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DELTA REPORT

10-Q

TRVI - TREVI THERAPEUTICS, INC.

10-Q - MARCH 31, 2024 COMPARED TO 10-Q - SEPTEMBER 30, 2023

The following comparison report has been automatically generated

TOTAL DELTAS	1512
CHANGES	146
DELETIONS	690
ADDITIONS	676

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, March 31, 2023 2024

OR

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

For the transition period from to

Commission File Number: 001-38886

TREVI THERAPEUTICS, INC.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**45-0834299**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
195 Church Street, 16th Floor New Haven, Connecticut	**06510**
(Address of principal executive offices)	**(Zip Code)**

(203) 304-2499

(Registrant's telephone number, including area code)

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

	Trading

Title of each class	Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	TRVI	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 ☒

As of November 9, 2023 May 7, 2024, the registrant had 63,857,622 70,435,093 shares of common stock, $0.001 par value per share, outstanding.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenues and profitability, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,”

“estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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

- our clinical trials, including our planned trials Phase 2b CORAL clinical trial of Haduvio for the treatment of chronic cough in idiopathic pulmonary fibrosis, or IPF, our Phase 2a RIVER clinical trial of Haduvio for the treatment of refractory chronic cough, or RCC, and our Phase 2b/3 PRISM 1b clinical trial to evaluate the effect of Haduvio for on respiratory physiology in patients with IPF of varying disease severity as well as our human abuse potential, or HAP, study to compare the treatment abuse potential of prurigo nodularis; oral nalbuphine to intravenous, or IV, butorphanol;
- our plans to develop and, if approved, subsequently commercialize Haduvio for the treatment of chronic cough in IPF and refractory chronic cough RCC and for the treatment of prurigo nodularis;
- our expectations regarding the timing for the initiation of clinical trials and the reporting of data from such trials;
- the timing of and our ability to submit applications for and to obtain and maintain regulatory approvals for Haduvio;
- our expectations regarding our ability to fund our operating expenses, including our ongoing and planned clinical trials, with our cash, cash equivalents and marketable securities;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and needs for additional financing;
- the impact of government laws and regulations;
- our competitive position; and
- our ability to establish and maintain collaborations.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Quarterly Report on Form 10-Q, particularly in the section titled “Risk Factors,” that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this Quarterly Report on Form 10-Q and the documents that we have filed as exhibits to this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may differ materially from what we expect. The forward-looking statements contained in this Quarterly Report on Form 10-Q are made as of the date of this Quarterly Report on Form 10-Q, and we do not assume any obligation to update any forward-looking statements except as required by applicable law.

This report includes statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties as well as our own estimates. All of the market data used in this report involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for Haduvio include several key assumptions based on our industry knowledge, industry publications, third-party

research, and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

We own or have rights to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. We own the trademarks Trevi® and Haduvio™. Other trademarks, service marks and trade names appearing in this Quarterly Report on Form 10-Q are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this Quarterly Report on Form 10-Q are listed without the ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names. We intend to propose Haduvio as the trade name for our oral nalbuphine ER investigational product.

RISK FACTOR SUMMARY

The following is a summary of the principal factors that make an investment in our company speculative or risky. This summary does not address all of the risks and uncertainties that we face. Additional risk risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Additional discussion of the risks summarized in this summary and other risks that we face, can be found in the “Risk Factors” section of this Quarterly Report on Form 10-Q and should be carefully considered, together with other information in this Quarterly Report on Form 10-Q and our other filings with the Securities and Exchange Commission, before making an investment decision regarding our common stock. The forward-looking statements discussed above are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

- We have incurred significant losses since inception and expect to continue to incur significant and increasing losses for the foreseeable future. We may never achieve or maintain profitability.
- We will need substantial additional funding. If we are unable to raise sufficient capital when needed on acceptable terms or a all, we could be forced to delay, reduce or abandon our product development programs or commercialization efforts.
- We are dependent on the successful development and commercialization of Haduvio, our sole product candidate. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize Haduvio or if we experience significant delays in doing so, our business would be substantially harmed.
- We are in the process of designing future clinical trials of Haduvio for the treatment of chronic cough in IPF and have initiated our Phase 2a RIVER trial of Haduvio for the treatment of refractory chronic cough. Before initiating the trials at sites in the U. we will need to submit an IND for Haduvio to the U.S. Food and Drug Administration, or FDA. Prior to initiating the trials at si outside the U.S., we will need to complete regulatory submissions in countries selected for the trials. Changes in the design ongoing or planned trials or regulatory Regulatory delays may affect the timing and costs of the our planned or ongoing clinic trials and changes in the timing or costs of the trials for these or other reasons may affect our ability to complete the planned or ongoing trials with our existing cash resources.

- The outcome of clinical trials may not be predictive of the success of later clinical trials. For instance, Haduvio may fail to sho the desired safety and efficacy in clinical development despite demonstrating positive results in earlier clinical trials. The resu of our Phase 2 clinical trial of Haduvio for the treatment of chronic cough in IPF, which we refer to as the Phase 2 CANAL tria may not be predictive of the results of future trials of Haduvio for the treatment of chronic cough in IPF or our Phase 2a RIVE clinical trial of Haduvio for the treatment of refractory other chronic cough and the results of our Phase 2b/3 PRISM trial in Haduvio for the treatment of prurigo nodularis may not be predictive of the results of any future trial in prurigo nodularis. indications such as RCC.
- We have experienced delays and difficulties in the enrollment of subjects patients in our clinical trials in the past, including in our Phase 2 CANAL trial and our Phase 2b/3 PRISM trial. If we experience delays or difficulties in the enrollment of subjects patients in current or future clinical trials, our receipt of necessary regulatory approvals could be delayed or prevente Other companies are conducting clinical trials or have announced plans for future clinical trials that are seeking or are likely t seek to enroll subjects patients with chronic cough with IPF, refractory chronic cough IPF, and prurigo nodularis, RCC, and subjects patients are generally only able to enroll in a single trial at a time. In addition, many patients use various treatments off-label to treat chronic cough associated with IPF refractory chronic cough and prurigo nodularis, RCC, and these patients and their physicians may be reluctant to forgo, discontinue or otherwise alter their use of such off-label therapeutic approach to participate in our clinical trials.
- Clinical drug development involves a lengthy and expensive process with an uncertain outcome. Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain, which may prevent us from obtaining approvals for the commercialization of Haduvio or any future product candidate.
- Adverse events or undesirable side effects caused by, or other unexpected properties of, Haduvio or any future project candidate may be identified during development and could delay or prevent the marketing approval or limit the use of Haduv or any future product. Haduvio, as a mixed κ-opioid receptor agonist and μ-opioid receptor antagonist, may be susceptible to side effects associated with drugs having either of those mechanisms of action, including psychiatric side effects, withdrawal effects, respiratory depression and potential cardiac risk, as well as endocrine side effects associated with opioids generally.
- The drug label for nalbuphine, the active ingredient in Haduvio, carries an opioid class label warning for serious, life-threatening or fatal respiratory depression and Haduvio, if approved for marketing in any indication, will likely carry a similar opioid class label. We intend to conduct a Phase 1b study of Haduvio to evaluate the effect of Haduvio on respiratory physiology in patients with IPF of varying disease severity. We cannot be certain that respiratory depression will not be observed or that the U.S. Food and Drug Administration, or FDA, will not require additional trials or impose more severe labeling restrictions related to respiratory depression. If there is a safety signal in the Phase 1b study, it could affect our abilit to conduct a trial in this patient population.
- Many currently approved μ-opioid products are subject to restrictive marketing and distribution regulations which, if applied t Haduvio, could potentially restrict its use and harm our ability to generate profits. We are conducting a human abuse

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potential, or HAP study to determine compare the abuse potential of oral nalbuphine ER relative to intravenous, or IV butorphanol. If the results of the HAP study suggest that Haduvio may carry risks of misuse, abuse or addiction or even if the trial indicates that Haduvio does not carry such risks, the FDA may require us to implement a Risk Evaluation and Mitigation Strategy in connection with any commercialization of Haduvio and the U.S. Drug Enforcement Agency could determine that Haduvio should be classified as a controlled substance.

- If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing Haduvio or any future product candidates if ar

when they are approved.

- We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do.
- We contract with third parties to conduct our clinical trials and for the manufacture, storage, packaging and distribution of Haduvio and other drug product for clinical trials, including a single supplier for the active ingredient in Haduvio. We expect t continue to rely on third parties for these services in connection with our future development and commercialization efforts fo Haduvio. If they do not perform satisfactorily, or if they experience delays or shortages, our business could be harmed.
- If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, including our license with Endo Pharmaceuticals Inc., we could lose license rights that are critical to our business or owe damages to the licensor of such intellectual property.
- If we are unable to obtain and maintain sufficient patent protection for Haduvio or any future product candidate and the disea indications for which we are developing or may in the future develop Haduvio or any other product candidate, or if the scope the patent protection is not sufficiently broad, competitors could develop and commercialize products similar or identical to such product candidate and our ability to successfully commercialize such product candidate may be adversely affected.
- The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity financings.

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PART I—FINANCIAL INFORMATION

Item 1. Condensed Consolidated Financial Statements.

Trevi Therapeutics, Inc.
Condensed Consolidated Balance Sheets
(Amounts in thousands, except share and per share amounts)

Assets	**September 30, 2023 (Unaudited)**	**December 31, 2022**	**March 31, 2024 Unaudited**	**December 31, 2023**
Current assets:				
Cash and cash equivalents	$ 25,965	$ 12,958	$ 13,811	$ 32,397
Marketable securities	62,903	107,921	59,009	50,574
Prepaid expenses	4,039	5,325	3,225	3,621
Other current assets	1,046	1,311	721	955

Total current assets	93,95 3	12 2,6 16	76,766	87,547
Operating lease right-of-use assets	1,1 90	24	1,084	1,137
Other non-current assets	29 7	20 5	311	297
Property, equipment and leasehold improvements, net	23 8	17 0	204	216
Finance lease right-of-use assets	21 8	—	194	206
Total assets	95,89 $ 6	12 3,0 $ 15	$ 78,559	$ 89,403
Liabilities and stockholders' equity				
Current liabilities:				
Accounts payable	1,2 $ 56	2,8 $ 57	$ 2,112	$ 1,809
Accrued expenses	3,6 25	3,5 18	2,842	3,709
Operating lease liabilities	17 1	25	198	184
Finance lease liabilities	12 1	—	124	122
Term loan	—	7,000		
Total current liabilities	5,173	13,040	5,276	5,824
Operating lease liabilities	1,051	2	949	1,001
Finance lease liabilities	62	—	—	31
Term loan	—	2,151		
Other non-current liabilities	—	3		

Total liabilities	6,286	15,556	6,225	6,856
Commitments and contingencies (Note 12)				
Stockholders' equity:				
Preferred stock: $0.001 par value; 5,000,000 shares authorized at September 30, 2023 and December 31, 2022; no shares issued or outstanding at September 30, 2023 and December 31, 2022.	—	—		
Common stock: $0.001 par value; 200,000,000 shares authorized at September 30, 2023 and December 31, 2022; and 63,855,330 and 59,943,430 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively.	64	60		
Preferred stock: $0.001 par value; 5,000,000 shares authorized at March 31, 2024 and December 31, 2023; no shares issued or outstanding at March 31, 2024 and December 31, 2023.			—	—
Common stock: $0.001 par value; 200,000,000 shares authorized at March 31, 2024 and December 31, 2023; and 68,960,167 and 68,283,699 shares issued and outstanding at March 31, 2024 and December 31, 2023, respectively.			69	68
Additional paid-in capital	321,076	317,590	322,368	321,642
Accumulated other comprehensive loss	(217)	(122)	(67)	(29)
Accumulated deficit	(231,306)	(210,139)	(250,036)	(239,134)
Total stockholders' equity	89,610	107,459	72,334	82,547
Total liabilities and stockholders' equity	95,896	123,015	$ 78,559	$ 89,403

The accompanying notes are an integral part of these condensed consolidated financial statements.

