDAPA drugs in existing functional categories will receive a post-TDAPA add-on payment set at 65 percent of the total trailing 12-months expenditure levels for the given renal dialysis drug or biological product. The post-TDAPA add-on payment will be applied to all ESRD PPS payments and paid for 3 years, adjusted annually. The add-on payments for KORSUVA injection commenced on April 1, 2024. The anticipated unfavorable CMS reimbursement codified in the final CY 2024 rule has resulted in a lack of sequential revenues growth for KORSUVA injection since its launch. For the three months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $2.7 million, which resulted in our profit share amount of negative $1.4 million. The negative net sales reported by CSL Vifor was primarily due to

higher rebates and chargebacks due to price decreases on KORSUVA injection related to the expiration of TDAPA in April 2024. Based on the terms of the agreement, the negative profit will be offset against net profits in future periods. However, we have recorded a liability in accrued professional fees and other within accounts payable and accrued expenses for $1.4 million and a corresponding expense in other G&A expense as a result of the negative profit share amount in the second quarter of 2024. For the six months ended June 30, 2024, CSL Vifor recorded net sales of KORSUVA injection in the United States of approximately negative $0.9 million. We expect no meaningful revenue contribution from KORSUVA injection post its TDAPA expiration.

In the third quarter of 2023, FMC decided to reallocate all remaining clinic level inventory within its network of clinics resulting in limited revenues in the fourth quarter of 2023 and the three months ended March 31, 2024 and no revenue in the three months ended June 30, 2024.

As of June 30, 2024, Vifor International owned 7,396,770, or 13.5%, of our common stock. CSL Vifor and its affiliates are all considered related parties as of June 30, 2024 and December 31, 2023 (see Note 18 of Notes to Condensed Consolidated Financial Statements, *Related Party Transactions*, in this Quarterly Report on Form 10-Q).

Cost of Goods Sold (COGS)

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

There was no commercial supply revenue recorded for the three months ended June 30, 2024. For the three months ended June 30, 2023, we recorded commercial supply revenue of $1.4 million, with associated COGS of $1.4 million. For the six months ended June 30, 2024 and 2023, we recorded commercial supply revenue of $0.6 million and $4.6 million, respectively, with associated COGS of $0.6 million for the 2024 period and $4.0 million for the 2023 period. We expect our COGS to be reflective of future KORSUVA injection sales.

Research and Development (R&D)

Our R&D expenses relate primarily to the development of oral difelikefalin. R&D expenses consist of expenses incurred in performing R&D activities, including compensation and benefits for full-time R&D employees, clinical trial and related clinical manufacturing expenses, third-party formulation expenses or milestone payments, fees paid to CROs and other vendors and 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 have been central to our business model. Based on our recent announcement that we are discontinuing our NP program, we presently expect that our R&D expenses will significantly decrease in the future as we focus on exploring strategic alternatives to maximize shareholder value. However, it is difficult to determine with certainty the duration and completion costs in connection with the discontinuation of our studies in NP or future nonclinical and clinical studies of our current or any future product candidates, should we resume the development of any future 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, should we resume the development of any future

product candidates. We may never succeed in achieving regulatory approval for oral difelikefalin or any future product candidates, should we resume the development of oral difelikefalin or any future product candidates.

The duration, costs and timing of clinical trials and development of future product candidates, should we resume the development of any future product candidates, will depend on a variety of factors including, but not limited to:

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

In addition, the probability of success for future product candidates, should we resume the development of any future product candidates, will depend on numerous factors, including competition, manufacturing capability and commercial viability. In the future, should we resume the development of any future product candidates, we will determine which, if any, other programs to pursue and how much to fund each program in response to the scientific and clinical success of future product candidates, as well as an assessment of our future product candidates' commercial potential.

General and Administrative (G&A)

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

We anticipate that our G&A expenses will decrease in the future as a result of our workforce reductions during the six months ended June 30, 2024. However, G&A expenses will continue to include costs related to remaining personnel, fees to outside consultants, lawyers, and accountants, as well as costs associated with our exploration of potential strategic alternatives, which could offset the decreases from workforce reductions. In addition, if any future product candidate obtains regulatory approval for marketing, should we resume the development of any future product candidates, we may incur expenses associated with building sales and marketing, commercial operations, and market access teams.

Our license agreements with CSL Vifor provide full U.S. commercialization rights of KORSUVA injection to CSL Vifor under profit-sharing arrangements. Under these profit-sharing arrangements, in consideration of CSL Vifor's conduct of the marketing, promotion, selling and distribution of KORSUVA injection in the United States, we pay a marketing and distribution fee to CSL Vifor based on the level of annual net sales. This fee as well as CSL Vifor's

COGS are deducted from product sales in calculating the net profits that are subject to the profit-sharing arrangement (see Note 12 of Notes to Condensed Consolidated Financial Statements, C*ollaboration and Licensing Arrangements*, in this Quarterly Report on Form 10-Q).

Restructuring

In January 2024, we announced a workforce reduction of up to 50% of our employees in order to reduce our operating expenses and focus our efforts on development of oral difelikefalin in chronic pruritus associated with NP. On June 14, 2024, our Board of Directors approved a streamlined operating plan exploring strategic alternatives focused on maximizing shareholder value after we announced our decision to discontinue the clinical program in NP on June 12, 2024. Our decision to discontinue the clinical program in NP followed the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. Our decision was not related to any safety or medical issues, or negative regulatory feedback related to our NP program. In connection with the streamlined operating plan, our Board of Directors also approved a second reduction in our workforce by approximately 70%, which we substantially completed by June 30, 2024.

Restructuring expenses consist of pre-tax severance and employee-related costs for those involuntary terminations associated with the discontinuation of our oral programs in atopic dermatitis and chronic kidney disease in December 2023 and January 2024, respectively, the discontinuation of our oral program in NP in June 2024, and the related workforce reductions in 2024 (see Note 17 of Notes to Condensed Consolidated Financial Statements, C*ommitments and Contingencies – Restructuring Actions*, in this Quarterly Report on Form 10-Q).

Other Income, Net

Other income, net consists of interest and dividend income earned on our cash, cash equivalents, and marketable securities, realized gains and losses on the sale of marketable securities and property and equipment, as well as accretion of discounts/amortization of premiums on purchases of marketable securities. In the event we record a credit loss expense on our available-for-sale debt securities, those expenses would be offset against other income.

Loss on Inventory Write-Down

We periodically analyze our inventory levels to identify inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value and write down such inventories as appropriate. In addition, our product is subject to strict quality control and monitoring which we perform throughout the manufacturing process. If certain batches or units of product no longer meet quality specifications or become obsolete due to expiration, we record a charge to write down such unmarketable inventory to its estimated realizable value.

Non-cash Interest Expense on Liability Related to Sales of Future Royalties and Milestones

Non-cash interest expense on liability related to sales of future royalties and milestone payments, which are received in conjunction with ex-U.S. sales of KORSUVA/Kapruvia under our agreements with CSL Vifor and Maruishi, consists of imputed interest on the carrying value of the liability and the amortization of the related issuance costs resulting from the HCR Agreement (see “Royalty Purchase and Sale Agreement” above). This non-cash interest expense is recognized separately on the Condensed Consolidated Statement of Comprehensive Loss for the three and six months ended June 30, 2024.

Income Taxes

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

The Inflation Reduction Act of 2022 included tax legislation that became effective early in 2023. Significant legislation for corporate taxpayers includes a corporate alternative minimum tax of 15.0% for companies with $1.0 billion or more in average net financial statement profits over the three previous years, as well as a 1.0% indirect excise tax on the repurchase of shares by a publicly traded company. We do not expect this legislation to have an effect on our tax provision as of June 30, 2024; however, we will continue to evaluate the effect on the tax provision each reporting period.

Results of Operations

Comparison of the Three and Six Months Ended June 30, 2024 and 2023

Revenue

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Collaborative revenue	$ —	$ 5,410	-100%	$ 788	$ 8,160	-90%
Commercial supply revenue	—	1,400	-100%	640	4,591	-86%
Royalty revenue	—	123	-100%	—	248	-100%
Clinical compound revenue	—	—	N/A	84	99	-15%
Other revenue	991	—	N/A	1,614	—	N/A
Total revenue	$ 991	$ 6,933	-86%	$ 3,126	$ 13,098	-76%

Collaborative Revenue

There was no collaborative revenue recognized for the three months ended June 30, 2024 due to negative net sales reported by CSL Vifor during the period. We recognized collaborative revenue of $5.4 million for the three months ended June 30, 2023, and $0.8 million and $8.2 million for the six months ended June 30, 2024 and 2023, respectively. This change in collaborative revenue for both periods was related to our share of the profit from CSL Vifor's sales of KORSUVA injection to third parties in the United States, which commercially launched in April 2022 (see Notes 12 and 13 of Notes to Condensed Consolidated Financial Statements, *Collaboration and Licensing Agreements* and *Revenue Recognition*, respectively, in this Quarterly Report on Form 10-Q).

Commercial Supply Revenue

There was no commercial supply revenue recognized for the three months ended June 30, 2024. We recognized commercial supply revenue of $1.4 million for the three months ended June 30, 2023, and $0.6 million and $4.6 million for the six months ended June 30, 2024 and 2023, respectively. This change in commercial supply revenue for both periods was related to our sales of KORSUVA injection to CSL Vifor, which commercially launched in April 2022.

Royalty revenue

We recognized royalty revenue of approximately $123,000 and $248,000 for the three and six months ended June 30, 2023, respectively, which was related to our royalties on the net sales of Kapruvia in Europe prior to October 1, 2023. Beginning on October 1, 2023, royalty revenue will no longer be recognized until we have fulfilled our obligations under the HCR Agreement (see "Royalty Purchase and Sale Agreement" above). As a result, there was no royalty revenue for the three and six months ended June 30, 2024.

Clinical compound revenue

There was no clinical compound revenue for the three months ended June 30, 2024 and 2023. We recognized clinical compound revenue of approximately $84,000 and $99,000 for the six months ended June 30, 2024 and 2023, respectively, which were related to sales of clinical compound to Maruishi.

Other revenue

We recognized non-cash revenue of approximately $1.0 million and $1.6 million for the three and six months ended June 30, 2024, which represent royalty payments earned in conjunction with ex-U.S. sales of KORSUVA/Kapruvia under our agreements with CSL Vifor and Maruishi, which were sold to HCR under the HCR Agreement. There was no non-cash revenue recognized for the three and six months ended June 30, 2023.

Cost of Goods Sold (COGS)

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Cost of Goods Sold	$ —	$ 1,418	-100%	$ 620	$ 4,008	-85%

We did not record COGS during the three months ended June 30, 2024 as there was no commercial supply revenue in the current period. We recorded COGS of $1.4 million for the three months ended June 30, 2023, and $0.6 million and $4.0 million for the six months ended June 30, 2024 and 2023, respectively, which were related to our commercial supply revenue for KORSUVA injection sales to CSL Vifor for these periods.

Research and Development Expense

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Direct clinical trial costs	$ 5,806	$ 20,538	-72%	$ 21,461	$ 34,287	-37%
Consultant services in support of clinical trials	490	1,358	-64%	1,069	2,429	-56%
Stock-based compensation	269	1,563	-83%	1,028	3,222	-68%
Depreciation and amortization	38	29	31%	50	58	-14%
Other R&D operating expenses	2,705	6,822	-60%	7,664	14,648	-48%
Total R&D expense	$ 9,308	$ 30,310	-69%	$ 31,272	$ 54,644	-43%

For the three months ended June 30, 2024 compared to the three months ended June 30, 2023, the $15.6 million decrease in direct clinical trial costs and consultant services in support of clinical trials was primarily due to decreases related to the discontinuation of our oral difelikefalin atopic dermatitis program due to the clinical trial results announced in December 2023, the discontinuation of our oral difelikefalin program in advanced chronic kidney disease in January 2024, and decreases in other general costs associated with oral difelikefalin, partially offset by increases related to our former oral difelikefalin NP program, which was discontinued due to the clinical trial results announced in June 2024. The decrease in stock compensation expense is primarily related to the reductions in workforce in January 2024 and June 2024, resulting in no additional vesting of options and restricted stock units for those terminated as part of the January 2024 workforce reduction, and a reversal of stock compensation expense for unvested stock options and restricted stock units that were forfeited in the current period as part of the June 2024 workforce reduction. The decrease in other R&D operating expenses for the three months ended June 30, 2024 compared to the three months ended June 30, 2023 was primarily related to decreases in payroll and related costs, travel costs and other related conference costs.

For the six months ended June 30, 2024 compared to the six months ended June 30, 2023, the $14.2 million decrease in direct clinical trial costs and consultant services in support of clinical trials was primarily due to decreases related to the discontinuation of our oral difelikefalin atopic dermatitis program due to the clinical trial results announced in December 2023, the discontinuation of our oral difelikefalin program in advanced chronic kidney disease in January 2024, and decreases in other general costs associated with oral difelikefalin, partially offset by increases related to our former oral difelikefalin NP program, which was discontinued due to the clinical trial results announced in June 2024. The decrease in stock compensation expense is primarily related to the reductions in workforce in January 2024 and June 2024, resulting in no additional vesting of options and restricted stock units for those terminated as part of the January

2024 workforce reduction, and a reversal of stock compensation expense for unvested stock options and restricted stock units that were forfeited in the current period as part of the January 2024 and June 2024 workforce reductions, partially offset by performance-based restricted stock units that were achieved during the six months ended June 30, 2024. The decrease in other R&D operating expenses for the six months ended June 30, 2024 compared to the six months ended June 30, 2023 was primarily related to decreases in payroll and related costs, travel costs and other related conference costs.

The following table summarizes our R&D expenses by program for the three and six months ended June 30, 2024 and 2023:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
External research and development expenses:						
Oral difelikefalin – Pruritus	$ 6,296	$ 21,869	-71%	$ 22,512	$ 36,675	-39%
Internal research and development expenses	3,012	8,441	-64%	8,760	17,969	-51%
Total research and development expenses	$ 9,308	$ 30,310	-69%	$ 31,272	$ 54,644	-43%

General and Administrative Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Professional fees and public/investor relations	$ 975	$ 1,796	-46%	$ 2,132	$ 3,440	-38%
Stock-based compensation	1,472	1,879	-22%	4,058	3,573	14%
Depreciation and amortization	39	31	25%	69	61	13%
Other G&A operating expenses	3,922	3,839	2%	6,965	7,362	-5%
Total G&A expense	$ 6,408	$ 7,545	-15%	$ 13,224	$ 14,436	-8%

For the three months ended June 30, 2024 compared to the three months ended June 30, 2023, the decrease in professional fees and public/investor relations was primarily due to decreases in legal costs. The decrease in stock compensation expense is primarily related to the reductions in workforce in January 2024 and June 2024, resulting in no additional vesting of options and restricted stock units for those terminated as part of the January 2024 workforce reduction, and a reversal of stock compensation expense for unvested stock options and restricted stock units that were forfeited in the current period as part of the June 2024 workforce reduction. The increase in other G&A operating expenses for the three months ended June 30, 2024 compared to the three months ended June 30, 2023 was primarily due to our negative profit share amount recorded for CSL Vifor's negative net sales for the second quarter of 2024, partially offset by decreases in payroll and related costs, travel costs and other related conference costs.