Trevi Therapeutics, Inc.
Condensed Consolidated Statements of Comprehensive Loss
(unaudited)
(Amounts in thousands, except share and per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,		Three Months Ended March 31,	
	2023	2022	2023	2022	2024	2023
Operating expenses:						
Research and development	6,323	$ 5,769	17,165	$ 15,517	$ 8,804	$ 5,000
General and administrative	2,722	2,636	7,825	7,733	3,102	2,563
Total operating expenses	9,045	8,405	24,990	23,250	11,906	7,563
Loss from operations	(9,045)	(8,405)	(24,990)	(23,250)	(11,906)	(7,563)
Other income (expense):						
Interest income, net	1,183	424	3,611	623	998	1,221
Other income, net	154	—	472	—		
Other (expense) income, net					(1)	165
Interest expense	(3)	(292)	(387)	(889)	(1)	(231)
Change in fair value of term loan derivative liability	—	—	—	(147)		
Total other income (expense), net	1,334	132	3,696	(413)		
Total other income, net					996	1,155
Loss before income taxes	(7,711)	(8,273)	(21,294)	(23,663)	(10,910)	(6,408)
Income tax benefit	13	7	50	16	8	7

Net loss	(7,69 $ 8)	(8,26 $ 6)	(21,2 $ 44)	(23,6 $ 47)	$ (10,902)	$ (6,401)
Basic and diluted net loss per common share outstanding	$ (0.08)	$ (0.12)	$ (0.21)	$ (0.44)	$ (0.11)	$ (0.06)
Weighted average common shares used in net loss per share attributable to common stockholders, basic and diluted	99,3 25,5 40	68,8 98,8 10	98,8 80,8 82	53,2 21,9 49	99,517,212	98,610,671
Net loss	(7,69 $ 8)	(8,26 $ 6)	(21,2 $ 44)	(23,6 $ 47)	$ (10,902)	$ (6,401)
Other comprehensive loss:						
Net unrealized gains (losses) on available-for-sale marketable securities	31	(128)	(95)	(263)		
Net unrealized (losses) gains on available-for-sale marketable securities					(38)	34
Comprehensive loss	(7,66 $ 7)	(8,39 $ 4)	(21,3 $ 39)	(23,9 $ 10)	$ (10,940)	$ (6,367)

The accompanying notes are an integral part of these condensed consolidated financial statements.

Trevi Therapeutics, Inc.

Condensed Consolidated Statements of Stockholders' Equity

(unaudited)

(Amounts in thousands, except share amounts)

	Common Stock Shares	Common Stock Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders’ Equity	Common Stock Shares	Common Stock Amount	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders’ Equity
Balance at June 30, 2023	63,098,455	$ 63	$ 318,873	$ (248)	$ (223,615)	$ 95,073						
Balance at December 31, 2023							68,283,699	$ 68	$ 321,642	$ (29)	$ (239,134)	$ 82,547
Stock-based compensation	—	—	530	—	—	530	—	—	723	—	—	723
Issuance of common stock from exercise of stock options	6,875	—	3	—	—	3	2,631	—	4	—	—	4

Issuance of common stock under the at-the-market sales agreement, net of commissions and allocated fees	7 5 0, 0 0 0		1, 6 7 0			1 , 6 7 1						
Issuance of common stock from pre-funded warrant exercise				673,837	1	(1)	—	—	—			
Unrealized losses on available-for-sale marketable securities				—	—	—	(38)	—	(38)			
Net loss				—	—	—	—	(10,902)	(10,902)			
Balance at March 31, 2024				68,960,167	$ 69	$ 322,368	$ (67)	$ (250,036)	$ 72,334			
Balance at December 31, 2022				59,943,430	$ 60	$ 317,590	$ (122)	$ (210,069)	$ 107,459			
Stock-based compensation				—	—	578	—	—	578			
Issuance of common stock from exercise of stock options				121,978	—	62	—	—	62			

Unrealized gains on available-for-sale marketable securities	—	—	—	31	—	31	—	—	—	34	—	34
Net loss	—	—	—	—	(7,698)	(7,698)	—	—	—	—	(6,401)	(6,401)
Balance at September 30, 2023	63,855,330	$ 64	$ 321,076	$ (217)	$ (231,313)	$ 89,610						
Balance at June 30, 2022	39,719,572	$ 40	$ 256,908	$ (135)	$ (196,298)	$ 60,515						
Stock-based compensation	—	—	569	—	—	569						
Issuance of common stock from exercise of stock options	51,005	—	139	—	—	139						

Issuance of common stock and warrants in public offering, less issuance costs	14,252,670	14	51,170	—	—	51,184
Issuance of common stock from warrant exercise	4,299,270	4	5,886	—	—	5,890
Unrealized losses on available-for-sale marketable securities	—	—	—	(128)	—	(128)
Net loss	—	—	—	—	(8,266)	(8,266)
Balance at September 30, 2022	58,322,517	$ 58	$ 314,672	$ (263)	$ (204,564)	$ 109,903
Balance at March 31, 2023	60,065,408	$ 60	$ 318,230	$ (88)	$ (216,470)	$ 101,732

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2022	59,943,430	$ 60	$ 317,590	$ (122)	$ (210,069)	$ 107,459
Stock-based compensation	—	—	1,713	—	—	1,713
Issuance of common stock from exercise of stock options	143,789	—	73	—	—	73
Issuance of common stock under the at-the-market sales agreement, net of commissions and allocated fees	750,000	1	1,670	—	—	1,671
Issuance of common stock from Employee Stock Purchase Plan	19,273	—	33	—	—	33
Issuance of common stock from pre-funded warrant exercise	2,998,838	3	(3)	—	—	—
Unrealized losses on available-for-sale marketable securities	—	—	—	(95)	—	(95)
Net loss	—	—	—	—	(21,244)	(21,244)
Balance at September 30, 2023	63,855,330	$ 64	$ 321,076	$ (217)	$ (231,313)	$ 89,610
Balance at December 31, 2021	28,505,804	$ 29	$ 197,963	$ —	$ (180,917)	$ 17,075
Stock-based compensation	—	—	1,826	—	—	1,826
Issuance of common stock from exercise of stock options	51,005	—	139	—	—	139
Issuance of common stock under the at-the-market sales agreement, net of commissions and allocated fees	—	—	(42)	—	—	(42)
Issuance of common stock from Employee Stock Purchase Plan	33,972	—	23	—	—	23
Issuance of common stock and warrants in public offering, less issuance costs	18,833,196	19	102,991	—	—	103,010

Issuance of common stock from warrant exercise	10,898,540	10	11,772	—	—	11,782
Unrealized losses on available-for-sale marketable securities	—	—	—	(263)	—	(263)
Net loss	—	—	—	—	(23,647)	(23,647)
Balance at September 30, 2022	58,322,517	$ 58	$ 314,672	$ (263)	$ (204,564)	109,903

The accompanying notes are an integral part of these condensed consolidated financial statements.

Trevi Therapeutics, Inc.
Condensed Consolidated Statements of Cash Flows
(unaudited)
(Amounts in thousands)

	Nine Months Ended September 30,		Three Months Ended March 31,	
	2023	2022	2024	2023
Operating activities:				
Net loss	$ (21,244)	$ (23,647)	$ (10,902)	$ (6,401)
Adjustments to reconcile net loss to net cash used in operating activities:				
Stock-based compensation	1,713	1,826	723	578
Operating lease right-of-use assets	259	100	120	—
Depreciation and amortization			35	19
Accretion of available-for-sale marketable securities, net			(381)	(671)
Accretion/accrual of term loan discounts and debt issuance costs	180	419	—	81
Depreciation and amortization	88	28		
Loss on disposal of property, equipment and leasehold improvements	10	—	—	10
Accretion of available-for-sale marketable securities, net	(1,774)	(268)		

Change in fair value of term loan derivative liability	—	147		
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(2,935)	(579)	584	(836)
Accounts payable	(1,676)	(527)	294	(914)
Accrued expenses and other liabilities	28	657	(940)	(63)
Net cash used in operating activities	(25,351)	(21,844)	(10,467)	(8,197)
Investing activities:				
Proceeds from maturities of available-for-sale marketable securities	55,679	2,001	22,173	18,000
Purchases of available-for-sale marketable securities	(8,981)	(61,025)	(30,264)	(8,981)
Purchases of property, equipment and leasehold improvements	(115)	(43)	—	(57)
Net cash provided by (used in) investing activities	46,583	(59,067)		
Net cash (used in) provided by investing activities			(8,091)	8,962
Financing activities:				
Proceeds from at-the-market sales, net of commissions	1,710	—		
Proceeds from exercises of stock options	73	139	4	62
Proceeds from employee stock purchase plan	33	23		
Repayments of term loan, term loan final fee and prepayment premium	(9,409)	(4,083)		
Payments of finance lease			(32)	—
Repayments of term loan			—	(1,750)
Payments of offering costs	(200)	(195)	—	(15)
Payments of finance lease	(63)	—		
Proceeds from sale of common stock and warrants in public offering and private placement, net of issuance costs	—	103,010		
Proceeds from exercises of warrants	—	11,782		
Payments of financing costs of term loan	—	(21)		
Net cash (used in) provided by financing activities	(7,856)	110,655		
Net increase in cash and cash equivalents	13,376	29,744		
Net cash used in financing activities			(28)	(1,703)

Net decrease in cash and cash equivalents			(18,586)	(938)
Cash and cash equivalents at beginning of period	12,589	36,830	32,397	12,589
Cash and cash equivalents at end of period	$ 25,965	$ 66,574	$ 13,811	$ 11,651

The accompanying notes are an integral part of these condensed consolidated financial statements.

Trevi Therapeutics, Inc.
Notes to Condensed Consolidated Financial Statements
(unaudited)
(in thousands, except share and per share data)

1. Nature of the Business

Trevi Therapeutics, Inc. ("Trevi" or the "Company") is a clinical-stage biopharmaceutical company focused on the development and commercialization of the investigational therapy Haduvio (oral nalbuphine ER) for the treatment of chronic cough in idiopathic pulmonary fibrosis ("IPF") and refractory chronic cough and for the treatment of prurigo nodularis. cough. These conditions share a common pathophysiology that is mediated through opioid receptors in the central and peripheral nervous systems. Due to nalbuphine's mechanism of action as a modulator of opioid receptors, the Company believes Haduvio has the potential to be effective in treating each of these conditions.

Haduvio is an oral extended-release formulation of nalbuphine. Nalbuphine is a mixed κ-opioid receptor agonist and μ-opioid receptor antagonist that has been approved and marketed as an injectable for pain indications for more than 20 years in the United States ("U.S.") and Europe. The κ- and μ-opioid receptors are known to be critical mediators of cough and itch. Nalbuphine's mechanism of action also mitigates the risk of abuse associated with μ-opioid agonists because it antagonizes, or blocks, the μ-opioid receptor. Parenteral nalbuphine is not scheduled as a controlled substance in the U.S. and most of Europe.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited interim Condensed Consolidated Financial Statements for the three and nine months ended September 30, 2023 March 31, 2024 and 2022 2023 included herein have been prepared in accordance with accounting principles generally accepted in the U.S. ("GAAP") for interim financial information and the rules and regulations of the Securities and Exchange Commission ("SEC") for interim information. Certain information and footnote disclosures typically prepared in accordance with GAAP have been condensed or omitted pursuant to SEC rules and regulations. The accompanying unaudited Condensed Consolidated Financial Statements and notes should be read in conjunction with the audited consolidated financial statements and related notes included in the Company's Annual Report on Form 10-K for the year ended December 31,

2022 December 31, 2023. Certain prior year balances have been reclassified to conform to the current year presentation. Such reclassifications did not affect loss from operations or net loss.

The accompanying Condensed Consolidated Financial Statements include the accounts of Trevi Therapeutics, Inc. and its wholly-owned subsidiary Trevi Therapeutics Limited. Intercompany balances and transactions have been eliminated.

All amounts presented are in thousands of dollars, except share and per share amounts, unless noted otherwise. The Company has evaluated events occurring subsequent to September 30, 2023 March 31, 2024 for potential recognition or disclosure in the Condensed Consolidated Financial Statements and concluded there were no subsequent events that required recognition or disclosure. disclosure other than those provided in Note 8.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amounts of the expenses during the reporting periods. Significant estimates and assumptions reflected in these Condensed Consolidated Financial Statements include but are not limited to the recognition of research and development ("R&D") expenses, the valuation of stock-based awards and the valuation allowance of deferred tax assets. In addition, management's assessment of the Company's ability to continue as a going concern involves the estimation of the amount and timing of future cash inflows and outflows. Changes in estimates are recorded in the period in which they become known. Actual results could differ from those estimates.