For the six months ended June 30, 2024 compared to the six months ended June 30, 2023, the decrease in professional fees and public/investor relations was primarily due to decreases in legal costs. The increase in stock compensation expense is primarily related to performance-based restricted stock units that were achieved during the six months ended June 30, 2024, partially offset by the reductions in workforce in January 2024 and June 2024, resulting in no additional vesting of options and restricted stock units for those terminated as part of the January 2024 workforce reduction, and a reversal of stock compensation expense for unvested stock options and restricted stock units that were forfeited in the current period as part of the January 2024 and June 2024 workforce reductions. The decrease in other G&A operating expenses for the six months ended June 30, 2024 compared to the six months ended June 30, 2023 was

primarily related to decreases in payroll and related costs, travel costs and other related conference costs, partially offset by our negative profit share amount recorded for CSL Vifor's negative net sales for the second quarter of 2024.

Restructuring Expenses

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Restructuring expenses	$ 2,581	$ —	N/A	$ 4,982	$ —	N/A

For the three months ended June 30, 2024, restructuring expenses were $2.6 million, which were related to the discontinuation of our oral program in NP, our exploration of strategic alternatives to maximize shareholder value, and the associated workforce reduction announced in June 2024. There were no restructuring expenses recorded during the three months ended June 30, 2023.

For the six months ended June 30, 2024, restructuring expenses were $5.0 million which were related to our strategic prioritization of NP in January 2024 and the resulting discontinuation of our NP program in June 2024, our exploration of strategic alternatives to maximize shareholder value, and the associated workforce reductions announced in January 2024 and June 2024, respectively. There were no restructuring expenses recorded during the six months ended June 30, 2023.

Other Income, Net

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Other income, net	$ 689	$ 861	-20%	$ 1,641	$ 1,846	-11%

For the three months ended June 30, 2024 compared to the three months ended June 30, 2023, the decrease in other income, net was primarily due to a decrease in interest income resulting from a lower balance in our portfolio of investments in 2024 as compared to 2023.

For the six months ended June 30, 2024 compared to the six months ended June 30, 2023, the decrease in other income, net was primarily due to a decrease in interest income resulting from a lower balance in our portfolio of investments in 2024 as compared to 2023, partially offset by an increase in accretion income from our available-for-sale marketable securities in the 2024 period as compared to the prior period.

Loss on Inventory Write-Down

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Loss on inventory write-down	$ 1,489	$ —	N/A	$ 1,489	$ —	N/A

For the three and six months ended June 30, 2024, we wrote down approximately $1.5 million of commercial supply inventory due to obsolescence.

Non-cash Interest Expense on Liability Related to the Sales of Future Royalties and Milestones

	Three Months Ended June 30,			Six Months Ended June 30,		
	2024	2023	% change	2024	2023	% change
	Dollar amounts in thousands			Dollar amounts in thousands		
Non-cash interest expense on liability related to sales of future royalties and milestones	$ 1,910	$ —	N/A	$ 3,892	$ —	N/A

We recognized $1.9 million and $3.9 million of non-cash interest expense on the liability related to sales of future royalties and milestones for the three and six months ended June 30, 2024, respectively, which represented imputed interest on the carrying value of the liability to HCR, and the amortization of the related issuance costs associated with the HCR Agreement. There was no non-cash interest expense on liability recognized during the three and six months ended June 30, 2023 as the HCR Agreement was entered into in the fourth quarter of 2023 (see "Royalty Purchase and Sale Agreement" above).

Benefit from Income Taxes

We have not exchanged our R&D tax credit for cash for the three and six months ended June 30, 2024, and were not eligible to exchange our R&D tax credit for cash for the three and six months ended June 30, 2023, therefore there was no benefit from income taxes for each of the three and six months ended June 30, 2024 and 2023. As of June 30, 2024, we recorded $0.7 million within income tax receivable which related to the 2020 R&D credit.

We recognized a full valuation allowance against deferred tax assets at June 30, 2024 and December 31, 2023. The tax benefit related to the exercise of stock options is recognized as a deferred tax asset that is offset by a corresponding valuation allowance. As such, our effective tax rate is zero for each of the three and six months ended June 30, 2024 and 2023.

Capital Requirements, Liquidity, and Capital Resources

Short-Term and Long-Term Cash Requirements

Our primary uses of capital have been third-party clinical R&D services, clinical costs related to the oral difelikefalin program, and compensation and related expenses.

As of June 30, 2024, we have no commitments for capital expenditures in either the short-term or long-term. The following discussion summarizes our current and long-term material cash requirements as of June 30, 2024, which we expect to fund primarily with current unrestricted cash and cash equivalents and available-for-sale marketable securities:

	Material Cash Requirements *(amounts in thousands)*						
	Total	2024	2025	2026	2027	2028	Thereafter
Operating lease obligation[1]	$ 14,371	$ 108	$ 1,298	$ 1,330	$ 1,363	$ 1,398	$ 8,874
Manufacturing purchase obligations[2]	1,467	1,467	—	—	—	—	—
Other obligations[3]	1,500	—	—	—	—	—	1,500
Total	$ 17,338	$ 1,575	$ 1,298	$ 1,330	$ 1,363	$ 1,398	$ 10,374

(1) Operating lease obligations in 2024 and beyond relate to our new Stamford operating lease entered into in May 2023 for our new principal office, for which rent payments are expected to begin in late 2024. See Note 17 of Notes to Condensed Consolidated Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q for details about our operating lease obligations.

(2) Based on our MSA with Patheon that we entered into in July 2019, we have a purchase capacity reservation through December 31, 2024. In December 2023, we entered into an agreement with Patheon to reimburse Patheon approximately $1.7 million for forecasted manufacturing commitments that were no longer needed due to the reduced demand expectations of KORSUVA in the United States. As of June 30, 2024, $0.2 million of the $1.7 million remained within accounts payable and accrued expenses on our Condensed Consolidated Balance Sheet. In the event the purchase capacity reservation is not met in 2024, it will rollover into 2025. We expect a portion of this capacity reservation will be reimbursed in accordance with the supply agreement with CSL Vifor. See Note 17 of Notes to Condensed Consolidated Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q for details about our MSA with Patheon. We have no other material non-cancelable purchase commitments with any other contract manufacturers or service providers, as we have generally contracted on a cancelable purchase order basis.

(3) We are required to maintain a stand-by letter of credit as a security deposit under our new lease for office space in Stamford, Connecticut. After the first and second anniversaries of the rent commencement date, the face amount of the letter of credit can be reduced by $0.5 million each period if we are not in default of our lease obligations. See Note 6 of Notes to Condensed Consolidated Financial Statements, *Restricted Cash*, in this Quarterly Report on Form 10-Q for details about our letter of credit for our new lease for our principal office in Stamford, Connecticut.

Based on the Enteris License Agreement that we entered into in August 2019, we are obligated to pay (1) milestone payments upon the achievement of certain development, regulatory and commercial milestones and (2) low-single digit royalty percentages on net sales of licensed products, subject to reductions in specified circumstances. As these milestone payments may or may not be achieved, and royalties may or may not be owed depending on our future commercial success, there were no future potential payments that were considered cash requirements in the table above as of June 30, 2024. We did not make any milestone payments to Enteris during the three and six months ended June 30, 2024 and 2023. See Note 17 of Notes to Condensed Consolidated Financial Statements, *Commitments and Contingencies*, in this Quarterly Report on Form 10-Q for details about our Enteris License Agreement.

During the fourth quarter of 2023, we, through our wholly-owned subsidiary Cara Royalty Sub, entered into the HCR Agreement with HCR pursuant to which Cara Royalty Sub sold to HCR certain of its rights to the Royalties, due and payable to Cara Royalty Sub (as our assignee) under our agreements with CSL Vifor and Maruishi, in exchange for up to $40.0 million. We have retained all of our rights, title and interest in, to and under the Covered License Agreements that relate to any non-intravenous formulation of difelikefalin. These future payments to HCR were not included in the table above since the amounts and timing of royalty and milestone payments received under the agreements with CSL Vifor and Maruishi could change in the future as they are subject to CSL Vifor's and Maruishi's commercialization efforts (see "Royalty Purchase and Sale Agreement" above).

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

Since inception, we have incurred significant operating and net losses. We incurred net losses of $20.0 million and $31.5 million for the three months ended June 30, 2024 and 2023, respectively, and $50.7 million and $58.1 million for the six months ended June 30, 2024. As of June 30, 2024, we had an accumulated deficit of $735.5 million. Our financial results may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials, should we resume the development of any future product candidates, and the future sales of KORSUVA.

We anticipate that our expenses will be focused on:

- the discontinuation of our clinical program for oral difelikefalin for chronic pruritus associated with NP; and
- the exploration of strategic alternatives to maximize shareholder value.

Should we resume the development of any future product candidate, the successful development of any future product candidate is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing

and costs of the efforts that will be necessary to complete the development of any future product candidate, should we resume the development of future product candidates. We are also unable to predict when, if ever, we will generate any further material net cash inflows from difelikefalin or any other future product candidate. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

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

A change in the outcome of any of these variables with respect to the development of oral difelikefalin or any of our future product candidates, should we resume the development of oral difelikefalin or any future product candidates, would significantly change the costs and timing associated with the development of that product candidate. Further, the timing of any of the above may be impacted by global economic conditions and significant global events, should we resume the development of oral difelikefalin or any future product candidate, introducing additional uncertainty.

We currently are exploring strategic alternatives to maximize shareholder value. Should we resume development of our product candidate or any future product candidates, we would require additional capital beyond our current balances of cash and cash equivalents and available-for-sale marketable securities and anticipated amounts as described above, and this additional capital may not be available when needed, on reasonable terms, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and continuing disruptions to and volatility in the credit and equity markets in the United States and worldwide, including impacts from global health crises, geopolitical tensions, such as the ongoing conflicts between Russia and Ukraine, conflict in the Middle East, and increasing tensions between China and Taiwan, and government actions implemented as a result of the foregoing, fluctuations in inflation, rising interest rates, uncertainty and liquidity concerns in the broader financial services industry, and a potential recession in the United States. To the extent that we raise additional capital through the future sale of equity or convertible debt, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. If we raise additional funds through the issuance of debt securities, these securities could contain covenants that would restrict our operations. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Sources of Liquidity

Since our inception to date, we have raised an aggregate of $943.8 million to fund our operations, including (1) net proceeds of $447.4 million from the sale of shares of our common stock in five public offerings, including our initial public offering; as well as the sale of our common stock under our open market sales agreement in 2023; (2) proceeds of $73.3 million from the sale of shares of our convertible preferred stock and from debt financings prior to our initial public offering; (3) $258.8 million under our license and supply agreements (including commercial supply sales and royalty payments), primarily with CSL Vifor, Maruishi, CKDP, and an earlier product candidate for which development efforts ceased in 2007; (4) our share of the profit generated by KORSUVA injection sales of $29.8 million; (5) net proceeds of $98.0 million from the purchase of our common stock in relation to the license agreements with CSL Vifor; and (6) net proceeds of $36.5 million from the sale of future ex-U.S. royalties and milestones to HCR under our agreements with CSL Vifor and Maruishi (see Note 12 of Notes to Condensed Consolidated Financial Statements, *Collaboration and Licensing Agreements*, in this Quarterly Report on Form 10-Q).

On June 14, 2024, our Board of Directors approved a streamlined operating plan exploring strategic alternatives focused on maximizing shareholder value after we announced our decision to discontinue the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP on June 12, 2024. This exploration includes substantial uncertainties, including whether we are able to identify and implement any potential strategic alternatives, in a timely manner or at all, whether we realize all or any of the anticipated benefits of any such transaction and whether any such transactions would generate value for stockholders.

During the fourth quarter of 2023, we, through our wholly-owned subsidiary Cara Royalty Sub, entered into the HCR Agreement with HCR pursuant to which Cara Royalty Sub sold to HCR certain of its rights to receive the Royalties, due and payable to Cara Royalty Sub (as our assignee) under the Covered License Agreements, in exchange for up to $40.0 million. We have retained all of our rights, title and interest in, to and under the Covered License Agreements that relate to any non-intravenous formulation of difelikefalin.

Under the terms of the HCR Agreement, Cara Royalty Sub received an initial payment of $17.5 million less certain transaction costs in November 2023. In December 2023, we received an additional $20.0 million, less certain advisory fees, upon satisfying the milestone event for pricing for Kapruvia® (difelikefalin) in Germany being approved above a certain threshold amount per dose. The terms of the HCR Agreement also provide for an additional $2.5 million milestone payment to Cara Royalty Sub upon achievement of a 2024 sales milestone of KORSUVA in Japan.

In order to fund our future operations, including our planned clinical trials at the time, on March 1, 2022, we filed a universal shelf registration statement, or the Shelf Registration Statement, which provides for aggregate offerings of up to $300.0 million of common stock, preferred stock, debt securities, warrants or any combination thereof. The Shelf Registration Statement was declared effective by the Securities and Exchange Commission on May 11, 2022. The securities registered under the Shelf Registration Statement include $154.5 million of unsold securities that had been registered under our previous Registration Statement on Form S-3 (File No. 333-230333) that was declared effective on April 4, 2019. On March 6, 2024, the date we filed our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, we became subject to the offering limits in General Instruction I.B.6 of Form S-3. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell shares of our common stock under our Shelf Registration Statement with a value of more than one-third of our public float in any 12-month period, so long as our public float is less than $75.0 million. We have not offered and sold any shares of our common stock pursuant to General Instruction I.B.6 to Form S-3 during the prior 12 calendar month period that ends on and includes the date hereof.

On March 1, 2022, we entered into an open market sales agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $80.0 million in an at-the-market offering pursuant to the Shelf Registration Statement. Jefferies is acting as sole sales agent for any sales made under the Sales Agreement for a 3% commission on gross proceeds. In June 2024, we filed an amendment to the prospectus dated May 11, 2022 for the at-the-market offering, or the ATM Prospectus, to update the amount of shares of our common stock we are eligible to sell under General Instruction I.B.6 of Form S-3, as described above, and pursuant to the Sales Agreement. Pursuant to General Instruction I.B.6 of Form S-3, in no event

will we sell shares of our common stock pursuant to the ATM Prospectus, as amended, with a value of more than one-third of our public float in any 12-month period, so long as our public float is less than $75.0 million. If our public float increases above $75.0 million such that we may sell additional amounts under the Sales Agreement and the ATM Prospectus, we will file another amendment to the ATM Prospectus prior to making additional sales in excess of the limitations of General Instruction I.B.6 of Form S-3. The common stock will be sold at prevailing market prices at the time of the sale, and, as a result, prices may vary. Unless otherwise terminated earlier, the Sales Agreement continues until all shares available under the Sales Agreement have been sold. No shares were sold under the Sales Agreement during the three and six months ended June 30, 2024 and 2023. In recognition of the decision by our Board of Directors to approve a streamlined operating plan exploring strategic alternatives, as described elsewhere in this report, we currently do not have any intention to sell shares pursuant to the Sales Agreement.

We may offer additional securities under our Shelf Registration Statement from time to time in response to market conditions or other circumstances if we believe such a plan of financing is in the best interests of our stockholders.