Unaudited Interim Financial Information

The accompanying interim Condensed Consolidated Balance Sheet as of September 30, 2023, March 31, 2024 and the Condensed Consolidated Statements of Comprehensive Loss, and the Condensed Consolidated Statements of Stockholders' Equity for the three and nine months ended September 30, 2023 and 2022 and the Condensed Consolidated Statements of Cash Flows for the nine three months ended September 30, 2023 March 31, 2024 and 2022 2023 are unaudited. The unaudited interim Condensed Consolidated Financial Statements have been prepared on the same basis as the audited annual consolidated financial statements and, in the Company's opinion, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statements of its financial position as of September 30, 2023 March 31, 2024 and the results of its operations and its cash flows for the three and nine months ended September 30, 2023 March 31, 2024 and 2022. 2023. The results for the three and nine months ended September 30, 2023 March 31, 2024 and 2022 2023 are not necessarily indicative of results to be expected for the year ending December 31, 2023 December 31, 2024 or any other interim period or any future year or period.

Cash Equivalents

The Company classifies short-term, highly liquid investments with an original term of three months or less at the date of purchase as cash equivalents.

Marketable Securities

The Company generally invests its excess cash in money market funds and investment grade short- to intermediate-term fixed income securities. Such investments are included in cash and cash equivalents or marketable securities on the Condensed Consolidated Balance Sheets. Marketable securities with an original maturity date greater than 90 days at each balance sheet date are classified as

short-term. Marketable securities are classified as current assets as these investments are intended to be available to the Company for use in funding current operations. All of the Company's marketable securities are considered available-for-sale and are reported at fair value value. For securities with unrealized gains and losses, when the Company expects to receive cash flows sufficient to recover the amortized cost basis of a security, such gains and losses are included in accumulated other comprehensive income as a component of stockholders' equity. Credit losses are identified when the Company does not expect to receive cash flows sufficient to recover the amortized cost basis of a security. In the event of a credit loss, only the amount associated with the credit loss is recognized in interest income, net on the Condensed Consolidated Statements of Comprehensive Loss. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income, net on the Condensed Consolidated Statements of Comprehensive Loss. Realized gains and losses, and declines in value judged to be other than temporary, if any, on marketable securities are included in interest income, net on the Condensed Consolidated Statements of Comprehensive Loss. The cost of securities sold is determined using specific identification.

The Company evaluates whether declines in the fair values of its marketable securities below their amortized cost are other than temporary credit losses on a quarterly basis. This evaluation consists of several qualitative and quantitative factors regarding the severity and duration of the unrealized loss, as well as the Company's ability and intent to hold the marketable security until a forecasted recovery occurs. Additionally, the Company assesses whether it has plans to sell the marketable security or whether it is more likely than not that it will be required to sell any marketable securities before recovery of its amortized cost basis. Factors considered include quoted market prices, recent financial results and operating trends, implied values from any recent transactions or offers of investee securities, credit quality of debt instrument issuers, other publicly available information that may affect the value of the marketable security, duration and severity of the decline in value, and the Company's strategy and intentions for holding the marketable security.

Fair Value Measurements

The Company's financial instruments have consisted of cash and cash equivalents, available-for-sale marketable securities, other current assets, accounts payable, accrued expenses, term loans and warrants to acquire the Company's common stock. Fair value estimates of these instruments are made at a specific point in time, based on relevant market information. The carrying amounts of cash and cash equivalents, other current assets, accounts payable and accrued expenses are generally considered to be representative of their respective fair values because of the short-term nature of those instruments. Available-for-sale marketable securities are reported at their fair values, based upon pricing of securities with the same or similar investment characteristics as provided by third-party pricing services, as described below. The carrying amount of the term loan approximates its fair value due to its floating market-based interest rate. The fair value of the term loan derivative liability is estimated utilizing a probability-weighted cash flow approach. The warrants to acquire the Company's common stock are not required to be accounted for at fair value.

Current accounting guidance defines fair value, establishes a framework for measuring fair value in accordance with Accounting Standards Codification ("ASC") 820, *Fair Value Measurements and Disclosures,* and requires certain disclosures about fair value measurements. The valuation techniques included in the guidance are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect market assumptions and are classified into the following fair value hierarchy:

Level 1—Observable inputs—quoted prices in active markets for identical assets and liabilities.

Level 2—Observable inputs other than the quoted prices in active markets for identical assets and liabilities—such as quoted prices for similar instruments, quoted prices for identical or similar instruments in inactive markets, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs—includes amounts derived from valuation models where one or more significant inputs are unobservable and require the company to develop relevant assumptions.

Valuation Techniques - Level 2 Inputs

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

Property, Equipment and Leasehold Improvements

Property, equipment and leasehold improvements (consisting of furniture, computer and office equipment and leasehold improvements) are stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the respective assets (three years for computer equipment, five years for furniture and office equipment, and the shorter of the term of the lease or useful life for leasehold improvements).

Foreign Currency Transactions

The Company, at times, contracts with vendors and consultants outside of the U.S., resulting in liabilities denominated in foreign currency. The transactions are recorded in U.S. dollars on the transaction dates and any currency fluctuation through the

payment date is recorded as currency gains or losses in other income, net in the Condensed Consolidated Statements of Comprehensive Loss.

Deferred Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of an equity financing, these costs are recorded in stockholders' equity as a reduction of additional paid-in capital generated as a result of the financings. Should the planned equity financing no longer be considered probable of being consummated, the deferred offering

costs are expensed immediately as a charge to general and administrative expenses. The deferred offering costs are included in Other current and non-current assets on the Condensed Consolidated Balance Sheets.

Research and Development ("R&D") Expenses

All of the Company's R&D expenses consist of expenses incurred in connection with the development of Haduvio. These expenses include certain payroll and personnel expenses, including stock-based compensation, consulting costs, contract manufacturing costs and fees paid to contract research organizations ("CROs") to conduct certain R&D activities on the Company's behalf. The Company expenses both internal and external R&D expenses as they are incurred.

Accrued R&D Expenses

The Company has entered into agreements with CROs, contract manufacturing organizations ("CMOs") and other companies that provide services in connection with the Company's R&D activities. The Company's R&D accruals are estimated based on the level of services performed, progress of the studies, including the phase or completion of events and contracted costs. The estimated costs of R&D provided, but not yet invoiced, are included in accrued expenses on the Condensed Consolidated Balance Sheets. If the actual timing of the performance of services or the level of effort varies from the original estimates, the Company will adjust the accrual accordingly. Payments made to CROs, CMOs and other companies under these arrangements in advance of the performance of the related services are recorded as prepaid expenses or as other non-current assets, as applicable, and are recognized as expenses as the goods are delivered or the related services are performed.

Patent Costs

All patent-related costs in connection with filing and prosecuting patent applications are expensed to general and administrative expense as incurred, as recoverability of such expenditures is uncertain.

Warrants

The Company determines the accounting classification of warrants that are issued, as either liability or equity, by first assessing whether the warrants meet liability classification in accordance with ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480"), and then in accordance with ASC 815, *Derivatives and Hedging* ("ASC 815"), depending on the specific terms of the warrant. Under ASC 480, warrants are considered liability classified if the warrants are mandatorily redeemable, obligate the issuer to settle the warrants or the underlying shares by paying cash or other assets, or must or may require settlement by issuing variable number of shares.

If the warrants do not meet liability classification under ASC 480, the Company assesses the requirements under ASC 815, which states that contracts that require or may require the issuer to settle the contract for cash are liabilities recorded at fair value, irrespective of the likelihood of the transaction occurring that triggers the net cash settlement feature. If the warrants do not require liability classification under ASC 815, in order to conclude equity classification, the Company assesses whether the warrants are indexed to its common stock and whether the warrants are classified as equity under ASC 815 or other applicable GAAP. After all relevant assessments are made, the Company concludes whether the warrants are classified as liability or equity. Liability classified warrants are required to be accounted for at fair value both on the date of issuance and on subsequent accounting period ending dates, with all changes in fair value after the issuance date recorded in the statements of comprehensive loss as a gain or loss. For equity classified warrants, no changes in fair value are recognized after the issuance date.

Stock-Based Compensation

The Company accounts for stock-based compensation arrangements with employees and non-employees for consultancy services in accordance with ASC 718, *Stock Compensation* (“ASC 718”). ASC 718 requires the recognition of compensation expense, using a fair-value based method, for costs related to all stock-based awards including stock options. The Company’s determination of the fair value of stock-based awards on the date of grant utilizes the Black-Scholes valuation model for stock options with time-based and performance-based vesting and is impacted by the price of its common stock as well as changes in assumptions regarding a number of subjective variables. These variables include the expected term that stock options will remain outstanding, expected common stock price volatility over the term of the stock options, risk-free interest rates and expected dividends.

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Changes in the variables can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require analysis and judgment to develop.

Expected Term—The expected term assumption represents the weighted average period that the stock-based awards are expected to be outstanding. The Company has elected to use the “simplified method” for estimating the expected term of its stock options, whereby the expected term equals the arithmetic average of the vesting term and the original contractual term of the stock option.

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Expected Volatility—For all stock options granted to date, the volatility data was estimated based on a study of publicly traded industry peer companies. For purposes of identifying these peer companies, the Company considered the industry, stage of development, size and financial leverage of potential comparable companies.

Expected Dividend—The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company currently has no history or expectation of paying cash dividends on its common stock.

Risk-Free Interest Rate—The risk-free interest rate is based on the yield available on U.S. Treasury zero-coupon issues similar in duration to the expected term of the stock-based award.

The fair value is recognized over the period during which an optionee is required to provide services in exchange for the stock option, known as the requisite service period (usually the vesting period) on a straight-line basis. For performance-based vesting, the fair value is recognized when it is probable the performance conditions will be achieved. The Company reassesses the probability of achieving the performance conditions at each reporting date. Forfeitures are accounted for as they occur.

Income Taxes

The Company accounts for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are determined based on differences between the financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

The Company applies the provisions of ASC 740, *Income Taxes* (“ASC 740”), which prescribes a comprehensive model for how a company should recognize, measure, present and disclose in its financial statements uncertain tax positions that the Company company has taken or expects to take on a tax return. These Condensed Consolidated Financial Statements reflect expected future tax consequences of such positions presuming the taxing authorities possess full knowledge of the position and all relevant facts. There are no material uncertainties regarding the tax positions that the Company has taken through September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023. The Company does not have any interest or penalties accrued related to tax positions as it does not have any unrecognized tax benefits.

Leases

Under ASC 842, *Leases* (“ASC 842”), the Company determines if an arrangement is a lease at its inception. Leases are classified as either operating or finance, based on the Company’s evaluation of certain criteria. If a lease has a term greater than one year, the lease is recognized in the balance sheet as a right-of-use asset and a lease liability at lease commencement. The Company elected the short-term lease practical expedient, therefore, if a lease has a term less than one year, the Company will not recognize the lease on its balance sheet. The right-of-use asset represents the Company’s right of use to an underlying asset for the term of the lease and the lease liability represents the Company’s obligation to make lease payments arising from the lease. If the Company’s leases do not provide an implicit rate within the lease, the Company uses its incremental borrowing rate, based on information available at the commencement date of the lease to determine the present value of the lease payments.

Operating lease right-of-use assets and operating lease liabilities are determined and recognized on the commencement date of the lease based on the present value of lease payments over the term of the lease. For operating leases, rent expense is recognized on a straight-line basis over the term of the lease, and right-of-use assets are subsequently re-measured to reflect the effect of uneven lease payments.

For finance leases, right-of-use assets are amortized on a straight-line basis over the shorter of the lease term or the useful life of the underlying asset. Expenses for finance leases include the amortization of right-of-use assets, which is recorded as depreciation and amortization expense, and interest expense, which reflects interest accrued on the lease liability.

Basic and Diluted Net Loss per Common Share

Basic and diluted net loss per common share outstanding is determined by dividing net loss by the weighted average common shares outstanding during the period. Basic shares outstanding includes the weighted average effect of the Company’s outstanding pre-funded warrants, the exercise of which requires little or no consideration for the delivery of shares of common stock.

For all periods presented, shares issuable upon exercise of stock options and warrants to purchase shares of common stock (other than pre-funded warrants) have been excluded from the calculation because their effects would be anti-dilutive. Therefore, the

weighted average common shares used to calculate both basic and diluted net loss per share are the same for each of the periods presented.

Segments

The Company has one reporting segment which is also the Company's only operating segment. Management uses one measurement of profitability and does not segregate its business for internal reporting. All long-lived assets are maintained in the U.S.