Under our agreement with CSL Vifor for the commercialization of KORSUVA injection, we are eligible to receive commercial milestone payments in the aggregate of up to $240.0 million from CSL Vifor upon the achievement of certain sales-based milestones. In October 2021, we received a $50.0 million milestone payment from CSL Vifor in exchange for the issuance of 3,282,391 shares of our common stock to CSL Vifor as a result of the regulatory approval of KORSUVA injection in August 2021. To date, we have received $50.0 million of regulatory milestones from CSL Vifor under this agreement.

Under a separate agreement with CSL Vifor, we are eligible to receive commercial milestone payments in the aggregate of up to $440.0 million, all of which are sales related. We are also eligible to receive tiered double-digit royalty payments based on annual net sales of difelikefalin injection in the licensed territories. To date, we have received $30.0 million of regulatory milestones from CSL Vifor. During the fourth quarter of 2023, we entered into the HCR Agreement where we sold our future royalties and milestone payments under this agreement to HCR (see “Royalty Purchase and Sale Agreement” above).

Under the Maruishi Agreement, we are also potentially eligible to earn up to an aggregate of $6.0 million in clinical development milestones and $4.5 million in regulatory milestones, before any foreign exchange adjustment, as well as tiered royalties, with percentages ranging from the low double digits to the low twenties, based on net sales of products containing difelikefalin in Japan, if any, and share in any sub-license fees. In September 2023, Maruishi received manufacturing and marketing approval from Japan’s Ministry of Health, Labour and Welfare for KORSUVA IV Injection Syringe for the treatment of pruritus in hemodialysis patients. To date, we have received $6.5 million (before contractual foreign currency exchange adjustments) for clinical development and regulatory milestones from Maruishi. During the fourth quarter of 2023, we entered into the HCR Agreement where we sold our future royalties and milestone payments to HCR (see “Royalty Purchase and Sale Agreement” above).

Under the CKDP Agreement, we are potentially eligible to earn up to an aggregate of $2.3 million in clinical development milestones and $1.5 million in regulatory milestones, before South Korean withholding tax, as well as tiered royalties with percentages ranging from the high single digits to the high teens, based on net sales of products containing difelikefalin in South Korea, if any, and share in any sub-license fees. To date, $2.3 million (before South Korean withholding tax) of development and regulatory milestones have been received under the CKDP Agreement.

In December 2021, CMS granted TDAPA designation to KORSUVA injection in the anti-pruritic functional category. TDAPA went into effect on April 1, 2022, for two years. On October 27, 2023, CMS published the final CY 2024 rule, which finalized the post-TDAPA add-on as proposed in the draft CY 2024 rule. Under the final rule, TDAPA drugs in existing functional categories will receive a post-TDAPA add-on payment set at 65 percent of the total trailing 12-months expenditure levels for the given renal dialysis drug or biological product. The post-TDAPA add-on payment adjustment will be applied to all ESRD PPS payments and paid for 3 years, adjusted annually. The add-on payments for KORSUVA injection commenced on April 1, 2024. The unfavorable CMS reimbursement codified in the final CY2024 rule has resulted in a lack of sequential revenues growth for KORSUVA injection since its launch. As a result, we expect no meaningful revenue contribution from KORSUVA injection post its TDAPA expiration.

Our ability to earn these milestone and royalty payments and their timing is dependent upon successful commercialization of KORSUVA injection/Kapruvia, and successful future repayments made to HCR using CSL Vifor and Maruishi milestones and royalties under the HCR Agreement. However, our receipt of any further such amounts is uncertain at this time and we may never receive any more of these amounts.

Outlook

As a result of the discontinuation of our clinical NP program, our workforce reductions in 2024, and our exploration of strategic alternatives to maximize shareholder value, we expect that our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient to fund our currently anticipated operating plan for at least the next 12 months. Our anticipated operating expenses include contractually committed costs as well as non-contractually committed clinical trial costs for trials that are closing based on our Board of Directors' new strategic plan. It is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we presently expect.

Cash Flows

The following is a summary of the net cash flows provided by (used in) our operating, investing and financing activities for the six months ended June 30, 2024 and 2023:

	Six Months Ended June 30,	
	2024	2023
	Dollar amounts in thousands	
Net cash used in operating activities	$ (42,890)	$ (55,063)
Net cash provided by investing activities	41,241	50,511
Net cash (used in) provided by financing activities	(1,295)	560
Net decrease in cash, cash equivalents and restricted cash	$ (2,944)	$ (3,992)

Net cash used in operating activities

Net cash used in operating activities for the six months ended June 30, 2024 consisted primarily of a net loss of $50.7 million and a $2.7 million cash outflow from net changes in operating assets and liabilities, partially offset by a $10.6 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of a decrease of $11.1 million in accounts payable and accrued expenses primarily due to operating payments made during the period, partially offset by a decrease in prepaid expenses of $4.4 million, primarily related to a decrease in prepaid clinical costs, a decrease in accounts receivable, net – related party of $2.4 million, and an increase of $2.1 million for lease incentives reimbursed to us. Net non-cash charges primarily consisted of stock-based compensation expense of $5.1 million, non-cash interest expense related to the HCR Agreement of $3.9 million, and a loss on inventory write-down of $1.5 million.

Net cash used in operating activities for the six months ended June 30, 2023 consisted primarily of a net loss of $58.1 million and a $4.5 million cash outflow from net changes in operating assets and liabilities, partially offset by a $7.6 million cash inflow from net non-cash charges. The change in operating assets and liabilities primarily consisted of cash outflows of $6.9 million from an increase in accounts receivable, net – related party primarily relating to amounts due from CSL Vifor for our share of the profit generated by KORSUVA injection sales, for commercial supply of KORSUVA injection to CSL Vifor, and for royalty revenue from sales of Kapruvia outside of the United States by CSL Vifor, an increase in inventory, net of $1.0 million, and a cash outflow of $0.9 million relating to operating lease liabilities associated with our lease agreements for our prior operating facility in Stamford, Connecticut. These cash outflows were partially offset by an increase of $2.9 million in accounts payable and accrued expenses primarily relating to decreased payments made in the first half of 2023, and a decrease in prepaid expenses of $1.3 million primarily related to prepaid clinical costs. Net non-cash charges primarily consisted of stock-based compensation expense of $6.8 million, and non-cash lease expense of $0.8 million relating to our prior Stamford operating leases.

Net cash provided by investing activities

Net cash provided by investing activities was $41.2 million for the six months ended June 30, 2024, which primarily included cash inflows of $74.5 million from maturities of available-for-sale marketable securities, partially offset by cash outflows of $32.2 million for the purchases of available-for-sale marketable securities and $1.0 million for the purchases of property and equipment.

Net cash provided by investing activities was $50.5 million for the six months ended June 30, 2023, which primarily included cash inflows of $76.3 million from maturities and redemptions of available-for-sale marketable securities, partially offset by cash outflows of $25.8 million for the purchases of available-for-sale marketable securities.

Net cash (used in) provided by financing activities

Net cash used in financing activities for the six months ended June 30, 2024 consisted of payments made to HCR under the royalty purchase and sale agreement of approximately $1.3 million.

Net cash provided by financing activities for the six months ended June 30, 2023 consisted of proceeds of approximately $0.6 million received from the exercise of stock options.

Recent Accounting Pronouncements

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

Critical Accounting Estimates

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

We define our critical accounting estimates as those subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the

specific manner in which we apply U.S. GAAP. Our critical accounting policies that require significant judgments and estimates are more fully described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Estimates" in our Annual Report and in Note 2 to our audited financial statements contained in our Annual Report. There have been no significant changes to our critical accounting policies that require significant judgments and estimates from those disclosed in our Annual Report.

Accounting Pronouncements Recently Adopted; Recent Accounting Pronouncements Not Yet Adopted

We do not expect that any recently issued accounting pronouncements will have a material effect on our condensed consolidated financial statements. Refer to Note 2 of Notes to Condensed Consolidated Financial Statements within this Quarterly Report on Form 10-Q, as well as Note 2 of Notes to Consolidated Financial Statements*, Summary of Significant Accounting Policies* in our Annual Report for a full description of accounting pronouncements recently adopted, and issued but not yet adopted, if applicable.

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

Interest Rate Risk

Historically, we invested substantially all of our cash reserves in a variety of available-for-sale marketable securities, including investment-grade debt instruments, principally corporate bonds, commercial paper, municipal bonds and direct obligations of the U.S. government and U.S. government-sponsored entities, and in cash equivalents. See Note 3 of Notes to Condensed Consolidated Financial Statements, *Available-for-Sale Marketable Securities*, in this Quarterly Report on Form 10-Q for details about our available-for-sale marketable securities.

As of June 30, 2024, we had invested $7.4 million of our cash reserves in such marketable securities. Those marketable securities included $7.4 million of investment grade debt instruments with a yield of approximately 0.79% and maturities through November 2024. As of December 31, 2023, we had invested $49.0 million of our cash reserves in such marketable securities. Those marketable securities included $49.0 million of investment grade debt instruments with a yield of approximately 4.41% and maturities through November 2024.

We maintain an investment portfolio in accordance with our investment policy, which includes guidelines on acceptable investment securities, minimum credit quality, maturity parameters, and concentration and diversification. The primary objectives of our investment policy are to preserve principal, maintain proper liquidity and to meet operating needs. Our investments are subject to interest rate risk and will decrease in value if market interest rates increase. However, due to the conservative nature of our investments and relatively short duration, we do not believe we are materially exposed to changes in interest rates related to our investments. As a result, we do not currently use interest rate derivative instruments to manage exposure to interest rate changes.

Duration is a sensitivity measure that can be used to approximate the change in the fair value of a security that will result from a change in interest rates. Applying the duration model, a hypothetical 100 basis point, or 1%, increase in interest rates as of June 30, 2024 and December 31, 2023, would have resulted in immaterial decreases in the fair values of our portfolio of marketable securities at those dates.

Credit Quality Risk

Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. Nonetheless, deterioration of the credit quality of an investment security subsequent to purchase may subject us to the risk of not being able to recover the full principal value of the security. As of June 30, 2024 and December 31, 2023, the aggregate unrealized losses on our available-for-sale marketable securities were $0.1 million and $0.3 million, respectively. For each of the three and six months ended June 30, 2024 and 2023, we did not record any charges to credit loss expense for our available-for-sale securities. Refer to Note 3 of Notes to Condensed Consolidated Financial Statements, *Available-for-Sale Marketable Securities*, in this Quarterly Report on Form 10-Q.

As of June 30, 2024 and December 31, 2023, we had accounts receivable, net - related party from CSL Vifor of approximately $0.4 million and $2.8 million, respectively, which primarily related to royalty payments from CSL Vifor in the current period and our profit-sharing revenue from sales of KORSUVA injection in the United States by CSL Vifor, our commercial supply of KORSUVA injection to CSL Vifor, and royalty payments from CSL Vifor in the prior period. We also had $0.6 million and $0.4 million recorded within other receivables for Japan royalties/milestones owed to us from Maruishi which was included within other receivables as of June 30, 2024 and December 31, 2023, respectively. We believe that credit risk associated with CSL Vifor and Maruishi are not significant. We review the need for an allowance for credit losses for any receivable based on various factors including payment history and historical bad debt experience. We had an insignificant allowance for credit losses as of June 30, 2024 and December 31, 2023.

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

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of June 30, 2024. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that, as of June 30, 2024, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC, and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosures.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended June 30, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Limitations on Controls and Procedures

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

PART II

OTHER INFORMATION

Item 1. *Legal Proceedings*

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

Item 1A. *Risk Factors*

Our business is subject to risks and events that, if they occur, could adversely affect our financial condition and results of operations and trading price of our securities. You should carefully consider the following risks and uncertainties, together with all other information in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations" as well as our other filings with the SEC in evaluating our business and future prospects and an investment in our common stock. We may disclose changes to risk factors or disclose additional factors from time to time in our future filings with the SEC. If any of the following risks and uncertainties develop into actual events, our business, financial condition, results of operations and cash flows could be materially adversely affected. In that case, the price of our common stock could decline, and you may lose all or part of your investment. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations.

Risk Factors Summary

Investing in our common stock involves a high degree of risk because our business is subject to numerous risks and uncertainties, as fully described below. The principal factors and uncertainties that make investing in our common stock risky include, among others:

- We may not be successful in identifying and implementing any potential strategic alternatives in a timely manner or at all, and any strategic transactions that we may consummate in the future could have negative consequences.
- Even if we successfully consummate any strategic transaction, or series of transactions, from our strategic assessment, we may fail to realize all or any of the anticipated benefits of any such transaction, such benefits may take longer to realize than expected, we may encounter integration difficulties or we may be exposed to other operational and financial risks.
- The value to stockholders in the event of a strategic transaction or dissolution may depend on the extent to which we will be able to successfully satisfy our existing contractual obligations to third parties and regulatory commitments on favorable terms, which may include the outcome of our negotiations to reduce or terminate such commitments.
- We may become involved in litigation, including securities class action litigation, that could divert our management's attention and harm our business, and insurance coverage may not be sufficient to cover all costs and damages.
- We have incurred significant losses since inception, and we anticipate that we may incur losses in the foreseeable future. We may never achieve profitability.

- If we fail to comply or regain compliance with the continued listing standards of the Nasdaq Capital Market, we may be delisted and the price of our common stock, our ability to access the capital markets and our financial condition could be negatively impacted.

- The market price of our common stock has been, and is likely to continue to be, highly volatile, and you may not be able to resell your shares at or above the price you paid for them.

- If we decide to resume development of our product candidate or any future product candidate, we will need additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs.

- Should we resume development of our product candidate or future product candidates, if we are unable to successfully complete clinical development, obtain regulatory approvals and commercialize our product candidate or future product candidates, or experience significant delays in doing so, our business will be materially harmed.

- Should we resume development of our product candidate or any future product candidate, we expect to continue to rely on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

- Should we resume development of our product candidate or any future product candidate, manufacturers upon whom we may rely could fail to produce a product candidate in the volumes that we may require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, and we could face delays in the development of our product candidate.

- Should we resume development of our product candidate or any future product candidate, even if we obtain regulatory approvals for such, they may never be successfully launched or become profitable, in which case our business, prospects, operating results and financial condition may be materially harmed.

- If we or our collaborators are unable to establish effective marketing and sales capabilities, or if we are unable to enter into or maintain agreements with third parties to market and sell our product and, should we resume development of our product candidate or any future product candidate, any product candidate, if they are approved, we may be unable to generate product revenues.

- Any collaboration arrangements that we are a party to or may enter into in the future may not be successful, which could adversely affect our ability to develop and ultimately commercialize our product candidate or any potential future product candidate.

- We face significant competition from other pharmaceutical and biotechnology companies, academic institutions, government agencies and other R&D organizations. Our operating results will suffer if we fail to compete effectively.

- Should we resume development of our product candidate or any future product candidate, if we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. Should we resume development activities in the future, if we are not able to obtain, or if there are delays in obtaining, required additional regulatory approvals, we will not be able to commercialize any product candidates as expected, and our ability to generate revenue will be materially impaired.

- We are subject to stringent and evolving U.S. and foreign laws, regulations and standards, contracts, industry standards, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation (including class claims) and mass arbitration demands, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue and profits, and otherwise adversely affect our business, operations and financial performance.

- We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

Risks Related to Our Strategic Review Process

We may not be successful in identifying and implementing any potential strategic alternatives in a timely manner or at all, and any strategic transactions that we may consummate in the future could have negative consequences.

In June 2024, we announced that we are undertaking a comprehensive exploration of strategic alternatives focused on maximizing stockholder value. We expect to devote substantial time and resources to exploring strategic alternatives that our Board of Directors believes will maximize stockholder value. Despite management devoting significant efforts to identify and evaluate potential strategic alternatives, there can be no assurance that this strategic review process will result in us pursuing any transaction or that we will be able to successfully consummate any particular strategic transaction on attractive terms, on a timely basis, or at all. For example, certain types of strategic transactions may require third party consents, such as stockholder approval, which could be difficult or costly to obtain. We have not set a timetable for completion of this strategic review process, and our Board of Directors has not approved a definitive course of action. Additionally, there can be no assurance that any particular course of action, business arrangement or transaction, or series of transactions, will be pursued, successfully consummated or lead to increased stockholder value or that we will make any cash distributions to our stockholders.

The process of continuing to evaluate our strategic alternatives may be costly, time-consuming and complex, and we may incur significant legal, accounting and advisory fees and other expenses, some of which may be incurred regardless of whether we successfully enter into a transaction. We may also incur additional unanticipated expenses in connection with this process. Any such expenses will decrease the remaining cash available for use in our business. Our ability to pursue or consummate strategic transactions also depends upon our ability to retain certain of our employees, the loss of whose services may adversely impact the ability to identify, negotiate and consummate such transaction. If we are unable to successfully retain certain of our key remaining personnel, we are at risk of a disruption to our exploration and consummation of one or more strategic transactions.

In addition, potential counterparties in a strategic transaction involving us may place minimal or no value on our assets and our public listing. Further, should we resume the development of future product candidates, such as one or more of the programs in our pipeline for which we halted further development in December 2023, January 2024 and June 2024, the development and any potential commercialization of our future product candidates will require substantial additional cash to fund the costs associated with conducting the necessary preclinical and clinical testing and obtaining regulatory approval. Consequently, any potential counterparty in a strategic transaction involving us may choose not to spend additional resources to resume or continue development of our future product candidates and may attribute little or no value, in such a transaction, to our future product candidates.

In addition, any strategic transactions that we may pursue could have a variety of negative consequences, and we may enter into a transaction that yields unexpected results that adversely affect our business and decreases the remaining cash available for use in our business. Any potential transaction would be dependent on a number of factors that may be beyond our control, including, among other things, market conditions, industry trends, the interest of third parties in a potential transaction with us, obtaining stockholder approval and the availability of financing to third parties in a potential transaction with us on reasonable terms. There can be no assurance that any particular course of action, business arrangement or transaction, or series of transactions, will be pursued, successfully consummated, lead to increased stockholder value, or achieve the anticipated results.

If we are not successful in setting forth a new strategic path for us, or if our plans are not executed in a timely fashion, this may cause reputational harm with our stockholders and the value of our securities may be adversely impacted. In addition, speculation regarding any developments related to the review of strategic alternatives and perceived uncertainties related to the future of us could cause our stock price to fluctuate significantly.

Even if we successfully consummate any strategic transaction, or series of transactions, from our strategic assessment, we may fail to realize all or any of the anticipated benefits of any such transaction, such benefits may take longer to realize than expected, we may encounter integration difficulties or we may be exposed to other operational and financial risks.

Our ability to realize the anticipated benefits of any potential strategic transaction will depend on a number of factors, including our ability to integrate with any future business partner, our ability to obtain value for portions of our business, if divested, and our ability to generate future stockholder value. The process may be disruptive to our business and the expected benefits may not be achieved within the anticipated time frame, or at all. The failure to meet the challenges involved and to realize the anticipated benefits of any potential transaction could adversely affect our business and financial condition. The negotiation and consummation of any potential strategic transaction will require significant time on the part of our management, and the diversion of management's attention may disrupt our business.

The negotiation and consummation of any such transaction may also require more time or greater cash resources than we anticipate and expose us to other operational and financial risks, including, but not limited to, increased near-term and long-term expenditures, exposure to unknown liabilities, higher than expected acquisition or integration costs, incurrence of substantial debt or dilutive issuances of equity securities to fund future operations, including financings in connection with a strategic transaction, write-downs of assets or goodwill or incurrence of non-recurring, impairment or other charges, increased amortization expenses, difficulty and cost in combining the operations and personnel of any acquired or acquiring business with our operations and personnel, impairment of relationships with key suppliers or customers of any acquired or acquiring business due to changes in management and ownership, inability to retain our key employees or any acquired or acquiring business and possibility of future litigation. Any of the foregoing risks could have a material adverse effect on our business, financial condition and prospects.

If a strategic transaction is not consummated, our Board of Directors may decide to pursue a dissolution and liquidation. In such an event, the amount of cash available for distribution to our stockholders will depend significantly on the timing of such liquidation as well as the amount of cash that may need to be reserved for commitments and contingent liabilities.

There can be no assurance that a strategic transaction will be completed. If a strategic transaction is not completed, our Board of Directors may decide to pursue a dissolution and liquidation. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such decision and, with the passage of time, the amount of cash available for distribution will be reduced as we continue to fund our operations. In addition, if our Board of Directors were to approve and recommend, and our stockholders were to approve, a dissolution and liquidation, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our stockholders. As a result of this requirement, a portion of our assets may need to be reserved pending the resolution of such obligations and the timing of any such resolution is uncertain. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation. If a dissolution and liquidation were pursued, our Board of Directors, in consultation with our advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of our common stock could lose all or a significant portion of their investment in the event of a liquidation, dissolution or winding up.

The value to stockholders in the event of a strategic transaction or dissolution may depend on the extent to which we will be able to successfully satisfy our existing contractual obligations to third parties and regulatory commitments on favorable terms, which may include the outcome of our negotiations to reduce or terminate such commitments.

We are currently subject to certain contractual and regulatory obligations and commitments. In connection with our comprehensive exploration of strategic alternatives, we may seek to negotiate with third parties in order to reduce or

eliminate such obligations and commitments. Our ability to successfully negotiate such obligations or commitments on favorable terms, or at all, or our ability to satisfy any such obligations may impact our ability to pursue a strategic transaction on terms favorable to us, the resulting value to stockholders in a strategic transaction or the cash available for distribution to our stockholders in the event of our dissolution. We may also incur substantial costs in connection with or as a result of such negotiations or termination of any of our commitments. There can be no assurance that we will be successful in negotiating to reduce or eliminate any of our existing contractual or regulatory obligations and commitments, or that we will be able to satisfy any such obligations on a timetable that will allow us to maximize potential value to our stockholders.

We may become involved in litigation, including securities class action litigation, that could divert our management's attention and harm our business, and insurance coverage may not be sufficient to cover all costs and damages.

In the past, litigation, including securities class action litigation, has often followed certain significant business transactions, such as the sale of a company or announcement of any other strategic transaction, or the announcement of negative events. These events may also result in investigations by the SEC. We may be exposed to such litigation even if no wrongdoing occurred. Litigation is usually expensive and diverts management's attention and resources, which could adversely affect our business and cash resources and our ability to consummate a potential strategic transaction or the ultimate value our stockholders receive in any such transaction.

Risks Related to Our Financial Condition and Capital Requirements

We have incurred significant losses from our inception, and we anticipate that we may incur losses in the foreseeable future.

We are a biopharmaceutical company. Until recently, we had focused our efforts primarily on developing KORSUVA injection, Kapruvia and oral difelikefalin for a number of indications with the goal of achieving regulatory approval and, more recently, commercializing KORSUVA injection and Kapruvia. However, the commercial launches of KORSUVA injection and Kapruvia did not achieve meaningful success and, in January 2024, we made the strategic decision to focus our efforts on developing oral difelikefalin for the treatment of pruritus associated with NP. In June 2024, we discontinued the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. We are undertaking a comprehensive exploration of strategic alternatives focused on maximizing stockholder value. Since inception, we have incurred significant operating and net losses. We incurred net losses of $118.5 million, $85.5 million and $88.4 million for the years ended December 31, 2023, 2022 and 2021, respectively. We also incurred net losses of $20.0 million and $31.5 million for the three months ended June 30, 2024 and 2023, respectively, and $50.7 million and $58.1 million for the six months ended June 30, 2024 and 2023, respectively. As of June 30, 2024, we had an accumulated deficit of $735.5 million. In connection with the termination of all ongoing clinical programs noted above, our research and development expenses have decreased. We expect to continue to incur costs and expenditures in connection with the process of evaluating our strategic alternatives.

Should we resume development activities in the future, we expect that research and development costs would increase significantly and we would continue to incur significant expenses and operating and net losses, as we develop and seek regulatory approval for such product candidates.

Our financial results may fluctuate significantly from year to year, depending on whether we resume development of our product candidate or any future product candidates, the timing of any clinical trials, the receipt of payments under any future agreements we may enter into, and our expenditures on other R&D activities as well as any payments owed under the License Agreement with Enteris and any future similar agreements.

Should we resume the development activities in the future, we expect we would to continue to incur significant losses for the foreseeable future as we:

- continue the development of any product candidate;

- seek regulatory approvals for any product candidate that successfully completes clinical trials;
- establish a sales, marketing and distribution infrastructure in the United States and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- maintain, expand and protect our global intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development and potential future commercialization efforts.

Revenues from KORSUVA injection will not be sufficient to enable us to reach profitability. To become and remain profitable from product sales, we must succeed in developing and eventually commercializing one or more products that generate significant revenue. In order to commercialize any product candidate, we will need to be successful in a range of challenging activities, including, should we resume the development of our product candidate or any future product candidate, successful registration of oral difelikefalin, discovering, developing, licensing or acquiring additional product candidates and completing preclinical testing and clinical trials for those product candidates, potentially entering into collaboration and license agreements, obtaining regulatory approval for product candidates and manufacturing, marketing and selling approved products and product candidates for which we may obtain regulatory approval. We may never succeed in these activities and, even if we do, may never achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA or foreign regulatory authorities, to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of our product candidate, our expenses could increase.

Even if we do achieve profitability from product sales, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, should we resume the development of our product candidate or any future product candidate, maintain our R&D efforts and diversify our product offerings, or even continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

If we decide to resume development of our product candidate or any future product candidate, we will need additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs.

Conducting clinical trials, pursuing regulatory approvals, establishing outsourced manufacturing relationships, and successfully manufacturing and commercializing products and product candidates is expensive. If we resume development of our product candidate or any future product candidate, we will need to raise additional capital to resume the development of oral difelikefalin and potentially in-license or acquire other product candidates.

In January 2024, we announced a prioritization of our pipeline to focus our resources on our late-stage clinical program evaluating oral difelikefalin in chronic pruritus associated with NP and terminate our Phase 3 clinical program evaluating oral difelikefalin in pruritus associated with advanced chronic kidney disease, including our KICK 1 and KICK 2 Phase 3 clinical trials. As part of this strategic update, in the first quarter of 2024, we reduced our global workforce by approximately 50%. In June 2024, we discontinued the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. Following the discontinuation of the clinical program in NP, we announced that we are

undertaking a comprehensive exploration of strategic alternatives focused on maximizing stockholder value. In connection with our streamlined operating plan, we further reduced our headcount by approximately 70%.

After taking into account the discontinuation of our clinical development programs, reduction in workforce and comprehensive exploration of strategic alternatives, we expect that our current unrestricted cash and cash equivalents and available-for-sale marketable securities will be sufficient to fund our currently anticipated operating plan for at least the next 12 months. In connection with the termination of all ongoing clinical programs, our research and development expenses have decreased. We expect to continue to incur costs and expenditures in connection with the process of evaluating our strategic alternatives. Should we resume development activities in the future, we expect that research and development costs would increase significantly. It is possible that the assumptions upon which we have based this estimate may prove to be wrong, and we could use our capital resources sooner than we presently expect.

Our future funding requirements will depend on many factors, including, but not limited to:

- the discontinuation of our clinical program for oral difelikefalin for chronic pruritus associated with NP;
- the exploration of strategic alternatives to maximize shareholder value;
- should we resume development activities in the future, the rate of progress and costs related development of and any trials for product candidates;
- should we resume development activities in the future, the rate of progress and costs for any product candidates that we may in-license or acquire in the future;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with any product candidate, including any such costs we may be required to expend if our licensors are unwilling or unable to do so;
- the effect of competing technological and market developments; and
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies. Until we can generate a sufficient amount of product revenue, if ever, we may seek to finance future cash needs through public or private equity offerings, debt financings, milestone and royalty payments from corporate collaboration and licensing arrangements, as well as through interest income earned on cash and investment balances. We cannot be certain that additional funding will be available on acceptable terms, or at all, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions, including high rates of inflation and interest rates, the continuing disruptions to and volatility in the credit and financial markets in the United States and worldwide, including resulting from the ongoing conflicts between Russia and the Ukraine, conflicts in the Middle East, and increasing tensions between China and Taiwan.

Risks Related to Our Business and the Development and Commercialization of Our Product and Potential Product Candidates

Should we resume development of our product candidate or future product candidates, if we are unable to successfully complete clinical development, obtain regulatory approvals and commercialize our product candidate or future product candidates, or experience significant delays in doing so, our business will be materially harmed.

Should we resume development of our product candidate or any future product candidates, our business will depend on the successful development, regulatory approval, and commercialization of such product candidates. In January 2024, we announced a prioritization of our pipeline to focus our resources on our late-stage clinical program evaluating oral difelikefalin in chronic pruritus associated with NP and terminate our Phase 3 clinical program

evaluating oral difelikefalin in pruritus associated with advanced chronic kidney disease, including our KICK 1 and KICK 2 Phase 3 clinical trials. In June 2024, we discontinued the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. Should we resume development activities in the future, we cannot be certain that any such product candidates will be successful in clinical trials or receive regulatory approval. Regulatory authorities may interpret our data differently than we do. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and, should we resume development activities in the future we may never receive such regulatory approval for oral difelikefalin or any future product candidates.

Should we resume development of our product candidate or any future product candidates, the success of such product candidates will depend on many factors, including but not limited to:

- successful enrollment in, and completion of, clinical trials, as well as completion of preclinical studies;
- favorable efficacy and acceptable safety data from our clinical trials and other studies;
- receipt of additional regulatory approvals;
- managing our reliance on sole-source third parties such as our third-party vendors, suppliers, and manufacturers;
- the performance by CROs or other third parties and consultants we may retain of their duties to us in a manner that complies with our protocols and applicable laws and that protects the integrity of the resulting data;
- obtaining and maintaining patent, trade secret and other intellectual property protection and regulatory exclusivity;
- ensuring we do not infringe, misappropriate or otherwise violate the valid patent, trade secret or other intellectual property rights of third parties;
- successfully launching, either alone or with a commercial partner, any product candidate for which regulatory approval is received;
- obtaining and maintaining favorable reimbursement from third-party payers and governments for products and product candidates;
- competition with other products;
- post-marketing commitments, if any, to regulatory agencies following regulatory approval of any product candidate;
- continued acceptable safety profile following regulatory approval; and
- manufacturing or obtaining sufficient supplies of our products and any product candidate that may be necessary for use in clinical trials for evaluation of any product candidate and commercialization of any approved product.

If we do not achieve and maintain one or more of these factors in a timely manner or at all, we could experience significant delays in our ability to, or be unable to obtain regulatory approvals for, and/or to successfully commercialize

any products or product candidates, which would materially harm our business and we may not be able to generate sufficient revenues and cash flows to continue our operations.