Recently Adopted Accounting Pronouncements

There have been no new pronouncements adopted during the nine three months ended September 30, 2023 March 31, 2024.

Recently Issued Accounting Pronouncements

There have been no new pronouncements 8

In November 2023, the Financial Accounting Standards Board ("FASB") issued during the nine months ended September 30, 2023 Accounting Standards Update ("ASU") 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, which could requires public entities to disclose information about their reportable segments' significant expenses and other segment items on an interim and annual basis. Public entities with a single reportable segment are required to apply the disclosure requirements in ASU 2023-07, as well as all existing segment disclosures and reconciliation requirements in ASC 280, *Segment Reporting*, on an interim and annual basis. ASU 2023-07 is effective for fiscal years beginning after December 15, 2023, and for interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact of adopting ASU 2023-07.

In December 2023, the FASB issued ASU 2023-09, *Improvements to Income Tax Disclosures*, which requires entities to disclose disaggregated information about their effective tax rate reconciliation as well as expanded information on income taxes paid by jurisdiction. The disclosure requirements will be expected applied on a prospective basis, with the option to materially apply them retrospectively. The standard is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. The Company is currently evaluating the impact the Company's Condensed Consolidated Financial Statements. of adopting ASU 2023-09.

3. Marketable Securities

The fair value and amortized cost of available-for-sale marketable securities by major security type as of September 30, 2023 and December 31, 2022 are presented in the following table (in thousands): tables as of the periods presented:

	September 30, 2023				March 31, 2024			
Type of security	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate bonds	54,1 $ 52	$ 18	$ (218)	53,95 $ 2	$ 37,888	$ 13	$ (36)	$ 37,865

U.S. government agency securities	4,993	—	(15)	4,978	11,904	—	(18)	11,886
Commercial paper	1,994	—	—	1,994				
U.S. treasury securities					5,621	1	(17)	5,605
Asset backed securities	1,981	—	(2)	1,979	3,663	—	(10)	3,653
Total marketable securities	63,120	$ 18	$ (235)	62,903	$ 59,076	$ 14	$ (81)	$ 59,009

	December 31, 2022				December 31, 2023			
Type of Security	**Amortized Cost**	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Estimated Fair Value**	**Amortized Cost**	**Gross Unrealized Gains**	**Gross Unrealized Losses**	**Estimated Fair Value**
Corporate bonds	62,573	$ 83	$ (143)	62,513	$ 45,686	$ 20	$ (53)	$ 45,653
Commercial paper	30,739	—	—	30,739				
U.S. treasury securities	9,914	—	(62)	9,852				
U.S. government agency securities	2,905	2	(4)	2,903	4,917	9	(5)	4,921
Asset backed securities	1,912	2	—	1,914				
Total marketable securities	108,043	$ 87	$ (209)	107,921	$ 50,603	$ 29	$ (58)	$ 50,574

The net amortized cost and fair value of available-for-sale marketable securities at September 30, 2023 and December 31, 2022, respectively, are shown below presented in the following table as of the periods presented by contractual maturity. Actual maturities may differ from contractual maturities because securities may be restructured, called or prepaid, or the Company may intend to sell a security prior to maturity.

	September 30, 2023		March 31, 2024	
	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Due to mature:				
Less than one year	$ 57,666	$ 57,469	$ 52,313	$ 52,269
One year through two years	5,454	5,434	6,763	6,740
Total	$ 63,120	$ 62,903	$ 59,076	$ 59,009

	December 31, 2022		December 31, 2023	
	Amortized Cost	Fair Value	Amortized Cost	Fair Value
Due to mature:				
Less than one year	$ 69,527	$ 69,367	$ 49,651	$ 49,618
One year through two years	38,516	38,554	952	956
Total	$ 108,043	$ 107,921	$ 50,603	$ 50,574

During the three and nine months ended September 30, 2023 March 31, 2024 and 2022, 2023, there were no realized gains or losses on available-for-sale marketable securities.

10 During the three months ended March 31, 2024 and 2023, no marketable securities had been in a continuous unrealized loss position for more than 12 months and the Company considered all losses to be temporary in nature. The Company reviewed the securities in the tables above and considered the decline in market value for these securities to be primarily attributable to economic and market conditions. As of the periods noted in the tables above, the Company did not intend to sell these securities and did not believe it was more likely than not that it would be required to sell these securities before recovery of their amortized cost basis.

Accordingly, the Company did not recognize any credit losses related to its marketable securities in an unrealized loss position during any of the periods noted in the table above.

4. Fair Value Measurements

The following table summarizes the Company's financial assets and financial liabilities measured at fair value on a recurring basis as of September 30, 2023 and December 31, 2022, and the basis for that measurement, by level within the fair value hierarchy: hierarchy, as follows:

Balance Sheet Classification	Type of Instrument	Fair Value Measurement Using: Level 1	Level 2	Level 3	Total	Type of Instrument	Fair Value Measurement Using: Level 1	Level 2	Level 3	Total
September 30, 2023										
March 31, 2024										
Financial assets:										
Cash equivalents	Money market funds	$ 25,771	$ —	$ —	$ 25,771	Money market funds	$ 13,036	$ —	$ —	$ 13,036
Marketable securities	Corporate bonds	—	53,995	—	53,995	Corporate bonds	—	37,865	—	37,865
Marketable securities	U.S. government agency securities	—	48	—	48	U.S. government agency securities	—	11,886	—	11,886
Marketable securities	Commercial paper	—	1,999	—	1,999	U.S. treasury securities	—	5,605	—	5,605

Marketable securities	Asset backed securities	—	1,997	—	1,997	Asset backed securities	—	3,653	—	3,653
Total assets		25,791	2,979		28,770		$ 13,036	$ 59,009	$ —	$ 72,045
		$ 5	$ 3	$ —	$ 8					

Balance Sheet Classification	Type of Instrument	Fair Value Measurement Using: Level 1	Level 2	Level 3	Total	Type of Instrument	Fair Value Measurement Using: Level 1	Level 2	Level 3	Total
December 31, 2022										
December 31, 2023										
Financial assets:										
Cash equivalents	Money market funds	11,581			11,581	Money market funds				
		$ 9	$ —	$ —	$ 9		$ 30,404	$ —	$ —	$ 30,404
Marketable securities	Corporate bonds		62,551		62,551	Corporate bonds				
		—	3	—	3		—	45,653	—	45,653
Marketable securities	Commercial paper		30,739		30,739	U.S. government agency securities				
		—	9	—	9		—	4,921	—	4,921

Marketable securities	U.S. treasury securities	9,852	—	—	9,852				
Marketable securities	U.S. government agency securities	—	2,990	—	2,990				
Marketable securities	Asset backed securities	—	1,991	—	1,991				
Total assets		$ 1,842,461	$ 8,981	$ —	$ 1,851,442		$ 30,404	$ 50,574	$ —	$ 80,978

5. Leases

The Company entered into a lease for office space in New Haven, Connecticut, effective March 1, 2013, and entered into a First Amendment (the “First Amendment”) to such lease on December 5, 2017 and a Second Amendment (the “Second Amendment”) to such lease on November 21, 2022 (collectively, the “Office Space Lease”). The leased space approximated 5,600 square feet and, prior to the Second Amendment, the Office Space Lease had a term of 60 months expiring on February 28, 2023. Under the First Amendment, the Company was required to make monthly payments ranging from approximately $10 to $12 through February 1, 2023 and received two designated months of free rent. As a result of the Company entering into the Second Amendment, the leased space increased to 12,500 square feet effective in March 2023 and the term for the Office Space Lease was extended for an additional 60 months from its prior termination date, until February 28, 2028. The Second Amendment requires monthly payments ranging from approximately $23 to $32 effective in March 2023 through February 2028. The first year of payments are based on 10,500 square feet of occupied space, the second year of payments are based on 11,500 square feet of occupied space and the remaining lease payments are based on 12,500 square feet of occupied space.

In December 2022, the Company entered into a 24-month month lease for the financing of the furniture installed in the Company’s new office space. The furniture lease requires monthly payments of approximately $11 starting in March 2023. The Company also entered into an immaterial office equipment lease during 2022 that has a term of 36 months.

The following table presents the Company’s Company's lease-related assets and liabilities as of September 30, 2023 and December 31, 2022: presented on its Condensed Consolidated Balance Sheets:

	Classification on the Condensed Consolidated Balance Sheet	March 31, 2024	December 31, 2023
Assets:			
Operating lease assets	Operating lease right-of-use assets	$ 1,084	$ 1,137
Finance lease assets	Finance lease right-of-use assets	194	206
Total lease assets		$ 1,278	$ 1,343
Liabilities:			
Current			
Operating lease liabilities	Operating lease liabilities, current portion	$ 198	$ 184
Finance lease liabilities	Finance lease liabilities, current portion	124	122
Non-current			
Operating lease liabilities	Operating lease liabilities, non-current portion	949	1,001
Finance lease liabilities	Finance lease liabilities, non-current portion	—	31
Total lease liabilities		$ 1,271	$ 1,338

	Classification on the Condensed Consolidated Balance Sheet	September 30, 2023	December 31, 2022
Assets:			
Operating lease assets	Operating lease right-of-use assets	$ 1,190	$ 24
Finance lease assets	Finance lease right-of-use assets	218	—
Total lease assets		$ 1,408	$ 24
Liabilities:			
Current			
Operating lease liabilities	Operating lease liabilities, current portion	$ 171	$ 25
Finance lease liabilities	Finance lease liabilities, current portion	121	—
Non-current			
Operating lease liabilities	Operating lease liabilities, non-current portion	1,051	2
Finance lease liabilities	Finance lease liabilities, non-current portion	62	—
Total lease liabilities		$ 1,405	$ 27

The following table presents information related to the Company's lease expense for the three and nine months ended September 30, 2023 and 2022: periods shown:

	Three Months Ended	Nine Months Ended

	September 30,		September 30,	
	2023	2022	2023	2022
Operating lease expense	$ 85	$ 31	$ 202	$ 92
Finance lease expense	12	—	24	—
Total lease expense	$ 97	$ 31	$ 226	$ 92

	Three Months Ended March 31,	
	2024	2023
Operating lease expense	$ 85	$ 31
Finance lease expense	12	—
Total lease expense	$ 97	$ 31

Future minimum lease payments from September 30, 2023 March 31, 2024 until the expiration of the leases are as follows:

	Operating Leases	Finance Leases	Operating Leases	Finance Leases
2023	$ 69	$ 32		
2024	303	126	$ 234	$ 95
2025	349	32	349	32
2026	368	—	368	—
2027	377	—	377	—
Thereafter	95	—		
2028			95	—
Total minimum lease payments	1,561	190	1,423	127
Less: Amount of lease payments representing interest	(339)	(7)	(276)	(3)
Present value of future minimum lease payments	$ 1,222	$ 183	$ 1,147	$ 124

The following table presents certain information related to the lease terms and discount rates for the Company's leases as of September 30, 2023 and December 31, 2022: Company's leases:

	September 30, 2023	December 31, 2022	March 31, 2024	December 31, 2023
Weighted average remaining lease term:				
Operating leases	4.5 years	0.3 years	3.6 years	4.3 years
Finance leases	1.5 years	not applicable	1.0 years	1.3 years

Weighted average discount rate:				
Operating leases	11.00%	13.00%	11.00%	11.00%
Finance leases	4.37%	not applicable	4.37%	4.37%

The following table presents supplemental cash flow information related to the Company's leases for the periods shown:

	Three Months Ended September 30,		Nine Months Ended September 30,		Three Months Ended March 31,	
	2023	2022	2023	2022	2024	2023
Cash paid for amounts included in the measurement of lease liabilities:						
Operating cash outflows relating to operating leases	$ 69	$ 36	$ 162	$ 5	$ 69	$ 24
Finance lease payments	$ 32	$ —	$ 63	$ —	$ 32	$ —
Supplemental non-cash information:						
Right-of-use assets obtained in exchange for new operating lease liabilities	$ —	$ 4	$ 9	$ 4	$ —	$ 1,289
Right-of-use assets obtained in exchange for new finance lease liabilities	$ —	$ —	$ 242	$ —	$ —	$ 242

6. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2023	December 31, 2022	March 31, 2024	December 31, 2023
Accrued R&D projects	$ 1,842	$ 1,130	$ 1,069	$ 1,579
Accrued compensation and benefits	1,221	1,508	906	1,614
Accrued consulting and professional fees	490	382	808	510
Accrued other	72	498	59	6
Total accrued expenses	$ 3,625	$ 3,518	$ 2,842	$ 3,709

7. Debt

Silicon Valley Bank Term Loan

On May 9, 2023, the Company paid the remaining amount due under the SVB Loan Agreement, (as described below), resulting in the full extinguishment of the SVB Term Loan as (as described below. below). As a result, after May 9, 2023, the Company had no outstanding debt. The total payoff amount was $6.5 million, consisting of the remaining principal amount due of $5.2 million, the final payment fee of

$1.2 million, and $0.1 million $0.1 million of accrued interest and prepayment premium.