Clinical and preclinical drug development involves a lengthy and expensive process with uncertain timelines and outcomes, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Should we resume development of our product candidate or any potential future product candidate, such product candidate may not achieve favorable results in clinical trials or preclinical studies or receive regulatory approval on a timely basis, if at all.

Drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. Should we resume development of our product candidate or any future product candidate, we cannot guarantee that any clinical trials or preclinical studies will be conducted as planned, including whether we are able to meet expected timeframes for data readouts, or complete on schedule, if at all, and failure can occur at any time during the trial or study process, including due to factors that are beyond our control.

Should we resume development activities in the future, the results from preclinical studies or clinical trials of oral difelikefalin, any potential future product candidates, or a competitor's product candidate in the same class may not predict the results of later clinical trials, and interim, topline or preliminary results of a clinical trial are not necessarily indicative of final results. Oral difelikefalin or any future product candidate in later stages of clinical trials may fail to show the desired characteristics despite having progressed through preclinical studies and initial clinical trials. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials, and many product candidates fail in clinical trials despite very promising early results. For example, in December 2023, we announced the outcome from the dose-finding Part A of the KIND 1 study evaluating the efficacy and safety of oral difelikefalin in moderate-to-severe pruritus associated with atopic dermatitis as an adjunct to topical corticosteroids. In the study, oral difelikefalin did not demonstrate a meaningful clinical benefit, which resulted in our decision to discontinue the clinical program in atopic dermatitis. Further, in June 2024, we discontinued the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo.

Moreover, preclinical and clinical data may be susceptible to varying interpretations and analyses. A number of companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies. Such setbacks have occurred and may occur for many reasons, including, but not limited to: clinical sites and investigators may deviate from clinical trial protocols, whether due to lack of training or otherwise, and we may fail to detect any such deviations in a timely manner; patients may fail to adhere to any required clinical trial procedures, including any requirements for post-treatment follow-up; product candidates may fail to demonstrate safety, potency (or efficacy) in certain patient subpopulations, which has not been observed in earlier trials due to limited sample size, lack of analysis or otherwise; or, should we resume development of our product candidate or any future product candidate, our clinical trials may not adequately represent the patient populations we intend to treat, whether due to limitations in our trial designs or otherwise, such as where one patient subgroup is overrepresented in the clinical trial. There can be no assurance that we will not suffer similar setbacks despite the data we may observe in earlier studies. Based upon negative or inconclusive results, we or any current or any future collaborator may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials, which would cause us to incur additional operating expenses and delays and may not be sufficient to support regulatory approval on a timely basis or at all.

As a result, we cannot be certain that, should we resume development of our product candidate or any future product candidate, any clinical trials or preclinical studies will be successful. Any safety concerns observed in any clinical trials, should we resume development of our product candidate or any future product candidate, could limit the prospects for regulatory approval of such product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Should we resume development of our product candidate or any future product candidate, if we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Should we resume development of our product candidate or any future product candidate, we may not be able to initiate or continue conducting clinical trials for any such product candidate if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Our competitors may have ongoing clinical trials for product candidates that treat the same indications as our future product candidates, should we resume development activities in the future, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the eligibility criteria for, and design of, the trial in question;
- the perceived risks and benefits of the product candidate under study;
- competition in recruiting and enrolling patients in clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- delays or difficulties due to public health crises, such as pandemics or other similar outbreaks.

For example, we experienced a delay in patient enrollment for our Phase 2 clinical trial of oral difelikefalin for the treatment of pruritus in patients with hepatic impairment due to primary biliary cholangitis that led to our decision to discontinue and unblind this trial. Should we resume development of our product candidate or any future product candidate, we could in the future experience similar delays in programs for such product candidates.

Should we resume development of our product candidate or any future product candidate, our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. We may encounter difficulties and/or delays in completing any future enrollments, should we resume development activities in the future. Enrollment delays in our clinical trials may result in increased development costs for our product candidate, or the inability to complete development of our product candidate, which would cause the value of our company to decline, limit our ability to obtain additional financing, and materially impair our ability to generate revenues.

Should we resume development of our product candidate or any future product candidate, we expect to continue to rely on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

Should we resume development of our product candidate or any future product candidate, we expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our preclinical studies and clinical trials. Any agreements we may enter into might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements

that would delay our product development activities, should we resume development of our product candidate or any future product candidate, and adversely affect our business.

Our reliance on these third parties for development activities will reduce our control over these activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. For example, should we resume development activities in the future, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical trials are conducted in accordance with FDA's good laboratory practice, or GLP, as appropriate. Moreover, the FDA and comparable foreign regulatory authorities require us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced, under current good manufacturing practices, or cGMP, regulations. Our failure to comply with these regulations should we resume development activities in the future, may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register certain clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Should we resume development activities in the future, CROs we engage may also have relationships with other entities, some of which may be our competitors. In addition, our CROs would not be our employees, and except for remedies available to us under our agreements with such CROs, we would not be able to control whether or not they devote sufficient time and resources to our clinical, non-clinical and preclinical programs. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct any future preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to any future clinical protocols, regulatory requirements or for other reasons, our clinical trials, should we resume development activities in the future, may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for any such product candidate and will not be able to, or may be delayed in our efforts to, successfully commercialize our products and product candidates. As a result, our results of operations and the commercial prospects for our products and product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

If any of our relationships with a third-party CRO that we engage terminates, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our CROs, should we resume development activities in the future, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

Should we resume development of our product candidate or any future product candidate, manufacturers upon whom we may rely could fail to produce a product candidate in the volumes that we may require on a timely basis, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, and we could face delays in the development of a product candidate.

Should we resume development of our product candidate or any future product candidate, we expect to continue to rely on third parties for the manufacture of any such product candidate for preclinical and clinical testing. If we were to

experience an unexpected loss of supply of a product candidate for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any clinical studies.

Should we resume development of our product candidate or any future product candidate, any problems or delays we experience in preparing for commercial-scale manufacturing of a product or product candidate may result in a delay in FDA approval of the product or product candidate or may impair our ability to manufacture commercial quantities, which would adversely affect our business. For example, our manufacturers would need to produce specific batches of a product or product candidate to demonstrate acceptable stability under various conditions and for commercially viable lengths of time. We and our contract manufacturers would need to demonstrate to the FDA and other regulatory authorities acceptable stability data for any product candidate, as well as validate methods and manufacturing processes, in order to receive and maintain regulatory approval to commercialize any approved product candidates. Furthermore, if our commercial manufacturers fail to deliver the required commercial quantities of bulk drug substance or finished product on a timely basis and at commercially reasonable prices, we would likely be unable to meet demand for our product and we would lose potential revenues.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up initial production. These problems include difficulties with production costs and yields, quality control, including stability of the products and product candidates and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Manufacturers that we engage may not perform as agreed. If manufacturers we engage were to encounter any of these difficulties, our ability to provide products for commercialization and product candidates to patients in any future clinical trials, should we resume development activities in the future, would be jeopardized. This could, among other things, lead to increased costs, lost revenue, damage to customer relationships, time and expense spent investigating the cause and, depending on the cause, similar losses with respect to other batches or products. If problems are not discovered before the product is released to the market, recall and product liability costs may also be incurred.

Further, should we resume development of our product candidate or any future product candidate, we may rely on proprietary technology developed by contract manufacturers for purposes of manufacturing certain of our products and product candidates and our failure to negotiate or maintain the long-term use of any such proprietary technology or the inability for our contract manufacturers to produce any products and product candidates or components of any products and product candidates in the volumes that we require on a timely basis, may lead to delays or interruptions in the regulatory approval or commercialization process, as well as increased costs. For example, in August 2019, we entered into the Enteris License Agreement and intended to use Enteris's Peptelligence® technology to develop, manufacture and commercialize oral difelikefalin. In light of decision to discontinue the development of oral difelikefalin, it is possible that the Enteris License Agreement will be terminated. If we decide to resume development of oral difelikefalin in the future, if the Enteris License Agreement has been terminated or, for any other reason, we experience any interruptions in the manufacture, delivery or scale-up of the Enteris formulation technology, we may experience delays in the development and commercialization of oral difelikefalin. Further, if we are unable to maintain our relationship with Enteris, we may be forced to reformulate oral difelikefalin which could result in significantly delaying commercializing oral difelikefalin and require us to incur additional costs in connection with such reformulation and potentially needed to seek additional approvals from the FDA. The operations of our third-party manufacturers have been and, should we resume development of our product candidate or any future product candidate, may in the future be constrained or disrupted and their operating capacity may be reduced by public health crises, such as pandemics or other similar outbreaks, which could negatively impact our clinical development and commercialization timelines.

In addition, should we resume development of our product candidate or any future product candidate, any manufacturers must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our products and product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory

authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, regulatory agencies subject an approved product, its manufacturer and the manufacturer's facilities to continual review and inspections, including periodic unannounced inspections. The subsequent discovery of previously unknown problems with our current or any future approved products, including adverse events of unanticipated severity or frequency, or problems with the facilities where our current or any future approved products are manufactured, may result in restrictions on the marketing of our current or any such future approved products, up to and including withdrawal of the affected product from the market. We have little control over our manufacturers' compliance with these regulations and standards. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our products and product candidate or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products and any product candidate, should we resume development of our product candidate or any future product candidate, if approved. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension, delay or denial of product approval, product seizure or recall, or withdrawal of product approval. If the safety of any quantities supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products and any potential future product candidates.

Should we resume development of our product candidate or any future product candidate, even if we obtain regulatory approvals for such product candidate, they may never be successfully launched or become profitable, in which case our business, prospects, operating results and financial condition may be materially harmed.

In order to successfully launch a product and have it become profitable, should we resume development of our product candidate or any future product candidate, we anticipate that we will have to dedicate substantial time and resources. Our ability to generate revenues from any commercialized products will depend on a number of factors, including, but not limited to:

- achievement of broad market acceptance and coverage by government and third-party payers for our product;
- our or our partners' effectiveness in marketing and selling our product;
- our ability to have manufactured commercial quantities of our product at acceptable cost levels and in compliance with regulatory requirements;
- our ability to maintain a cost-efficient organization and, to the extent we seek to do so, to collaborate successfully with additional third parties;
- our ability to expand and maintain intellectual property protection for our product successfully;
- the efficacy and safety of our product; and
- our ability to comply with regulatory requirements, which are subject to change.

Because of the numerous risks and uncertainties associated with our commercialization efforts, we may not be able to achieve profitability. For example, we previously successfully developed KORSUVA injection through regulatory approval, for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis. However, this product failed to achieve meaningful commercial success.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. A failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

If we or our collaborators are unable to establish effective marketing and sales capabilities, or if we are unable to enter into or maintain agreements with third parties to market and sell our product and, should we resume development of our product candidate or any future product candidate, any product candidate, if they are approved, we may be unable to generate product revenues.

We currently do not have an internal commercial infrastructure for the marketing, sale, and distribution of pharmaceutical products. Should we resume development of our product candidate or any future product candidate, in order to commercialize any such product candidate (if approved) in the United States, we will need to build our marketing, sales and distribution capabilities. We have no prior experience in the marketing, sale and distribution of pharmaceutical products, and there are significant risks involved in the building and managing of a commercial infrastructure to the extent we choose to do so in the future. The establishment and development of our own sales force and related plans to market any products in the United States we may develop will be expensive and time-consuming and could delay any product launch, and we may not be able to successfully develop this capability. Should we resume development activities in the future, if oral difelikefalin or any future product candidate is approved for marketing outside of the United States, we intend to make and maintain arrangements with third parties to perform these services.

We, or our partners or collaborators, will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, manage and retain marketing and sales personnel. In the event that we or our partners or our collaborators are unable to develop a marketing and sales infrastructure, we may not be able to commercialize any potential future product candidate, which would limit our ability to generate product revenues. Factors that may inhibit our or our partners' or collaborators' efforts to commercialize any potential future product candidate, if approved, include:

- inability to recruit, train, manage and retain adequate numbers of effective sales and marketing personnel;
- inability of sales personnel to obtain access to physicians and other providers or educate adequate numbers of physicians and other providers on the benefits of prescribing the product;
- inability to effectively oversee a geographically dispersed sales and marketing team;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Our or our partners' or our collaborators' sales force and marketing teams may not be successful in commercializing any approved product candidate that may receive regulatory approval. For example, we previously partnered with CSL Vifor for the commercialization of KORSUVA injection, but that product has not achieved meaningful commercial success.

In the event that we are unable to successfully collaborate with a third-party marketing and sales organization to commercialize any approved product candidate outside the United States, our ability to generate product revenues may be limited. To the extent that we rely on third parties to commercialize products for which we obtain regulatory approval, we may receive less revenues than if we commercialized these products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts.

We face significant competition from other pharmaceutical and biotechnology companies, academic institutions, government agencies and other research organizations. Our operating results will suffer if we fail to compete effectively.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product, KORSUVA injection and, should we resume development of our product candidate or any future product candidate, we will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and

biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of pruritus. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Among the companies that currently market or are developing therapies in the pruritus space that, if approved, our oral difelikefalin would potentially compete with include: Pfizer, AbbVie, Eli Lilly, Amgen, Regeneron, Leo Pharma, Galderma, Chugai, Incyte and others.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than our product or any future product candidates. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products. Should we resume development of our product candidate or any future product candidate, generic products may be approved or used in clinical practice in some markets for the indication that such product candidate is intended to treat. We expect that any potential future product candidates, if approved, would be priced at a significant premium over competitive generic products, if any.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in R&D, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient recruitment for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability and, should we resume development of our product candidate or any future product candidate, may have to limit commercialization of a product candidate.

We face an inherent risk of product liability lawsuits related to the sale of our products to, use of our products by, and testing of any product candidate in, seriously ill patients. For example, product liability claims might be brought against us by consumers, healthcare providers or others using, administering or selling our products. We may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- loss of revenue from decreased demand for our products and/or any potential product candidate;
- impairment of our business reputation or financial stability;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- diversion of management attention and scientific resources from our business operations;

- withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs;
- the inability to successfully commercialize our products and/or any potential product candidate;
- significant negative media attention;
- initiation of investigations by regulators or increased regulatory scrutiny;
- product recalls, withdrawals or labeling, marketing or promotional restrictions; and
- the inability to commercialize any potential product candidate.

Should we resume development of our product candidate or any future product candidate, for any product candidate that is approved for commercial sale, we will be highly dependent upon healthcare provider and patient perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. Because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our financial condition or results of operations.

We have obtained limited product liability insurance coverage for our products and our clinical trials with a $15.0 million annual aggregate coverage limit in the United States and various other coverage limits outside of the United States. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products for our product candidate in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing, or at all. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on our product candidate or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we have focused on developing product candidates for specific indications that we believed to be most likely to succeed, in terms of both regulatory approval and commercialization. As a result, we may have foregone or delayed, or, should we resume development activities in the future, may in the future forgo or delay, pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. For example, in 2023, we terminated the atopic dermatitis program as part of our strategy to focus on our advanced chronic kidney disease and NP programs. Further, in January 2024, we announced a prioritization of our pipeline to focus our resources on our late-stage clinical program evaluating oral difelikefalin in chronic pruritus associated with NP and terminate our Phase 3 clinical program evaluating oral difelikefalin in pruritus associated with advanced chronic kidney disease. In June 2024, we discontinued the clinical program in NP following the outcome from the dose-finding Part A of the KOURAGE-1 study evaluating the efficacy and safety of oral difelikefalin for moderate-to-severe pruritus in adult patients with NP in which oral difelikefalin did not demonstrate a meaningful clinical benefit at any dose compared to placebo. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Should we resume development activities in the future, our spending on future R&D programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through

collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Our future growth may depend on our ability to identify and develop products and, should we resume development activities in the future, if we do not successfully identify and develop product candidates or integrate them into our operations, we may have limited growth opportunities.

Should we resume development activities in the future, our business strategy may require that we develop a product that we believe is a strategic fit with our focus on pruritus therapeutics. However, these business activities may entail numerous operational and financial risks, including:

- difficulty or inability to secure financing to fund development activities for such development;
- disruption of our business and diversion of our management's time and attention;
- higher than expected development costs;
- exposure to unknown liabilities;
- difficulty in managing multiple clinical trials; and
- inability to successfully develop new products or clinical failure.

We have limited resources to identify and execute the development of products. Moreover, we may devote resources to potential developments that are never completed, or we may fail to realize the anticipated benefits of such efforts. If we do not successfully develop and commercialize product candidates, we may not be able to obtain product revenues in future periods.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. Should we resume development activities in the future, if we are not able to obtain, or if there are delays in obtaining, required additional regulatory approvals, we will not be able to commercialize any product candidates as expected, and our ability to generate revenue will be materially impaired.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Should we resume development of our product candidate or any future product candidate, it is possible that none of such potential product candidates we may seek to develop in the future will ever obtain regulatory approval.

Product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA, and similar regulatory authorities in other countries. Should we resume development of our product candidate or any future product candidate, failure to obtain marketing approval for a product candidate will prevent us from commercializing that product candidate. Should we resume development activities in the future, we expect we would continue to rely on third-party CROs, other vendors, and consultants to assist us in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy for that indication. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of any product candidates, should we resume development of our product candidate or any future product candidate, may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Should we resume development activities in the future, future clinical trial results may not be successful. We may also experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize any product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of any product candidate may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to suspend clinical trials, or terminate clinical trials of any potential product candidate for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- changes in marketing approval policies during the development period;
- changes in or the enactment of additional statutes or regulations;
- changes in regulatory review for each submitted product application;
- the cost of clinical trials of our product candidate may be greater than we anticipate;
- the supply or quality of our product candidate or other materials necessary to conduct clinical trials of any potential product candidate may be insufficient or inadequate; and
- any potential product candidate may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

In addition, unfavorable changes in our industry or the global economy, including as a result of macroeconomic factors related to inflation, rising interest rates, political turmoil, or public health crises such as pandemics or other similar outbreaks, could contribute to some of the events listed above and further impact our ability to progress any future clinical trials should we resume development activities in the future, submit for marketing approval or

commercialize any product candidates, if approved, as planned. Further, if and to the extent, global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process any additional regulatory submissions we may make, which could affect our ability to obtain marketing approval for our product candidate.

Should we resume development of our product candidate or any future product candidate, if we are unable to successfully complete clinical trials of a product candidate or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for any potential product candidate;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Furthermore, regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies, including with respect to third-party technology used in any potential product candidates. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Finally, even if we were to obtain approval, regulatory authorities may approve a product candidate for fewer or more limited indications than we request, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of these scenarios could compromise the commercial prospects for a product candidate to assure safe use of the product candidate, either as a condition of product candidate approval or on the basis of new safety information.

If we experience delays in obtaining approval, if we fail to obtain approval of a product candidate or if the label for a product candidate does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate, the commercial prospects for such product candidate may be harmed and our ability to generate revenues will be materially impaired.

Should we resume development of our product candidate or any future product candidate, such product candidate, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our product.

Should we resume development of our product candidate or any future product candidate, even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including any requirement to implement a Risk Evaluation and Mitigation Strategies, or REMS. If a product candidate receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA or other regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA and other regulatory authorities closely regulate the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved

indications and in accordance with the provisions of the approved labeling. The FDA and other regulatory authorities impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act or equivalent regulations outside the United States relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown AEs or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on the products, manufacturers, manufacturing facilities or manufacturing process;
- imposition of restrictions on operations, including costly new manufacturing requirements;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products and publicity requirements;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing or regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure, detentions or import bans; or
- injunctions or the imposition of civil or criminal penalties.

The FDA's or other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any product candidates should we resume development of our product candidate or any future product candidate. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained.

Regulatory approval is limited by the FDA and other regulatory authorities to those specific indications and conditions for which clinical safety and efficacy have been demonstrated, and we may be subject to fines, penalties or injunctions if we are determined to be promoting the use of our products for unapproved or "off-label" uses, resulting in damage to our reputation and business.

When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific indications for which a product is approved. If we are not able to obtain FDA approval for any desired future indications for our products and product candidates, should we resume

development of our product candidate or any future product candidate, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians may choose to prescribe drugs for uses that are not described in the product's labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, we are prohibited from marketing and promoting the products for indications that are not specifically approved by the FDA or other regulatory authorities. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States and other countries generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by pharmaceutical companies on off-label use. If the FDA or other regulatory authorities determine that our or our commercial partners' promotional activities constitute promotion of an off-label use, it could request that we modify our promotional materials. Further, off-label promotion could subject us to regulatory or enforcement actions by the FDA and other authorities, including issuance of warning letters or untitled letters, suspension or withdraw an approved product from the market, mandatory or voluntary recalls, civil fines, disgorgement of money, operating restrictions, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement, injunctions or criminal prosecution, any of which could significantly harm our business.

Should we resume development of our product candidate or any future product candidate, failure to obtain marketing approval in international jurisdictions would prevent a product candidate from being marketed abroad.

In order to market and sell products in the EU and many other jurisdictions, we or our collaborators or partners must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Even if we obtain FDA approval of a product candidate, the regulatory approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, the failure to obtain approval in one jurisdiction may compromise our or our collaborators' or partners' ability to obtain approval elsewhere. We or our collaborators or partners may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Our agreements with HCR contain various covenants and other provisions, which, if violated, could materially adversely affect our financial condition.

During the fourth quarter of 2023, we, through Cara Royalty Sub, entered into the HCR Agreement with HCR, pursuant to which Cara Royalty Sub sold, or agreed to sell, to HCR the Royalties under the Covered License Agreements, in exchange for up to $40.0 million. We have retained all of our right, title and interest in, to and under the Covered License Agreements that relate to any non-intravenous formulation of difelikefalin.

Under the terms of the HCR Agreement, Cara received an initial payment of $17.5 million in November 2023. In December 2023, we received an additional $20.0 million less certain advisory fees, upon satisfying the milestone event for pricing for Kapruvia® (difelikefalin) in Germany being approved above a certain threshold amount per dose. The terms of the HCR Agreement also provide for an additional $2.5 million milestone payment to Cara Royalty Sub upon achievement of a 2024 sales milestone of KORSUVA in Japan.

The HCR Agreement will automatically expire, and the payment of Royalties to HCR will cease, when HCR has received payments of Royalties equal to two times the aggregate amount of payments made by HCR under the HCR Agreement if achieved on or prior to December 31, 2029, or 2.8 times the aggregate amount of payments made by HCR under the HCR Agreement, if the 2029 Threshold is not achieved on or prior to December 31, 2029. In the event of a change of control, Cara Royalty Sub will pay to HCR an amount equal to 2.8 times the aggregate amount of payments

made by HCR less the total net amounts paid by Cara Royalty Sub to HCR as of the effective date of control. In certain situations, Cara Royalty Sub would not be obligated to pay the change of control payment to HCR. After the HCR Agreement expires, all rights to receive the Royalties return to Cara Royalty Sub.

In connection with the HCR Agreement, we entered into a Contribution and Servicing Agreement which contains various representations and warranties, covenants, indemnification obligations and other provisions related to the contribution of the Covered License Agreement to Cara Royalty Sub and our maintenance and servicing obligations with respect to the Royalties and the Covered License Agreements. In the event we violate these covenants or provisions, we may lose the right to act as the servicer of Cara Royalty Sub and a third-party servicer may be appointed at Cara Royalty Sub's expense. Our replacement as servicer, if it were to occur, could have a material adverse effect on our financial condition as HCR, by virtue of owning Cara Royalty Sub, would own the Royalties.

In connection with the HCR Agreement we also entered into a Pledge and Security Agreement containing various representations, warranties and covenants, and a limited recourse guaranty of Cara Royalty Sub's obligations under the Purchase and Sale Agreement which is secured by the pledge in favor of HCR all of the capital stock of Cara Royalty Sub. HCR is entitled to foreclose on the capital stock of Cara Royalty Sub following the occurrence of certain remedies events, including, without limitation, a bankruptcy of us or the failure of us to perform our obligations under the Contribution and Servicing Agreement. Such foreclosure, if it were to occur, could have a material adverse effect on our financial condition as HCR, by virtue of owning Cara Royalty Sub, would own the Royalties.

Our information systems, or those of others upon whom we rely (such as our CROs, contract manufacturers, contractors, consultants, service providers, collaborators and others) may fail or suffer cybersecurity breaches, loss or leakage of data or other disruptions, which could result in a material disruption of our development programs, compromise sensitive information related to our business, or prevent us from accessing critical information, potentially exposing us to liability that could adversely affect our business.

We are increasingly dependent upon information systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store, transmit and otherwise process confidential information (including but not limited to intellectual property, proprietary business information and personal data). We also have outsourced elements of our operations to third parties, and as a result we manage a number of service providers who have access to our data and information systems and infrastructure. Our reliance on service providers could introduce new cybersecurity risks and vulnerabilities, including supply-chain attacks, and other threats to our business operations. We rely on service providers and technologies to operate critical business systems to process sensitive data in a variety of contexts, including, without limitation, cloud-based infrastructure, data center facilities, encryption and authentication technology, personnel email, and other functions. We also rely on third-party service providers to provide other products, services, parts, or otherwise to operate our business. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

Cybersecurity risks have significantly increased in recent years in part because of the proliferation of new technologies, the use of the internet and telecommunication technologies to conduct financial transactions, especially as personnel are working remotely, and the increased sophistication and activities of organized crime, hackers, terrorists, nation-states and other external parties. To the extent that any disruption or cybersecurity breach were to result in a loss of, or damage to, our data or information systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability and reputational damage and, should we resume development of our product candidate or any future product candidate, the further development of such product candidates could be delayed.

Some actors now engage and are expected to continue to engage in cyberattacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, and the third parties upon which we rely, may be vulnerable to a heightened

risk of these attacks, including retaliatory cyberattacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations, ability to provide our products or services, loss of sensitive data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments.

We and the third parties upon which we rely are subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks, credential stuffing, credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, telecommunications failures, earthquakes, fires, floods, and other similar threats. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

While we have implemented security measures designed to protect against security incidents, there can be no assurance that these measures will be effective. We take steps designed to detect, mitigate, and remediate vulnerabilities in our information systems (such as our hardware and/or software, including that of third parties upon which we rely). We may not, however, detect and remediate all such vulnerabilities including on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive data or our information technology systems, or those of the third parties upon whom we rely. A security incident or other interruption could disrupt our ability (and that of third parties upon whom we rely) to provide our services.

We may expend significant resources or modify our business activities to try to protect against security incidents. Additionally, certain data privacy and security obligations may require us to implement and maintain specific security measures or industry-standard or reasonable security measures to protect our information technology systems and sensitive data.

Applicable data privacy and security obligations may require us to notify relevant stakeholders, including affected individuals, customers, regulators, and investors, of security incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences.

If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences, such as government enforcement actions (for example, investigations, fines, penalties, audits, and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive data (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm; monetary fund diversions; diversion of management attention; interruptions in our operations (including development and commercialization of any product candidate, should we resume development activities in the future, if approved, and availability of data); financial loss; and other similar harms. Security incidents and attendant consequences may prevent or cause customers to stop using our services, deter new customers from using our services, and negatively impact our ability to grow and operate our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that our insurance coverage will be adequate or sufficient to protect

us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

Risks Related to Our Dependence on Third Parties

Any collaboration arrangements that we are a party to or may enter into in the future may not be successful, which could adversely affect our ability to develop and ultimately commercialize our product candidate or any potential future product candidate.

Our business model in the past has been to develop and commercialize product candidates in the United States and generally to seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of product candidate in the rest of the world. We currently have license agreements with Maruishi and CKDP for the intravenous and oral formulations of difelikefalin, as well as license agreements with respect to our commercially approved products, KORSUVA Injection and Kapruvia with CSL Vifor. In addition to our existing agreements, we may enter into additional collaboration arrangements in the future on a selective basis. Our existing collaborations and future collaboration arrangements may not be successful. The success of our existing and future collaboration arrangements will depend heavily on the efforts and activities of our collaborators.

Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaboration arrangements. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Maruishi may terminate its agreement with us at will, and CKDP may terminate its agreement with us in certain circumstances relating to patent invalidity or unenforceability or generic entry by a third party, as further described in the section titled "*Management's Discussion and Analysis of Financial Condition and Results of Operations - Collaboration and License Agreements*". Any such termination or expiration could adversely affect us financially and could harm our business reputation. Our current collaborations and any future collaborations we might enter into, including related to development of our product candidate or any future product candidate should we resume development activities in the future, may pose a number of risks, including the following:

- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product or product candidate that achieves regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could fail to make timely regulatory submissions for a product or product candidate;
- collaborators may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of any potential product candidates;

- a collaborator with marketing and distribution rights to one or more of our products or product candidate that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of products and product candidates, might lead to additional responsibilities for us with respect to products and product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

- collaborations, including our collaboration with Maruishi, may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidate.

If our current collaborations or any other collaborations we might enter into in the future, including related to development of our product candidate or any future product candidate should we resume development activities in the future, do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of potential product candidates could be delayed and we may need additional resources to develop a product candidate and our product platform. All of the risks relating to our product development, regulatory approval and commercialization described in this Quarterly Report on Form 10-Q also apply to the activities of our collaborators in their respective jurisdictions.

Additionally, if any current or future collaborator of ours, including related to development of our product candidate or any future product candidate should we resume development activities in the future, is involved in a business combination, the collaborator might deemphasize or terminate development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation in the business and financial communities could be adversely affected.

If we determine to collaborate in the future with additional pharmaceutical or biotechnology companies for the development and potential commercialization of oral difelikefalin or any potential future product candidate, should we resume development activities in the future, we would face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to

undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform or successfully commercialize our products and our business may be materially and adversely affected.