On March 10, 2023 During the year ended December 31, 2023, Silicon Valley Bank ("SVB") an immaterial effect from early extinguishment of debt was closed by recorded in connection with the California Department of Financial Protection and Innovation and Company paying the Federal Deposit Insurance Corporation ("FDIC") remaining amounts due under the SVB Loan Agreement, which was appointed as receiver. While SVB was included in other income, net on the Company's primary bank at the time Condensed Consolidated Statement of its closure, the vast majority of the Company's total cash, cash equivalents and marketable securities resided in custodial accounts held by U.S. Bank for which SVB Asset Management was the advisor. The FDIC subsequently transferred all of SVB's deposits and loans to a newly created bridge bank, named Silicon Valley Bridge Bank, N.A., under a systemic risk exception approved by the United States Department of the Treasury, the Board of Governors of the Federal Reserve, and the FDIC. On March 27, 2023, First Citizens Bank & Trust Company ("First Citizens Bank") assumed all of SVB's deposits and certain other liabilities and acquired substantially all of SVB's loans and certain other assets from the FDIC. As a result, all of the Company's deposits that were at SVB and the Company's SVB Term Loan were then moved to First Citizens Bank. The Company has access to all cash, cash equivalents and marketable securities that had been in its SVB accounts, and does not expect losses or material disruptions to the Company's ongoing operations due to SVB's closure. Comprehensive Loss.

On August 13, 2020 (the "Effective Date"), the Company entered into a loan and security agreement (the "SVB Loan Agreement") with SVB, Silicon Valley Bank ("SVB"), as lender, pursuant to which SVB provided a term loan to the Company in the original principal amount of $14.0 million (the "SVB Term Loan"). The SVB Term Loan bore interest at a floating rate per annum equal to the greater of (A) the prime rate plus 1.00% and (B) 4.25%. If SVB received evidence satisfactory to it that the Company had (i) received positive data for the Phase 2b/3 clinical trial of Haduvio sufficient to advance Haduvio into a second Phase 3 clinical trial for prurigo nodularis, and (ii) raised sufficient financing to fund such Phase 3 clinical trial and the Company's operations, (together, the "Phase 3 Event"), the interest rate under the SVB Term Loan would have been adjusted to a floating rate equal to the greater of (A) the prime rate plus 3.00% and (B) 6.25% (see term loan derivative liability discussion below). Commencing on March 1, 2022 and on the first business day of each month thereafter, the Company was required to make monthly interest payments and to repay the SVB Term Loan in 24 consecutive installments of principal plus monthly payments of accrued interest. All outstanding principal and accrued and unpaid interest under the SVB Term Loan and all other outstanding obligations with respect to the SVB Term Loan were due and payable in full on February 1, 2024. The SVB Loan Agreement permitted voluntary prepayment of all, but not less than all, of the SVB Term Loan, subject to a prepayment premium. Such prepayment premium would have been 3.00% of the principal amount of the SVB Term Loan if prepaid prior to the first anniversary of the Effective Date, 2.00% of the principal amount of the SVB Term Loan if prepaid on or after the first anniversary of the Effective Date but prior to the second anniversary of the Effective Date, and 1.00% of the principal amount of the SVB Term Loan if prepaid

on or after the second anniversary of the Effective Date but prior to February 1, 2024. Upon repayment in full of the SVB Term Loan, the Company was required to pay a final payment fee equal to $1.2 million. The SVB Term

Loan and related obligations under the SVB Loan Agreement were secured by substantially all of the Company's properties, rights and assets, except for its intellectual property (which was subject to a negative pledge under the SVB Loan Agreement).

On July 6, 2021, the Company and SVB entered into a First Amendment (the "Loan Amendment") to the SVB Loan Agreement. The Loan Amendment modified the conditions under which the Company was required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement. Under the Loan Amendment, if the Company failed to receive positive data in its Phase 2b/3 PRISM trial or to raise by June 30, 2022 sufficient net proceeds from the sale of equity securities to finance its planned second Phase 3 clinical trial of Haduvio for prurigo nodularis and its ongoing operations (each a "Milestone Condition"), the Company would have been required to deposit unrestricted and unencumbered cash equal to 100% of all outstanding amounts owed to SVB in a cash collateral account with SVB, which could have been used by SVB to prepay the SVB Term Loan at any time. In addition, the Loan Amendment provided that if the Company failed to maintain at least $20.0 million in unrestricted and unencumbered cash in its accounts with SVB at any time prior to the satisfaction of all the Milestone Conditions (the "Minimum Required Cash"), the Company would have been required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement. The Company would also have been required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement if it did not raise at least $15.0 million in net proceeds from the sale of equity securities during the period from June 1, 2021 through October 31, 2021. The Company satisfied this equity funding condition through a combination of equity issuances under the Company's at-the-market ("ATM") Sales Agreement sales agreement entered into with SVB Securities LLC (formerly SVB Leerink LLC) ("SVB Securities") in June 2020 (the "ATM Sales Agreement") and two private placements, which took place in October 2021 (see Note 8).

On April 6, 2022, the Company and SVB entered into a Third Amendment (the "Third Amendment") to the SVB Loan Agreement. The Third Amendment principally modified the conditions under which the Company would have been required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement. Under the terms of the Third Amendment, if the Company raised $45.0 million in net proceeds from the sale of equity securities (the "2022 Equity Event"), the Company's obligations to achieve the Milestone Conditions and maintain the Minimum Required Cash would have terminated and the sole remaining trigger for cash collateralization would have been if the Company did not receive positive final data by December 31, 2022 from either its Phase 2b/3 PRISM trial of Haduvio for prurigo nodularis or its Phase 2 CANAL trial of Haduvio for the treatment of chronic cough in IPF. In addition, the Third Amendment modified the interest rate on the principal amount outstanding under the SVB Loan Agreement. As a result of the Third Amendment, amounts outstanding under the SVB Loan Agreement accrued interest at a floating per annum rate equal to (i) prior to the occurrence of the 2022 Equity Event, the greater of (A) the prime rate plus 1.00% and (B) 4.25%, and (ii) upon and after the occurrence of the 2022 Equity Event, the greater of (A) the prime rate plus 3.00% and (B) 6.25%. The closing of the April 2022 Private Placement, as discussed in Note 8 below, constituted the 2022 Equity Event and thereby terminated the Company's obligations to achieve the Milestone Conditions and maintain the Minimum Required Cash. On August 3, 2022, SVB confirmed that the reported data from the Phase 2b/3 PRISM trial satisfied the requirement for positive final data and that the cash collateralization requirements of the SVB Loan Agreement were no longer in effect.

The SVB Loan Agreement contained customary representations, warranties, events of default and covenants. The occurrence and continuation of an event of default could have caused interest to be charged at the rate that was otherwise

applicable plus 5.00% (unless SVB elected to impose a smaller increase) and would have provided SVB with the right to accelerate all obligations under the SVB Loan Agreement and exercise remedies against the Company and the collateral securing the SVB Term Loan and other

obligations under the SVB Loan Agreement, including foreclosure against assets securing the SVB Term Loan and other obligations under the SVB Loan Agreement, including the Company's cash. The SVB Loan Agreement also restricted the payment of dividends on the Company's common stock.

In August 2020, in connection with the SVB Term Loan, the Company paid $57 in financing costs to a third-party, which were recorded as deferred charges and were amortized over the life of the SVB Term Loan using the effective interest method. In connection with the Loan Amendment, the Company paid $68 in financing costs to a third-party, which were recorded as deferred charges and were amortized over the life of the SVB Term Loan using the effective interest method. In connection with the Third Amendment, the Company paid $21 in financing costs to a third party, which were recorded as deferred charges and were amortized over the life of the SVB Term Loan using the effective interest method.

In August 2020, in connection with the execution of the SVB Loan Agreement, the Company paid $27 in financing costs to SVB, which were recorded as loan discounts. These loan discounts were included as a reduction in the balance of the term loan payable on the Company's Condensed Consolidated Balance Sheets and were accreted over the life of the SVB Term Loan using the effective interest method.

In connection with the SVB Loan Agreement, the Company was obligated to pay a final payment fee of $1.2 million upon repayment in full of the SVB Term Loan. The final payment fee was accrued over the life of the SVB Term Loan using the effective interest method and was included as an increase in the balance of the term loan payable on the Company's Condensed Consolidated Balance Sheets. The Company paid this final payment fee of $1.2 million on May 9, 2023 in connection with the payoff in full of the SVB Term Loan.

Prior to the Third Amendment, the SVB Loan Agreement provided that upon SVB receiving evidence satisfactory to it that the Company had (i) received positive data for the Phase 2b/3 PRISM trial sufficient to advance Haduvio into a second Phase 3 clinical trial for prurigo nodularis and (ii) raised sufficient financing to fund such Phase 3 clinical trial and the Company's operations, the interest rate on the SVB Term Loan would increase by 2.00% (the "Contingent Interest Rate Increase") as described above. The Contingent Interest Rate Increase represented a free-standing financial instrument. Accordingly, the Company accounted for the Contingent Interest Rate Increase as a derivative under ASC 815, *Derivatives and Hedging* and therefore, recorded a term loan derivative liability for the Contingent Interest Rate Increase at its fair value of $187 on the Effective Date of the SVB Loan Agreement. The Company adjusted this liability to fair value at each reporting date it remained outstanding, with such adjustments recorded as non-cash charges in other income (expense), net in the Company's Condensed Consolidated Statements of Comprehensive Loss. The term loan derivative liability was previously presented as a current liability on the Company's Condensed Consolidated Balance Sheets. Upon recording such term loan derivative liability, the Company also recorded an offsetting term

loan discount – interest, that was amortized to interest expense in the Company's Condensed Consolidated Statements of Comprehensive Loss through the SVB Term Loan's maturity date using the effective interest method. Upon entering into the Third Amendment, the Contingent Interest Rate Increase became effective and the Company recorded an increase to the total fair value of the term loan derivative liability in 2022. The term loan derivative liability was then settled and reclassified to both current and non-current interest payable, which were presented as accrued liabilities and other non-current liabilities on the Company's Condensed Consolidated Balance Sheet.

During the nine months ended September 30, 2023, an immaterial effect from early extinguishment of debt was recorded in connection with the Company paying the remaining amounts due under the SVB Loan Agreement, which was included in other income, net on the Company's Condensed Consolidated Statements of Comprehensive Loss.

As of September 30, 2023, the Company had no outstanding borrowings, and as of December 31, 2022, the Company had outstanding borrowings of $8.2 million under the SVB Term Loan. The term loan payable balance as presented on the Company's Condensed Consolidated Balance Sheets as of September 30, 2023 was $0 and as of December 31, 2022 was as shown below.

	December 31, 2022
Principal outstanding under term loan	$ 8,167
Term loan discount-interest	(24)
Term loan discount-unamortized deferred charges	(29)
Term loan discount-financing costs, net of accretion	(3)
Term loan-final payment fee	1,040
	9,151
Less current portion	7,000
Term loan payable, non-current	$ 2,151

Interest expense on the SVB Term Loan, which is was comprised of interest payments, accretion and amortization of term loan discounts and the accrual of the final payment fee, is shown below for the three and nine months ended September 30, 2023 and 2022, respectively. March 31, 2023. For the three and nine months ended September 30, 2022 March 31, 2023, the weighted average interest rate applicable to borrowings under the SVB Term Loan was 6.97% and 5.27%, respectively. For the nine months ended September 30, 2023, the weighted average interest rate applicable to borrowings under the SVB Term Loan was 10.25 10.68%.