Risks Related to Legal and Compliance Matters

If we fail to comply with federal and state healthcare laws, including fraud and abuse, and transparency laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payers, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, transparency and patients' rights may be applicable to our business. The healthcare laws and regulations that may affect our ability, and our partners' and collaborators' ability, to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which regulates, among other things, our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, any person or entity from knowingly and willfully soliciting, receiving, offering or paying any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchase, recommendation, lease, order or furnishing of an item or service reimbursable, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs;

- federal civil and criminal false claims laws, including without limitation the federal civil False Claims Act, and civil monetary penalties law, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment or approval from a federal health care program (including Medicare and Medicaid);

- Federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any health care benefit program, regardless of the payer (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick, scheme or device a material fact or making any materially false statements in connection with the delivery of, or payment for, health care benefits, items or services relating to healthcare matters;

- federal transparency laws, including the federal Physician Payments Sunshine Act, that requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to CMS information related to payments and other transfers of value provided to physicians (defined to include doctors of medicine, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members;

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers; and

- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to the pricing of certain drugs, as

well as payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and local laws that require the registration of pharmaceutical sales representatives, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available under these laws, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Pharmaceutical and other healthcare companies continue to be prosecuted under the federal false claims laws for numerous activities, including those related to research, sales, marketing and promotional programs. In addition, recent health care reform legislation has strengthened these laws. For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or the Health Care Reform Law, among other things, amends the intent requirement of the federal Anti-Kickback Statute and certain other criminal healthcare fraud statutes. As a result, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to commit a violation. Moreover, the Health Care Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. To the extent that any product we make is sold in a foreign country, we may be subject to similar foreign laws and regulations. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, exclusion from participation in U.S. federal or state health care programs, contractual damages, reputational harm, imprisonment, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results. Although an effective compliance program can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state transparency and fraud and abuse laws may prove costly. If any of the physicians or other healthcare providers or entities with whom we do business, including our partners or collaborators, is found not to be in compliance with applicable laws, it may be subject to significant criminal, civil or administrative sanctions, including but not limited to, exclusions from participation in government healthcare programs, which could also materially affect our business.

We are subject to stringent and evolving U.S. and foreign laws, regulations and standards, contracts, industry standards, policies and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions, litigation (including class claims) and mass arbitration demands, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue and profits, and otherwise adversely affect our business, operations and financial performance.

We are subject to or affected by numerous domestic (both federal and state) and foreign laws and regulations, as well as regulatory guidance, contracts, industry standards, policies and other obligations governing the collection, use, disclosure, retention, security and other processing of personal data, such as information that we collect about participants and healthcare providers in connection with clinical trials in the United States and abroad. Obligations related to data privacy and security (and consumers' data privacy expectations) are quickly changing, becoming increasingly stringent, and creating uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. This evolving global data protection landscape may create uncertainty in our business, affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use, share and otherwise personal data, result in liability or impose additional costs on us. The cost of compliance with these obligations is high and is likely to increase in the future and may necessitate changes to our operations and to those of third parties that process personal data on our behalf. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, imposes certain requirements relating to the privacy, security and transmission of

individually identifiable health information without appropriate authorization by entities subject to the rule, including health plans, healthcare clearinghouses, certain healthcare providers, and their business associates and covered subcontractors that perform services for them that involve the creation, use, maintenance or disclosure of, individually identifiable health information. In the event we are subject to HIPAA and we or our business associates or subcontractors fail to properly maintain the privacy and security of certain individually identifiable health information, or we or our business associates or subcontractors are responsible for an inadvertent disclosure or security breach of such individually identifiable health information, we could be subject to enforcement measures, including civil and criminal penalties and fines for violations of state and federal privacy or security standards, such as HIPAA and HITECH, and their respective implementing regulations.

Additionally, certain states have adopted their own privacy and security laws and regulations for health information, some of which may be more stringent than HIPAA.

In the past few years, numerous U.S. states, following California's enactment of the CCPA - including Virginia, Colorado, Connecticut, and Utah-have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. To the extent that we are or may become subject to these laws, the exercise of these rights may impact our business and ability to provide our products and services. Similar laws are being considered in several other states, as well as at the federal and local levels, and we expect more states to pass similar laws in the future. These state laws may allow for statutory fines for noncompliance (for example, under the CCPA, fines can be levied up to $7,500 per intentional violation) and private rights of action. While some of these laws may exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us, and the third parties upon whom we rely. For example, Washington's My Health My Data Act ("MHMD") broadly defines consumer health data, places restrictions on processing consumer health data (including imposing stringent consent requirements), provides consumers certain rights with respect to their health data, and creates a private right of action to allow individuals to sue for violations of the law.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data privacy and security. For example, the EU GDPR and the UK GDPR impose strict requirements for processing personal data. GDPR may increase compliance burdens on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and otherwise process personal data. The processing of sensitive personal data, such as physical health conditions, may also be subject to heightened compliance burdens under the GDPR. Under the GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros under the EU GDPR, 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

In addition, we may be unable to transfer personal data from Europe and other jurisdictions to the United States or other countries due to data localization requirements or limitations on cross-border data flows. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the European Economic Area (EEA) and the United Kingdom (UK) have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA's standard contractual clauses, the UK's International Data Transfer Agreement/Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers to relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the

need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activities groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the GDPR's cross-border data transfer limitations.

In addition to data privacy and security laws, we are or may become contractually subject to industry standards adopted by industry groups. We are also bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful.

We publish privacy policies, marketing materials, and other statements, such as compliance with certain certifications or self-regulatory principles, regarding data privacy and security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims) and mass arbitration demands; additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials. In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations (including, as relevant, clinical trials should we resume development activities in the future); inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

We are subject to recent legislation, regulatory proposals and healthcare payer initiatives that may increase our costs of compliance and adversely affect our ability to market our products, obtain collaborators and raise capital.

In March 2010, President Obama signed the Health Care Reform Law, which includes provisions that have changed, and likely will continue to change, health care financing and the delivery of health care in the United States. The Health Care Reform Law, among other things, increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs, required collection of rebates for drugs paid by Medicaid managed care organizations, required manufacturers to participate in a coverage gap discount program, under which they must agree to offer point-of-sale discounts (increased to 70 percent, effective as of January 1, 2019) off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected expanded the types of entities eligible for the 340B drug discount program; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been executive, judicial, and Congressional challenges to certain aspects of the Health Care Reform Law. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Health Care Reform Law is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Further, prior to the Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the Health Care Reform Law marketplace, which began on February 15, 2021, and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the Health Care Reform Law. In addition, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in Health Care Reform Law marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is also unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the Health Care Reform Law and our business.

In addition, other legislative changes have been proposed and adopted since the Health Care Reform Law was enacted. These changes include, among other things, aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went effective on April 1, 2013, and, due to subsequent legislative amendments, will remain in effect until 2032, unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Congress is considering additional health reform measures. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations. Further, Congress is considering additional health reform measures.

We expect that the Health Care Reform Law, as well as other federal and state healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for KORSUVA injection or any approved product candidate, should we resume development of our product candidate or any future product candidate. Any reduction in reimbursement from Medicare or other government healthcare programs may result in a similar reduction in payments from private payers. In addition, there have been several recent U.S. Presidential executive orders, Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Further, in July 2021, the Biden administration released an executive order that included multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform. The plan sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions take effect progressively starting in fiscal year 2023. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. It is unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.

Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program (SIP) proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be, should we resume development activities in the future. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements. Moreover, the Drug Supply Chain Security Act imposes obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing.

Legislation and regulations that, among other things, reduce drug prices or require the implementation of costly compliance measures could result in decreased net revenues from our pharmaceutical products and decrease potential returns from our development efforts, and we cannot predict what legislation will be enacted in the future.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. Should we resume development activities in the future, to obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of a product candidate to other available therapies. There can be no assurance that our products will be considered cost-effective by third-party payers, that an adequate level of reimbursement will be available or that the third-party payers' reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Our employees, independent contractors, consultants, and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants and commercial partners. Misconduct by such individuals could include inadvertent or intentional failures to:

- comply with FDA regulations and other similar foreign regulations;

- provide true, complete and accurate information to the FDA;
- comply with manufacturing standards;
- comply with federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and similar foreign laws;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, including off label uses of our products, structuring and commission(s), certain customer incentive programs, patient assistance programs, and other business arrangements generally. Third party misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter such misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials owned by us. We and any third-party manufacturers and suppliers we engage are subject to numerous federal, state and local environmental, health and safety laws, regulations and permitting requirements, including those governing laboratory procedures; the generation, handling, use, storage, treatment, and disposal of hazardous and regulated materials and wastes; the emission and discharge of hazardous materials into the ground, air and water; and employee health and safety. Our partners' operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste. In some cases, these hazardous materials and various wastes resulting from their use are stored at our contract manufacturers' facilities pending their use and disposal. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes.

Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. Under certain environmental laws, we could be held responsible for costs relating to any contamination at our current or past facilities and at third-party facilities. In such an event, we may be held liable for any resulting damages and such liability

could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance.

Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our research, product development and manufacturing efforts.

Risks Related to Intellectual Property

It is difficult and costly to protect our proprietary rights and as a result we may not be able to ensure their protection and all patents will eventually expire.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for difelikefalin and, should we resume development activities in the future, for any other product candidates that we may develop, license or acquire and the methods we use to manufacture them, as well as successfully defending these patents and trade secrets against third-party challenges. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute to issuance all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we may fail to identify patentable aspects of our R&D output before it is too late to obtain patent protection. Moreover, should we enter into additional collaborations we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance and enforcement of our patents. Therefore, these patents and applications may not be successfully prosecuted to issuance and enforced in a manner consistent with the best interests of our business. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is also uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. The degree of future protection for our proprietary rights is uncertain, because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. Moreover, the patent application process is also subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting difelikefalin and, should we resume development activities in the future, any other product candidates that we may develop, license or acquire by obtaining and defending patents. For example:

- we may not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- we may not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our product candidates or technologies;
- it is possible that none of the pending patent applications will result in issued patents;
- the issued patents covering our product candidates may not provide a basis for commercially viable active products, may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable;
- patents of others may have an adverse effect on our business;

- competitors may file trademark infringement claims or challenges to the validity of our trademark(s);
- noncompliance with governmental patent agencies requirements can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction, potentially allowing competitors to enter the market earlier than would otherwise have been the case;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential product candidates; or
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of available patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The U.S. Patent Office has developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, including and in particular, the first to file provisions, became effective on March 16, 2013. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our currently pending and future patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Patent applications in the United States are generally maintained in confidence for at least 18 months after their earliest effective filing date and in certain circumstances not until granted when no foreign counterpart patent applications are filed. Furthermore, published patent applications may issue at a later date with new and/or amended claims substantially different from those published earlier. Consequently, we cannot be certain we were the first to invent or the first to file patent applications on difelikefalin or, should we resume development activities in the future, any other product candidates that we may develop, license or acquire.

Until recent changes to the U.S. Patent Laws, patents and patent applications relating to substantially similar claimed inventions were potentially subject to interference proceedings to determine the first applicant to invent the claimed subject matter. For an interference to be declared against our patents and patent applications, any such interference would be under the 1952 law which was eliminated by the America Invents Act, or AIA, enacted in 2011 and fully effective in 2013. Such an interference would therefore have to relate to a patent or application with an effective filing date before March 16, 2013. No interference with such a patent or application has been declared to date. Therefore, it seems extremely unlikely that we may have to participate in interference proceedings declared by the USPTO to determine priority of invention in the United States against one or more parties claiming the same or similar invention. However, in the unlikely event that such interference was to be declared, the costs of these proceedings could be substantial and it is possible that our efforts would be unsuccessful, resulting in a material adverse effect on our U.S. patent position. The results of these types of proceedings could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such results could have a material adverse effect on our results of operations.

In addition, the patentability of claims in pending patent applications covering KORSUVA injection or other difelikefalin-based product can be challenged by third parties during prosecution in the USPTO under the new AIA law

of 2013, for example by third party observations and derivation proceedings, and the validity of claims in issued patents can be challenged by third parties in various post-grant proceedings such as Post-Grant Review, Inter-partes Reexamination, and Inter-partes Review proceedings.

Furthermore, we may not have identified all U.S. and foreign patents or published applications that affect our business either by blocking our ability to commercialize our drugs or by covering similar technologies that affect our drug market. In addition, some countries, including many in Europe, do not grant patent claims directed to methods of treating humans, and in these countries patent protection may not be available at all to protect our product candidates. Even if patents issue, we cannot guarantee that the claims of those patents will be valid and enforceable or provide us with any significant protection against competitive products, or otherwise be commercially valuable to us.

We also rely on trade secrets to protect our technology, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. While we use reasonable efforts to protect our trade secrets, our licensors, employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third party illegally obtained and is using our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we fail to obtain or maintain patent protection or trade secret protection for difelikefalin or, should we resume development activities in the future, any other product candidate that we may develop, license or acquire, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and achieve profitability.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we or any current or future collaboration partner are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market and sell difelikefalin or, should we resume development activities in the future, any potential future product candidate will depend upon our ability to avoid infringing the proprietary rights of third parties, and our commercial success will depend upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the general field of pain management and cover the use of numerous compounds and formulations in our targeted markets. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and our licensors may not be successful in defending intellectual property claims by third parties, which could have a material adverse effect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management. In addition,

because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that current or potential future product candidates may infringe. There could also be existing patents of which we are not aware that our current or potential future product candidates may inadvertently infringe.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third-party claims that we infringe on their products or technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, can be expensive and time consuming to litigate and can divert management's attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor's patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our processes so they do not infringe, which may not be possible or could require substantial funds and time.

If we are found to infringe on a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidate or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and may ultimately be unsuccessful.

Competitors may infringe on our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Most of our competitors are larger than we are and have substantially greater resources. They are, therefore, likely to be able to sustain the costs of complex patent litigation longer than we could. In addition, should we resume development activities in the future, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our internal research programs, in-license needed technology, or enter into development partnerships that would help us bring any product candidate to market.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development or commercialization of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms or at all, which could materially harm our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees, or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement rights are not as strong as those in the United States. These products may compete with our product candidate, should we resume development activities, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

The validity and enforceability of the patents and applications that cover difelikefalin can be challenged by competitors.

Should we resume development activities in the future, in the event that oral difelikefalin or any potential future product candidate is approved by the FDA, one or more third parties may challenge the patents covering these products and product candidates, which could result in the invalidation of, or render unenforceable, some or all of the relevant patent claims. For example, if a third party files an Abbreviated New Drug Application, or ANDA, for a generic drug product containing difelikefalin, and relies in whole or in part on studies conducted by or for us, the third party will be required to certify to the FDA that either: (1) the patents listed in the Orange Book have expired; (2) the listed patents have not expired, but will expire on a particular date and approval is sought after patent expiration; or (3) the listed patents are invalid or will not be infringed by the manufacture, use or sale of the third-party's generic drug product. A

certification that the new product will not infringe the Orange Book-listed patents for difelikefalin, or that such patents are invalid, is called a paragraph IV certification. If the third party submits a paragraph IV certification to the FDA, a notice of the paragraph IV certification must also be sent to us once the third-party's ANDA is accepted for filing by the FDA. We may then initiate a lawsuit to defend the patents identified in the notice. The filing of a patent infringement lawsuit within 45 days of receipt of the notice automatically prevents the FDA from approving the third-party's ANDA until the earliest of 30 months or the date on which the patent expires, the lawsuit is settled, or the court reaches a decision in the infringement lawsuit in favor of the third party. If we do not file a patent infringement lawsuit within the required 45-day period, the third-party's ANDA will not be subject to the 30-month stay. Litigation or other proceedings to enforce or defend intellectual property rights are often very complex in nature, may be very expensive and time-consuming, may divert our management's attention from our core business, and may result in unfavorable results that could adversely impact our ability to prevent third parties from competing with our products.

Risks Related to Employee Matters and Managing Growth

We depend on skilled personnel to operate our business effectively in a rapidly changing market, and if we are unable to retain existing or hire additional personnel when needed, our ability to develop and sell our products could be harmed.