	Three Months Ended September 30,		Nine Months Ended September 30,		Three Months Ended March 31,
	2023	2022	2023	2022	2023
Interest payments		17	20	47	
	$ —	$ 0	$ 2	$ 0	$ 150
Accrual of the final payment			15	30	
fee	—	89	0	9	59

Accretion and amortization of term loan discounts	—	33	30	11 0	22
		29	38	88	
	$ —	$ 2	$ 2	$ 9	$ 231

8. Stockholders' Equity

As of September 30, 2023 and December 31, 2022, the The Company had reserved shares of common stock for future issuance as shown in the table below:

	September 30, 2023	December 31, 2022
Shares of common stock reserved for future issuance upon exercise of outstanding warrants and pre-funded warrants	45,330,707	48,330,707
Shares of common stock reserved for future issuance under the 2019 Stock Incentive Plan	6,549,024	4,553,202
Shares of common stock reserved for future issuance under the 2019 Employee Stock Purchase Plan	1,208,274	701,232
Shares of common stock reserved for future issuance under the 2012 Stock Incentive Plan	568,243	602,231
Shares of common stock reserved for future issuance upon sales under the LPC Purchase Agreement	—	30,000,000
	53,656,248	84,187,372

	March 31, 2024	December 31, 2023
Shares of common stock reserved for future issuance upon exercise of outstanding warrants and pre-funded warrants	40,257,447	40,931,506
Shares of common stock reserved for future issuance under the 2019 Stock Incentive Plan	8,683,520	6,549,183
Shares of common stock reserved for future issuance under the 2019 Employee Stock Purchase Plan	1,177,456	1,177,456
Shares of common stock reserved for future issuance under the 2012 Stock Incentive Plan	534,447	565,792
	50,652,870	49,223,937

At-the-Market Offering

In June 2020, the Company entered into the ATM Sales Agreement with SVB Securities under which the Company was able to issue and sell shares of its common stock, from time to time, having an aggregate offering price of up to $12.0 million. In May 2022, the Company and SVB Securities amended the ATM Sales Agreement to increase the maximum aggregate offering price of common stock that it was able to issue and sell from time to time under the ATM Sales Agreement by $50.0 million, from $12.0 million to up to $62.0 million.

Sales of common stock under the ATM Sales Agreement were able to be made by any method that was deemed an “at-the-market” offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. The Company was not obligated to make any sales of its common stock under the ATM Sales Agreement. The Company began making sales pursuant to the ATM Sales Agreement in July 2020. As of September 30, 2023 August 15, 2023, the date of termination of the ATM Sales Agreement, the Company had issued and sold an aggregate of 4,333,394 shares of common stock for gross proceeds of $12.7 million pursuant to the ATM Sales Agreement, before deducting estimated commissions and allocated fees of $1.0 million.

In June 2023, the Company filed with the SEC a universal shelf registration statement on Form S-3 (the “Shelf Registration Statement”), which allows the Company to offer and sell up to $200.0 200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The Shelf Registration Statement was filed to replace the Company’s prior universal shelf registration statement on Form S-3 and was declared effective on August 15, 2023. Further, in June 2023, the Company entered into a new ATM at-the-market sales agreement with Leerink Partners, LLC (formerly SVB Securities) (the “New “2023 ATM Sales Agreement”), under which the Company may issue and sell shares of common stock, from time to time by any method that is deemed an “at-the-market” offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. The Company is not obligated to make any sales of its common stock under the New 2023 ATM Sales Agreement. The Company filed a prospectus under the Shelf Registration Statement for the offer and sale of shares of the Company’s common stock having an aggregate offering price of up to $75.0 million pursuant to the New 2023 ATM Sales Agreement. In accordance with the terms of the New 2023 ATM Sales Agreement, the ATM Sales Agreement terminated upon effectiveness of the Shelf Registration Statement, at which point the Company was no longer able to issue and sell shares of its common stock under the ATM Sales Agreement. As of September 30, 2023 March 31, 2024, the Company had not made any sales pursuant to the New 2023 ATM Sales Agreement.

Equity Purchase Agreement

On June 18, 2021 Subsequent to March 31, 2024, and through May 7, 2024, the Company entered into a common stock purchase agreement (“LPC Purchase Agreement”) with Lincoln Park Capital Fund, LLC (“Lincoln Park”). The LPC Purchase Agreement provided that, subject to the terms issued and conditions therein, the Company had the right, but not the obligation, to sell, at its discretion, to Lincoln Park up to $ sold 15.0 million of shares of common stock over a 24-month period commencing on July 23, 2021. The Company issued 170,088 1,474,926 shares of common stock to Lincoln Park as consideration for Lincoln Park’s commitment to purchase shares gross proceeds of the Company’s common stock $5.0 million, before deducting estimated commissions and allocated fees of $0.2 million under the LPC Purchase 2023 ATM Sales Agreement. As of July 23, 2023, no shares had been sold to Lincoln Park and the LPC Purchase Agreement terminated by its terms.

Private Placements

On October 5, 2021, the Company issued and sold to an initial investor, in a private placement priced at-the-market under Nasdaq rules, (i) 2,373,201 shares of the Company’s common stock and accompanying warrants to purchase an aggregate of 4,746,402 shares of the Company’s common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 4,926,069 shares of the Company’s common stock and accompanying warrants to purchase an aggregate of 9,852,138 shares of the

Company's common stock. Each share of the Company's common stock and accompanying common stock warrants were sold together at a combined price

of $1.62, and each pre-funded warrant and accompanying common stock warrants were sold together at a combined price of $1.619, for gross proceeds of approximately $11.8 million. Each pre-funded warrant had an exercise price of $0.001 per share, became exercisable immediately upon issuance and was exercisable until exercised in full. Of the accompanying common stock warrants, warrants to purchase an aggregate of 7,299,270 shares will expire on April 5, 2025, and warrants to purchase an aggregate of 7,299,270 shares will expire on October 5, 2028. The accompanying common stock warrants have an exercise price of $1.37 per share and became exercisable immediately upon issuance. Of the accompanying common stock warrants, warrants to purchase an aggregate of 7,299,270 shares had an expiration date of April 5, 2025, and warrants to purchase an aggregate of 7,299,270 shares had an expiration date of October 5, 2028. All of the accompanying common stock warrants expiring on April 5, 2025 have been exercised and accompanying common stock warrants to purchase 1,299,270 shares expiring on October 5, 2028 have been exercised.

On October 18, 2021, the Company issued and sold to New Enterprise Associates 16, L.P., an existing stockholder of the Company ("NEA") and related party, in a private placement, 1,851,852 shares of the Company's common stock and accompanying warrants to purchase an aggregate of 3,703,704 shares of the Company's common stock. Each share of the Company's common stock and accompanying common stock warrants were sold together at a combined price of $1.62 for gross proceeds of approximately $3.0 million. The accompanying common stock warrants have an exercise price of $1.37 per share and became exercisable immediately upon issuance. Of the accompanying common stock warrants, warrants to purchase an aggregate of 1,851,852 shares of the Company's common stock will expire on April 18, 2025, and warrants to purchase an aggregate of 1,851,852 shares of the Company's common stock will expire on October 18, 2028. The None of the accompanying common stock warrants expiring on April 18, 2025 and October 18, 2028, have an exercise price of $ been exercised. 1.37 per share and became exercisable immediately upon issuance.

Total net proceeds from the two October 2021 private placements were $13.7 million, after deducting issuance costs of $1.1 million.

On April 6, 2022, the Company entered into a securities purchase agreement with certain purchasers, pursuant to which the Company agreed to issue and sell to the purchasers, in a private placement priced at-the-market under Nasdaq rules, (i) 4,580,526 shares of the Company's common stock at a purchase price of $1.90 per share, and (ii) pre-funded warrants to purchase up to an aggregate of 24,379,673 shares of common stock at a purchase price of $1.899 per warrant (the "April 2022 Private Placement"). Each pre-funded warrant has an exercise price of $0.001 per share, is became exercisable immediately upon issuance and will be exercisable until the pre-funded warrant is exercised in full. The April 2022 Private Placement, which closed on April 11, 2022, resulted in gross proceeds to the Company of approximately $55.0 million. NEA, an existing stockholder of the Company and a related party, as well as an affiliate of NEA, participated in the offering.

Public Offering

On September 27, 2022, the Company issued and sold 14,252,670 shares of the Company's common stock and, in lieu of common stock to certain investors, pre-funded warrants to purchase 14,247,330 shares of common stock in a public offering (the "September 2022 Offering"), at a public offering price of $1.93 per share of common stock and $1.929 per pre-funded warrant

pursuant to an underwriting agreement (the “Underwriting Agreement”) with SVB Securities, Stifel, Nicolaus & Company, Incorporated and Oppenheimer & Co. Inc., as representatives of the several underwriters (the “Underwriters”). Each pre-funded warrant has an exercise price of $0.001 per share, is became exercisable immediately upon issuance and will be exercisable until the pre-funded warrant is exercised in full. Under the terms of the Underwriting Agreement, the Company agreed not to issue and sell additional shares until after November 21, 2022 except in certain circumstances, including the issuance and sale of additional shares pursuant to the Underwriting Agreement. Under the terms of the Underwriting Agreement, the Company granted the Underwriters an option (the “Option”), exercisable for 30 days, to purchase up to an additional 4,275,000 shares of common stock (the “Additional Shares”), at the public offering price of $1.93 per share. The Underwriters partially exercised the Option to purchase 1,600,428 Additional Shares, which shares were issued and sold on October 25, 2022. The September 2022 Offering, including the initial closing on September 27, 2022 and the Option closing on October 25, 2022, resulted in aggregate gross proceeds to the Company of approximately $58.1 million.

Warrants

Warrant activity, including activity related to pre-funded warrants, for the nine months ended September 30, 2023, is shown in the table below:

	Number of Pre-funded Warrant Shares	Number of Common Stock Warrant Shares	Total Number of Warrant Shares	Weighted Average Exercise Price
Outstanding as of December 31, 2022	38,627,003	9,703,704	48,330,707	$ 0.28
Exercised	(3,000,000)	—	(3,000,000)	$ 0.001
Outstanding as of September 30, 2023	35,627,003	9,703,704	45,330,707	$ 0.29

	Number of Pre-funded Warrant Shares	Number of Common Stock Warrant Shares	Total Number of Warrant Shares	Weighted Average Exercise Price
Outstanding as of December 31, 2023	31,227,802	9,703,704	40,931,506	$ 0.33
Exercised	(674,059)	—	(674,059)	$ 0.001
Outstanding as of March 31, 2024	30,553,743	9,703,704	40,257,447	$ 0.33

The pre-funded and common stock warrants are classified as equity in accordance with ASC 815 given that the pre-funded and common stock warrants are indexed to the Company’s own shares of common stock and meet the requirements to be classified in permanent equity.

Stock-Based Awards

The 2012 Stock Incentive Plan (the “2012 Plan”) was adopted by the Company’s board of directors and stockholders. The 2012 Plan provides for the issuance of stock-based awards to the Company’s employees, officers, directors, consultants and advisors. The Company’s board of directors administers the 2012 Plan. In April 2019, the Company’s board of directors adopted a resolution effective May 7, 2019, that no further equity-based awards may be granted under the 2012 Plan.

In April 2019, the Company’s board of directors adopted the 2019 Stock Incentive Plan (the “2019 Plan”), which became effective on May 7, 2019. The 2019 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The Company’s employees, officers, directors, consultants and advisors are eligible to receive awards under the 2019 Plan. The 2019 Plan is administered by the Company’s board of directors.

The total number of shares of common stock that may be issued under the 2019 Plan and the 2012 Plan was 7,117,267 9,217,967 as of September 30, 2023 March 31, 2024, of which 1,801,724 1,395,262 shares remained available for grant under the 2019 Plan. Awards may be made under the 2019 Plan for up to such number of shares of the Company’s common stock as is equal to the sum of: i) 1,578,947 shares; plus ii) the number of shares (up to 1,157,894 shares) of the Company’s common stock subject to outstanding awards under the 2012 Plan that expire, terminate or are otherwise cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right; plus iii) an annual increase to be added on the first day of each fiscal year, beginning with 2020 and continuing through 2029, equal to the least of (a) 2,105,623 shares of common stock, (b) 4% of the number of outstanding shares of the Company’s common stock on such date, and (c) an amount determined by the Company’s board of directors. Effective January 1, 2023 January 1, 2024 and January 1, 2022 January 1, 2023, respectively, the number of shares reserved for issuance under the 2019 Plan increased, pursuant to the terms of the 2019 Plan, by an additional 2,105,623 shares and 1,140,232 shares, in each case, equal to the 2019 Plan determined maximum and 4% of the Company’s then-outstanding common stock, respectively. for each year.