In January 2024, as part of our pipeline prioritization, we reduced our headcount by approximately 50%, including the separation of our former Chief Scientific Officer and SVP of Research & Development. Further, in June 2024, in connection with our streamlined operating plan, we further reduced our headcount by approximately 70%. Although we believe these employee transitions are in the best interest of our company and our stockholders, these transitions may result in the loss of personnel with deep institutional or technical knowledge. Further, the transition could potentially disrupt our operations and relationships with employees, suppliers, and partners and, as a result, create added costs, operational inefficiencies, decreased employee morale and productivity and increased turnover. In addition, our competitors may seek to use these transitions and the related potential disruptions to gain a competitive advantage over us. Furthermore, these changes increase our dependency on the remaining members of our leadership team and clinical and preclinical operations teams that remain with us, who are not contractually obligated to remain employed with us and may leave at any time. Any such departure could be particularly disruptive and, to the extent we experience additional turnover, competition for top talent is high such that it may take some time to find a candidate that meets our requirements. We may not be able to attract or retain qualified management and commercial, scientific, and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

If we lose additional members of our senior management team, our ability to successfully implement our business strategy could be seriously harmed. Replacing these employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate additional key personnel. We do not maintain "key person" insurance for any of our executives or other employees.

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

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act of 2002 and the rules and regulations of Nasdaq. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting and, in the past, we have also been required to have our independent registered public accounting firm issue an opinion on the effectiveness of our internal control over financial reporting on an annual basis as a large accelerated filer. However, based on our public float as of June 30, 2023, we qualified as a non-accelerated filer at the end of 2023, which

would allow us to forgo the auditor attestation requirement for the fiscal year ended December 31, 2023. However, we voluntarily complied with the auditor attestation requirement for the fiscal year ended December 31, 2023.

During the evaluation and testing process, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. Further, we may in the future discover weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Moreover, our internal controls over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. Moreover, we are aware that the increased prevalence of remote working arrangements potentially presents additional areas of risk, including cyber and privacy risks, and we are carefully monitoring any impact to our internal controls and procedures.

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

Risks Related to Ownership of Our Common Stock

If we fail to comply or regain compliance with the continued listing standards of the Nasdaq Capital Market, we may be delisted and the price of our common stock, our ability to access the capital markets and our financial condition could be negatively impacted.

Our common stock is currently listed on Nasdaq under the symbol "CARA." To maintain the listing of our common stock on the Nasdaq Capital Market, we are required to meet certain listing requirements, including, among others, maintaining a minimum closing bid price of $1.00 per share. On February 1, 2024, we received a letter from Nasdaq, notifying us that, for the previous 30 consecutive business day period prior to the date of the letter, the closing bid price for our common stock was below $1.00. In accordance with Nasdaq Listing Rule 5810(c)(3)(A) we were provided an initial period of 180 calendar days, or until July 30, 2024, to regain compliance with Nasdaq's bid price requirement. On July 31, 2024, we received the Extension Notice from the Listing Qualifications Department of Nasdaq informing us that Nasdaq granted us an additional 180 calendar days, or until January 27, 2025, to regain compliance with the minimum closing bid price requirement for continued listing on The Nasdaq Capital Market under the Rule. In connection with the Extension Notice, the listing of our common stock was transferred from the Nasdaq Global Market to the Nasdaq Capital Market, effective as of August 1, 2024. If we are not able to regain compliance within this additional compliance period offered by Nasdaq, we could be delisted, which would have a further material adverse effect on market prices of our common stock and stockholder liquidity. If at any time before January 27, 2025, the closing bid price of our common stock is at least $1.00 per share for a minimum of 10 consecutive business days, Nasdaq will provide written confirmation that we have achieved compliance with the Rule, unless Nasdaq staff exercises its discretion to extend this 10-day period pursuant to Nasdaq rules.

We intend to actively monitor the bid price of our common stock and will consider available options to regain compliance with the listing requirement. These options include, but are not limited to, effecting a reverse stock split, if necessary, to attempt to regain compliance. However, there can be no assurance that we will be able to regain compliance with the listing requirement or will otherwise be in compliance with other Nasdaq listing criteria. If the Nasdaq Capital Market delists our securities from trading on its exchange for failure to meet the listing standards, we and our stockholders could face significant negative consequences including: reducing the liquidity and market price of our common stock; reducing the number of investors willing to hold or acquire our common stock, which could negatively impact our ability to raise equity financing; decreasing the amount of news and analyst coverage of us; and limiting our ability to issue additional securities or obtain additional financing in the future. In addition, delisting from Nasdaq may negatively impact our reputation and, consequently, our business.

The market price of our common stock has been, and is likely to continue to be, highly volatile, and you may not be able to resell your shares at or above the price you paid for them.

Since our initial public offering in January 2014, our stock price has been volatile and it is likely that the trading price of our common stock will continue to be volatile. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the outcome of our exploration of strategic alternatives;
- actual or anticipated variations in quarterly or annual operating results;
- failure to meet or exceed financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community, including securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, or divestitures;
- introduction of competitive products or technologies;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- general trends in our industry or economic and market conditions and overall fluctuations in U.S. equity markets;
- developments concerning our sources of manufacturing supply, warehousing and inventory control;
- disputes or other developments relating to patents or other proprietary rights;
- additions or departures of key scientific or management personnel;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- capital commitments;
- investors' general perception of our company and our business;
- announcements and expectations of additional financing efforts, including the issuance of debt, equity or convertible securities or other security instruments;
- sales of our common stock, including sales by our directors and officers or significant stockholders;
- changes in the market valuations of companies similar to us;
- should we resume development activities in the future, (i) changes or developments in laws or regulations applicable to such product candidate;(ii) delays in the commencement, enrollment and ultimate completion of any clinical trials; (iii)results of any clinical trials or those of our competitors; or (iv)any delay or refusal on the part of the FDA or other regulatory authorities in approving marketing authorization for any potential product candidate;
- changes in the structure of healthcare payment systems; and

- the other factors described in this "Risk Factors" section.

In addition, the stock market in general, and the market for small pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors, such as those related to high rates of inflation and interest rates and concerns of a recession in the United States or other major markets, the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide, and geopolitical instability, including resulting from the ongoing conflicts between Russia and the Ukraine, conflicts in the Middle East, and increasing tensions between China and Taiwan, may negatively affect the market price of our common stock, regardless of our actual operating performance.

Further, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If equity research analysts cease to publish research or reports about us or if they publish unfavorable research or reports about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock is likely to be influenced by the research and reports that equity research analysts publish about us and our business. We do not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. Certain equity research analysts who covered us have ceased coverage, and if further analysts who cover us were to cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our operating results will be affected by numerous factors, including:

- our exploration of strategic alternatives to maximize stockholder value, including whether we are able to identify and implement any strategic alternatives, in a timely manner or at all, whether we realize all or any of the anticipated benefits of any such transaction and whether any such transactions would generate value for our stockholder;

- should we resume development of our product candidate or any future product candidate, the successful progress of any clinical trials for such product candidates;

- should we resume development of activities in the future, variations in the level of expenses related to our future development programs;

- should we resume development of our product candidate or any future product candidate, whether the FDA or other regulatory authorities require us to complete additional, unanticipated studies, tests or other activities prior to approving any product candidates, which would likely further delay any such approval;

- should we resume development of our product candidate or any future product candidate, our ability to identify, enter into and maintain third party manufacturing arrangements capable of manufacturing any potential product candidate in commercial quantities;

- our execution of other collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;

- any product liability or intellectual property infringement lawsuit in which we may become involved;

- regulatory developments affecting any potential product candidates, or the product candidates of our competitors; and

- if any potential product candidate receives regulatory approval, the level of underlying demand for such product and wholesaler buying patterns.

If our quarterly or annual operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly or annual fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Entry into an acquisition, merger, business combination, or other strategic transaction, or raising additional funds by issuing securities may cause dilution to existing stockholders and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

In June 2024, we announced that we are undertaking a comprehensive exploration of strategic alternatives focused on maximizing stockholder value. The terms of any strategic transaction that we might enter could result in the issuance of securities in the company, such as our common stock, which could result significant dilution to our stockholders. Additionally, in connection with such strategic alternatives, we may seek to finance our cash needs through a combination of equity offerings, debt financings, royalty arrangements, grants, license and development agreements in connection with any collaborations, and other financial instruments. We do not yet have any committed external source of funds. To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through strategic transactions, collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs, product candidate or grant licenses on terms that may not be favorable to us. Any debt financing that we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments.

The use of our net operating loss carryforwards and research tax credits may be limited.

A portion of our net operating loss, or NOL, carryforwards and R&D tax credits may expire and not be used. As of December 31, 2023, we had federal and state NOL carryforwards of approximately $467.0 million and $473.3 million, respectively, and we also had federal and state R&D tax credit carryforwards of approximately $27.5 million and $4.5 million, respectively. Our NOL carryforwards will begin expiring in 2026 for federal purposes (to the extent such federal NOLs are generated in taxable years beginning on or before December 31, 2017) and 2027 for state purposes if we have not used them prior to that time, and our federal R&D tax credits will begin expiring in 2025 unless previously used. The federal NOLs arising in 2018 and forward have an unlimited carryforward period and losses from 2018-2020 may be carried back five years due to the Coronavirus Aid, Relief, and Economic Security Act of 2020, or the CARES Act. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act of 2017, or TCJA, as modified by the CARES Act. To the extent that we have not exchanged our Connecticut R&D tax credits for a tax refund, those tax credits carry forward indefinitely. Additionally, our ability to use any NOL and R&D tax credit carryforwards to offset taxable income or tax, respectively, in the future will be limited under Internal Revenue Code Sections 382 and 383, respectively, if we have a cumulative change in ownership of our stock of more than 50% within a three-year period. The completion of our initial public offering in 2014 and our follow-on public offerings in 2015, 2017, 2018 and 2019, together with private placements and other transactions that have occurred, may have triggered such ownership changes. We conducted a 382 analysis in the first quarter of 2021. This analysis showed a limited change of ownership had occurred, and the amount of NOL carryforwards and R&D tax credits that could be utilized annually in the future to

offset taxable income or tax, respectively. In addition, since we will need to raise substantial additional funding to finance our operations, we may undergo ownership changes in the future. Any such annual limitation may significantly reduce the utilization of the NOL carryforwards and R&D tax credits before they expire. In addition, certain states have in the past suspended use of NOL carryforwards for certain taxable years (including Connecticut which currently limits the use of NOL carryforwards by 50% and California, which recently enacted legislation that temporarily suspends the use of California NOLs for three years beginning on or after January 1, 2024), and other states are considering similar measures. As a result, we may incur higher state income tax expense in the future. Depending on our future tax position, limitations on our ability to use NOL carryforwards in states in which we are subject to income tax could have an adverse impact on our results of operations and financial condition.

Changes to existing tax laws, or challenges to our tax positions could adversely affect our business and financial condition.

The tax regimes to which we are subject or under which we operate are unsettled and may be subject to significant change. The issuance of additional guidance related to existing or future tax laws, or changes to tax laws or regulations proposed or implemented by the current or a future U.S. presidential administration, Congress, or taxing authorities in other jurisdictions could materially affect our tax obligations. For example, beginning in 2022, the TCJA eliminated the option to deduct R&D expenditures in the year incurred and instead requires taxpayers to capitalize and subsequently amortize such expenditures over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. In January 2024, the U.S. House of Representatives passed the Tax Relief for American Families and Workers Act, which would retroactively repeal for 2022 and 2023, and defer until 2026, the requirement to capitalize R&D expenditures for research activities conducted in the United States. Uncertainty exists as to whether the bill will be enacted into law. In addition, U.S. federal, state and local tax laws are extremely complex and subject to various interpretations. Although we believe that our tax estimates and positions are reasonable, there can be no assurance that our tax positions will not be challenged by relevant tax authorities. If the relevant tax authorities assess additional taxes on us, this could result in adjustments to, or impact the timing or amount of, taxable income, deductions or other tax allocations, which may adversely affect our results of operations and financial position.

Because we do not intend to pay dividends on our common stock, your returns will be limited to any increase in the value of our stock.

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not anticipate declaring or paying any cash dividends on our common stock for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock, if any. Investors seeking cash dividends should not purchase our common stock.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws, as amended, that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our Board of Directors has the authority to issue up to 5,000,000 shares of preferred stock and to fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- our Board of Directors are divided into three classes, with only one class of directors elected each year;

- our stockholders are entitled to remove directors only for cause upon a 66 2/3% vote;
- our stockholders are not permitted to take actions by written consent;
- our stockholders are not permitted to call a special meeting of stockholders; and
- our stockholders must give us advance notice of their intent to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

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

None.

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

None.

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

Not applicable.

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

None.

Item 6. ***Exhibits.***

Exhibit No.	Description of Exhibit	Incorporated by Reference			
		Form	File No.	Exhibit No.	Date Filed
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-36279	3.1	February 7, 2014
3.2	Amended and Restated Bylaws.	8-K	001-36279	3.2	February 7, 2014
3.3	Certificate of Amendment to Amended and Restated Certificate of Incorporation.	8-K	001-36279	3.1	June 7, 2024
31.1†	Certification of Chief Executive Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
31.2†	Certification of Chief Financial Officer of Cara Therapeutics, Inc. pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934.				
32.1†*	Certifications of Chief Executive Officer and Chief Financial Officer of Cara Therapeutics, Inc. pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				
101.CAL†	Inline XBRL Taxonomy Extension Calculation Linkbase.				
101.INS†	Inline XBRL Instance Document.				
101.LAB†	Inline XBRL Taxonomy Extension Label Linkbase.				
101.PRE†	Inline XBRL Taxonomy Extension Presentation Linkbase.				
101.SCH†	Inline XBRL Taxonomy Extension Schema Linkbase.				
101.DEF†	Inline XBRL Taxonomy Extension Definition Linkbase Document.				
104†	Cover page interactive data file (formatted as Inline XBRL and contained in Exhibit 101).				

† Filed herewith.

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

SIGNATURES

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

CARA THERAPEUTICS, INC.

Date: August 14, 2024

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

Date: August 14, 2024

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

EXHIBIT 31.1

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

I, Christopher Posner, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 14, 2024

By: /s/ Christopher Posner
CHRISTOPHER POSNER
CHIEF EXECUTIVE OFFICER
(Principal Executive Officer)

EXHIBIT 31.2

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

I, Ryan Maynard, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: August 14, 2024

By: /s/ Ryan Maynard
RYAN MAYNARD
CHIEF FINANCIAL OFFICER
(Principal Financial Officer)

EXHIBIT 32.1

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

In connection with the Quarterly Report on Form 10-Q of Cara Therapeutics, Inc. (the "Company") for the quarter ended June 30, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Christopher Posner, Chief Executive Officer of the Company, and Ryan Maynard, Chief Financial Officer of the Company, each hereby certifies, pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), that, to the best of his knowledge, based upon a review of the Report:

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

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

/s/ CHRISTOPHER POSNER
Name: Christopher Posner
Title: Chief Executive Officer
(Principal Executive Officer)
Date: August 14, 2024

/s/ RYAN MAYNARD
Name: Ryan Maynard
Title: Chief Financial Officer
(Principal Financial Officer)
Date: August 14, 2024

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Cara Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.