Options granted under the 2019 Plan and the 2012 Plan have a maximum term of ten years. Options granted to employees, officers and non-employees generally vest over four years based on varying vesting schedules that primarily include: 25% vesting on the first anniversary date of grant and the balance ratably over the next 36 months or vesting in equal monthly or quarterly installments over four years. Options granted to directors generally vest over one to two years. The Company generally settles stock option exercises with newly issued shares of common stock. As of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, respectively, options to purchase 4,747,300 7,288,258 shares and 3,848,052 4,746,508 shares of common stock were granted and outstanding, net of cancellations, under the 2019 Plan. As of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, respectively, options to purchase 568,243 534,447 and 602,231 565,792 shares of common stock were granted and outstanding, net of cancellations, under the 2012 Plan.

In February 2024, the Company granted 832,250 stock options subject to performance-based vesting (“PSOs”) to employees of the Company. The PSOs granted in February 2024 vest based on the timing and results of the Company’s clinical trials.

A summary of the Company’s combined stock option activity for the 2019 Plan and the 2012 Plan for the nine months ended September 30, 2023 is as follows:

	Number of Option Shares	Weighted Average Exercise Price	Number of Option Shares	Weighted Average Exercise Price
Outstanding as of December 31, 2022	4,450,283	$ 3.26		
Outstanding as of December 31, 2023			5,312,300	$ 3.24
Granted	1,562,000	$ 2.62	2,541,750	$ 2.38
Forfeited	(318,075)	$ 1.77		
Expired	(234,876)	$ 3.23	(28,714)	$ 3.23
Exercised	(143,789)	$ 0.51	(2,631)	$ 1.43
Outstanding as of September 30, 2023	5,315,543	$ 3.24		
Options exercisable as of September 30, 2023	2,607,790	$ 4.32		
Options unvested as of September 30, 2023	2,707,753	$ 2.20		
Forfeited			—	$ —
Outstanding as of March 31, 2024			7,822,705	$ 2.96
Options exercisable as of March 31, 2024			3,264,598	$ 3.92
Options unvested as of March 31, 2024			4,558,107	$ 2.27

In April 2019, the Company's board of directors adopted the 2019 Employee Stock Purchase Plan (the "2019 ESPP"), which became effective on May 7, 2019. The 2019 ESPP is administered by the Company's board of directors.

The total number of shares of common stock that may be issued under the 2019 ESPP was 1,208,274 1,177,456 as of September 30, 2023. March 31, 2024, all of which remain available for issuance. The number of shares of the Company's common stock that have been approved to be issued under the 2019 ESPP is equal to the sum of i) 155,106 shares plus ii) an annual increase to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2020 and continuing for each fiscal year until and including, the fiscal year ending December 31, 2029, equal to the least of (a) 526,315 shares of common stock, (b) 1% of the number of outstanding shares of the Company's common stock on such date and (c) an amount determined by the Company's board of directors. Effective January 1, 2023 and January 1, 2022, respectively, the aggregate number of shares of the Company's common stock that may be issued under the 2019 ESPP increased, pursuant to the terms of the 2019 ESPP, by an additional 526,315 shares, and 285,058 shares, equal to the 2019 ESPP determined maximum and 1% of for the Company's then-outstanding common stock, respectively year. No increase was made on January 1, 2024.

The following table summarizes the classifications of stock-based compensation expenses for the 2012 Plan, the 2019 Plan and the 2019 ESPP recognized in the Condensed Consolidated Statements of Comprehensive Loss:

	Three Months Ended September 30,		Nine Months Ended September 30,		Three Months Ended March 31,	
	2023	2022	2023	2022	2024	2023
General and administrative expense	$ 319	$ 371	$ 1,056	$ 1,195	$ 425	$ 365
Research and development expense	211	198	657	631	298	213
	$ 530	$ 569	$ 1,713	$ 1,826		
Total stock-based compensation expenses					$ 723	$ 578

9. Income Taxes

As of September 30, 2023 March 31, 2024 and December 31, 2022 December 31, 2023, the Company maintained a full valuation allowance on deferred tax assets. The income tax benefit recorded during the three and nine months ended September 30, 2023 March 31, 2024 and 2022 2023 was for the Company’s estimates for its state research and development tax credits in each given year.

10. Net Loss per Share

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company:

Three Months Ended September 30,		Nine Months Ended September 30,		Three Months Ended March 31,	
2023	2022	2023	2022	2024	2023

Net loss	(7,69	(8,26	(21,2	(23,6		
	$ 8)	$ 6)	$ 44)	$ 47)	$ (10,902)	$ (6,401)
Weighted average common shares used in net loss per share attributable to common stockholders, basic and diluted	99,32	68,89	98,88	53,22	99,517,212	98,610,671
	5,540	8,810	0,882	1,949		
Basic and diluted net loss per common share outstanding	(0.	(0.	(0.	(0.		
	$ 08)	$ 12)	$ 21)	$ 44)	$ (0.11)	$ (0.06)

Basic shares outstanding includes the weighted average effect of the Company's pre-funded warrants from the date of issuance, the exercise of which requires little or no consideration for the delivery of shares of common stock. As of September 30, 2023 March 31, 2024 and December 31, 2023, the Company had pre-funded warrants to purchase 21,379,673 30,553,743 and 14,247,330 31,227,802 shares of common stock outstanding, respectively, which were issued in the April 2022 Private Placement and the September 2022 Offering, which warrants are included in the weighted average common shares used in calculating the net loss per share attributable to common stockholders, basic and diluted, for the three and nine months ended September 30, 2023 March 31, 2024 and 2022, respectively. 2023.

The Company's potential dilutive securities, which include stock options and warrants that are not pre-funded, have been excluded from the computation of diluted net loss per share attributable to common stockholders whenever the effect of including them would be to reduce the net loss per share. In periods where there is a net loss, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The following potential common shares, presented based on shares outstanding as of September 30, 2023 March 31, 2024 and 2022, 2023, respectively, were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Shares as of September 30,		Shares as of March 31,	
	2023	2022	2024	2023
Warrants	9,703,704	9,703,704	9,703,704	9,703,704
Stock Options	5,315,543	4,141,907	7,822,705	5,361,019
	15,019,247	13,845,611		
Total potential common shares			17,526,409	15,064,723

11. Collaborative and Licensing Agreements

The Company enters into collaborative and licensing agreements with pharmaceutical companies to in-license, develop, manufacture and/or market products that fit within its business strategy.

Endo Pharmaceuticals Inc.

In May 2011, the Company entered into an agreement with Penwest Pharmaceuticals Co., which subsequently merged into its parent, Endo Pharmaceuticals Inc. ("Endo"), for an exclusive worldwide sublicensable license under certain patent rights and

know-how controlled by Endo to develop and commercialize products incorporating nalbuphine hydrochloride in any formulation, including an extended-release formulation such as Haduvio, in all fields and for any use.

Under the license agreement, the Company paid Endo a non-creditable, non-refundable upfront license fee. The Company may also become obligated to make milestone payments to Endo of $0.3 million, which would become due upon the successful completion

of the first Phase 3 clinical trial of a licensed product candidate, and $0.8 million, which would become due upon the marketing approval of a licensed product in the U.S., and to pay royalties based on net sales of the licensed products by the Company, its affiliates and sublicensees. In addition, the Company is obligated to pay Endo a low-to-mid double-digit percentage of certain income it receives from sublicensees, based on the date of the definitive agreement under which the sublicense was granted.

The Company's royalty obligation with respect to each licensed product in each country commences upon the first commercial sale of the product in that country and extends until the later of the expiration, unenforceability or invalidation of the last valid claim of any licensed patent or application covering the licensed product in the country or the expiration of 10 years after the first commercial sale of the licensed product in the country, which period is referred to as the royalty term. Upon the expiration of the royalty term for a product in a country, the Company is thereafter obligated to pay a low single-digit know-how and trademark royalty.

Under the agreement, the Company has granted Endo a non-exclusive, royalty-free (except for pass-through payments to third parties), sublicensable license under its relevant patent rights to use any improvement the Company makes to Endo's controlled release technology for any product other than the products under which it is licensed by Endo.

Both the Company and Endo have the right to terminate the agreement if the other party materially breaches the agreement and fails to cure the breach within specified cure periods. Endo also has the right to terminate in the event the Company undergoes specified bankruptcy, insolvency or liquidation events. The Company has the right to terminate the agreement at its convenience at any time on 180 days' notice to Endo. Additionally, if the Company or any of the Company's sublicensees challenge the validity or

enforceability of any licensed patent rights covering a licensed product and that challenge is not terminated within a specified period, the agreement will immediately terminate and all licenses granted under the agreement shall be revoked.

Upon termination of the agreement, the Company must transfer to Endo all regulatory filings and approvals relating to the development, manufacture or commercialization of the licensed products and all trademarks, other than the Company's corporate trademarks, then being used in connection with the licensed products. If the agreement is terminated under certain specified circumstances, the Company will be deemed to have granted Endo a perpetual, royalty-free (except for pass-through payments to third parties), worldwide, exclusive, sublicensable license under any improvements the Company made to the licensed know-how and any related patent rights the Company has to manufacture and commercialize the licensed products.

12. Commitments and Contingencies

A significant portion of the Company's development activities are outsourced to third parties under agreements, including with CROs and contract manufacturers in connection with the production of clinical trial materials. These arrangements may require the Company to pay termination costs to the third parties for reimbursement of costs and expenses incurred in the event of the orderly termination of contractual services.

The Company also has commitments under lease and licensing agreements (Note 5 and Note 11).

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our Condensed Consolidated Financial Statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q and our audited consolidated financial statements and related notes for the year ended December 31, 2022 December 31, 2023 included in our Annual Report on Form 10-K, filed with the Securities and Exchange Commission, or SEC, on March 16, 2023 March 20, 2024. Some of the statements contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, constitute forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We have based these forward-looking statements on our current expectations and projections about future events. The following information and any forward-looking statements should be considered in light of factors discussed elsewhere in this Quarterly Report on Form 10-Q, particularly including those risks identified in Part II-Item 1A "Risk Factors" and our other filings with the SEC.

Our actual results and timing of certain events may differ materially from the results discussed, projected, anticipated, or indicated in any forward-looking statements. We caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this Quarterly Report on Form 10-Q. Statements made herein are as of the date of the filing of this Quarterly Report on Form 10-Q with the SEC and should not be relied upon as of any subsequent date. Even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this Quarterly Report on Form 10-Q, they may not be predictive of results or developments in future periods. We disclaim any obligation, except as specifically required by law and the

rules of the SEC, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

We caution readers not to place undue reliance on any forward-looking statements made by us, which speak only as of the date they are made.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of the investigational therapy Haduvio (oral nalbuphine ER) for the treatment of chronic cough in idiopathic pulmonary fibrosis, or IPF, and refractory chronic cough, or RCC. These conditions share a common pathophysiology that is mediated through opioid receptors in the central and for peripheral nervous systems. Due to nalbuphine's mechanism of action as a modulator of opioid receptors, we believe Haduvio has the treatment potential to be effective in treating each of prurigo nodularis. these conditions.

Chronic Cough. Haduvio is an oral extended-release formulation of nalbuphine. Nalbuphine is a mixed κ-opioid receptor agonist and μ-opioid receptor antagonist that has been approved and marketed as an injectable for pain indications for more than 20 years in the United States, or the U.S., and Europe. The κ- and μ-opioid receptors are known to be critical mediators of cough and itch. Nalbuphine's mechanism of action also mitigates the risk of abuse associated with μ-opioid agonists because it antagonizes, or blocks, the μ-opioid receptor. Parenteral nalbuphine is not scheduled as a controlled substance in the U.S. and most of Europe.

IPF Program. In September 2022, we announced positive data from the full set of patients in our Phase 2 clinical trial of Haduvio for the treatment of chronic cough in IPF, which we refer to as the Phase 2 CANAL trial. The Phase 2 CANAL trial was a randomized, double-blind, placebo controlled, two-treatment, two-period, crossover study that was designed to evaluate the efficacy,

safety, tolerability and dosing of Haduvio for chronic cough in IPF that we conducted at multiple sites in the United Kingdom. In total, we enrolled 38 subjects 42 patients in the study. study received Haduvio. In the full subject data set, Phase 2 CANAL trial, Haduvio demonstrated statistically significant results for the primary efficacy endpoint of daytime cough frequency reduction ($p<0.0001$) and for key secondary endpoints on patient and clinician reported outcomes. The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials in other patient populations.

In December 2023, we initiated our Phase 2b CORAL clinical trial, which is a dose-ranging study evaluating the efficacy, safety and tolerability of Haduvio for chronic cough in IPF. This trial is expected to be conducted at multiple sites in up to 11 countries and uses a randomized, double-blind, placebo-controlled, parallel-arm design, which evaluates three doses of Haduvio over six weeks as compared to placebo. The primary efficacy endpoint for the trial is the relative change in 24-hour cough frequency at the end of week six versus baseline for Haduvio compared to placebo, as measured via an objective cough monitor. We expect the trial to enroll approximately 160 patients. The protocol for the Phase 2b CORAL clinical trial provides for a sample size re-estimation, or SSRE, analysis once approximately 50% of the patients in the trial are evaluable for the primary endpoint. The SSRE is expected to occur in discussions with the second half of 2024, and topline data from the full trial are expected to be available in the first half of 2025 assuming there are no adjustments made to the sample size.

The U.S. Food and Drug Administration, or FDA, and other international regulatory authorities, regarding the design of the next clinical trials of Haduvio has cleared our investigational new drug application for the treatment of chronic cough in IPF. We are preparing for a Phase 2b dose ranging trial of Haduvio for the treatment of chronic cough in IPF. The purpose of this trial would be to determine the dose response and select the dose for the next study as well as to further characterize the safety in this specific patient population. We expect this trial to use a parallel arm design, which would study three doses and placebo over a six-week

period. The primary endpoint of this study is expected to be a reduction in 24-hour cough frequency using an objective cough monitor. We expect the study to enroll approximately 160 subjects. We are also preparing to conduct a our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respiratory physiology in patients with IPF of varying disease severity. Subject The objective for this clinical trial will be to agreement with further characterize the FDA and other international regulatory authorities, we intend safety of Haduvio in this specific patient population, specifically as it relates to respiratory depression. We expect to initiate the Phase 2b dose ranging this trial in the fourth third quarter of 2023 and the Phase 1b respiratory physiology trial in the first quarter of 2024. We will need to submit an IND for Haduvio before proceeding with our planned respiratory physiology study at sites in the United States.

*RCC Program.*We are also developing Haduvio for the treatment of refractory chronic cough. RCC. In November 2023, we initiated our Phase 2a RIVER clinical trial of Haduvio for RCC, which we refer to as the Phase 2a RIVER trial. The Phase 2a RIVER trial is a randomized, double-blind, placebo-controlled, two-treatment, two-period, crossover study that is designed to evaluate the efficacy, safety, tolerability and dosing of Haduvio for the treatment of refractory chronic cough. RCC. We intend to conduct are conducting this trial at multiple sites in the United Kingdom and Canada. This The trial uses a randomized, double-blind, placebo-controlled, two treatment period crossover design, which studies escalating doses of Haduvio over three weeks as compared was designed to placebo. enroll approximately 60 adult patients. The primary endpoint of the study is a mean change in 24-hour cough frequency using an objective cough monitor. monitor in the overall population. Patients are randomized with a 1:1 stratification between those with 10-19 coughs/hour (moderate 24-hour cough frequency) and those with at least 20 coughs/hour (high 24-hour cough frequency). The study will also explore secondary endpoints, including patient reported outcome measures for cough frequency and severity. We expect the study to enroll approximately 60 subjects and to report topline efficacy and safety data in the second half of 2024.

Human Abuse Potential. We initiated a human abuse potential, or HAP, study in the fourth quarter of 2022 to compare the abuse potential of oral nalbuphine to intravenous, or IV, butorphanol. The parenteral version of nalbuphine is currently unscheduled in the U.S. by the Drug Enforcement Agency. The study follows a randomized, double-blind, active and placebo-controlled five-way crossover design. The study is being conducted in two parts. The first part of the study characterized various IV butorphanol doses in order to select a dose to be studied and has been completed. The FDA requested that we submit the data from the first part of the study in support of our IV butorphanol dose selection for review and comment prior to commencing the second part of the study. We submitted the data to the FDA and the FDA agreed to the selected dose of IV butorphanol for the second part of the study. In the second part of the study, we are comparing oral nalbuphine with the selected dose of IV butorphanol using a drug-liking visual analog scale. We initiated dosing in the second part of the study in January 2024 and the study is now 75% enrolled. We expect to report topline data from the study in the second half of 2024.

Prurigo Nodularis Program. We also have a development program for the use of Haduvio for the treatment of prurigo nodularis. In June 2022, we reported positive results in our Phase 2b/3 clinical trial of Haduvio in patients with prurigo nodularis, which we refer to as the Phase 2b/3 PRISM trial. The Phase 2b/3 PRISM trial was a randomized, double-blind, placebo controlled, two-arm treatment study that was designed to evaluate the safety and efficacy of Haduvio in patients with prurigo nodularis in the United States and Europe. In total we enrolled 353 patients in the study. In the Phase 2b/3 PRISM trial, Haduvio demonstrated statistically significant results on the primary and all three key secondary endpoints. The safety results of the trial were generally consistent with the known safety profile of Haduvio from previous trials. trials in other patient populations.

In October 2023, we reported the preliminary analysis of the 52-week data from the open-label extension portion of the Phase 2b/3 PRISM trial. Following the completion of the initial 14-week portion of the trial, subjects patients were eligible to enroll

into an additional 38-week open-label extension period during which all participants received Haduvio 162mg twice a day (BID). Post hoc analyses demonstrated continued reduction in mean Worst Itch Numerical Rating Scale for those participants who remained on Haduvio through 52 weeks. 151 subjects patients completed the open-label extension portion of the trial, adding to the safety database for Haduvio. The safety data were generally consistent with the safety profile of Haduvio observed in the 14-week portion of the Phase 2b/3 PRISM trial and previous trials of Haduvio. Adverse events reported with a frequency greater than 5% five percent in the 38-week open-label period included nausea, dizziness, vomiting, fatigue, and somnolence. Study discontinuation due to treatment-related adverse events occurred in 13% of subjects patients during the 38-week open-label period, and serious adverse events were reported for 13 subjects, patients, although only 2 two of these events were considered potentially treatment related.

We expect that we will need to conduct an additional Phase 3 clinical trial to support the submission of a new drug application, or NDA, to the FDA, a marketing authorization application, or MAA, to the European Medicines Agency and an MAA to the Medicines and Healthcare Products Regulatory Agency in the United Kingdom for Haduvio for the treatment of prurigo nodularis, and we plan to request an end of Phase 2 meeting with the FDA. Following discussions with the FDA and other regulatory authorities, we plan to determine next steps with respect to our prurigo nodularis program, including with respect to the conduct of any future Phase 3 clinical trial. We are exploring entering may seek to enter into a strategic collaboration for the continued development of this program.

Human Abuse Potential. We initiated a human abuse potential, or HAP, study in the fourth quarter of 2022 to compare the abuse potential of oral nalbuphine to intravenous, or IV, butorphanol. The injectable version of nalbuphine is currently unscheduled in the U.S. by the Drug Enforcement Agency. The study is a randomized, double-blind, active and placebo-controlled 5-way crossover design. The study is being conducted in two parts. The first part of the study characterized various IV butorphanol doses in order to select a dose to be studied. The second part of the study is designed to utilize the selected dose and compare oral nalbuphine relative to IV butorphanol using the study metrics. We have completed part one of the study. The FDA requested that we submit the data from part one in support of our IV butorphanol dose selection for their review and comment prior to commencing part two of the study. We submitted this data to the FDA and they have agreed with the selected dose for IV butorphanol. Beginning in the first quarter of 2023, we were unable to obtain supply of IV butorphanol due to a worldwide shortage, and we had to delay the initiation of the second part of the study. In October 2023, we secured supply of IV butorphanol and we expect to initiate dosing in the second part of the study in the first quarter of 2024 as a result. We expect to report topline data from this study in the second half of 2024.

Since commencing operations in 2011, we have devoted substantially all of our efforts and financial resources to the clinical development of Haduvio. We have not generated any revenue from product sales and, as a result, we have never been profitable and have incurred net losses in each year since commencement of our operations. As of September 30, 2023 March 31, 2024, we had an accumulated deficit of $231.3 million $250.0 million, primarily as a result of research and development and general and administrative expenses. We do not expect to generate product revenue unless and until we obtain marketing approval for and commercialize Haduvio for the treatment of chronic cough in IPF and refractory chronic cough RCC or for the treatment of prurigo nodularis and we can provide no assurance that we will ever generate significant revenue or profits.

In May 2019, we issued and sold 5,500,000 shares of common stock in our initial public offering, or the IPO, and 1,500,000 shares of common stock in a concurrent private placement, in each case at an offering price of $10.00 per share, for combined net proceeds of $62.1 million after deducting aggregate underwriting discounts and commissions and private placement agent fees of $4.9 million and other offering expenses of $3.0 million. Upon the closing of the IPO, our preferred stock then outstanding converted into an aggregate of 10,381,234 shares of common stock.

In June 2020, we entered into a sales agreement with SVB Securities LLC (formerly SVB Leerink LLC), or SVB Securities, which we refer to as the ATM Sales Agreement, under which we were able to issue and sell shares of common stock, from time to time, having an aggregate offering price of up to $12.0 million. In May 2022, we and SVB Securities amended the ATM Sales Agreement to increase the maximum aggregate offering price of common stock that we were able to issue and sell from time to time under the ATM Sales Agreement by $50.0 million, from $12.0 million to up to $62.0 million. Sales of common stock under the ATM Sales Agreement were able to be made by any method that was deemed an “at-the-market” offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. We were not obligated to make any sales of our common stock under the ATM Sales Agreement. We began making sales pursuant to the ATM Sales Agreement in July 2020, and through September 30, 2023 as of August 15, 2023, the date of termination of the ATM Sales Agreement, we had issued and sold an aggregate of 4,333,394 shares of common stock for gross proceeds of $12.7 million pursuant to the ATM Sales Agreement, before deducting estimated commissions and allocated fees of $1.0 million.

In June 2023, we filed with the SEC a universal shelf registration statement on Form S-3, or the Shelf Registration Statement, which allows us to offer and sell up to $200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The Shelf Registration Statement was filed to replace our prior universal shelf registration statement on Form S-3 and was declared effective on August 15, 2023. Further, in June 2023, we entered into a new sales agreement with Leerink Partners, LLC (formerly SVB Securities), or Leerink Partners, which we refer to as the New 2023 ATM Sales Agreement, under which we may issue and sell shares of common stock, from time to time by any method that is deemed an “at-the-market” offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. We are not obligated to make any sales of our common stock under the New 2023 ATM Sales Agreement. We filed a prospectus under the Shelf Registration Statement for the offer and sale of shares of our common stock having an aggregate offering price of up to $75.0 million pursuant to the New 2023 ATM Sales Agreement. In accordance with the terms of the New 2023 ATM Sales Agreement, the ATM Sales Agreement terminated upon effectiveness of the Shelf Registration Statement, at which point we were no longer able to issue and sell shares of our common stock under the ATM Sales Agreement. As of September 30, 2023 March 31, 2024, we had not made any sales pursuant to the New 2023 ATM Sales Agreement. Subsequent to March 31, 2024, and through May 7, 2024, we issued and sold 1,474,926 shares of common stock for gross proceeds of $5.0 million, before deducting estimated commissions and allocated fees of $0.2 million under the 2023 ATM Sales Agreement.

On October 5, 2021 and October 18, 2021, we issued and sold in two private placements, or the October 2021 Private Placements, in the aggregate (i) 4,225,053 shares of our common stock and accompanying warrants to purchase an aggregate of 8,450,106 shares of our common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 4,926,069 shares of our common stock and accompanying warrants to purchase an aggregate of 9,852,138 shares of our common stock. Each share of our common stock and accompanying common stock warrants were sold together at a combined price of $1.62, and each pre-funded warrant and accompanying common stock warrants were sold together at a combined price of $1.619, for gross proceeds of approximately $14.8 million. Each pre-funded warrant had an exercise price of $0.001 per share, became exercisable immediately upon issuance and continued to be exercisable until exercised in full. Of the accompanying common stock warrants, we issued

warrants to purchase an aggregate of 9,151,122 shares that are to expire in April 2025 and warrants to purchase an aggregate of 9,151,122 shares that are to expire in October 2028. The accompanying common stock warrants have an exercise price of $1.37 per share and became exercisable immediately upon issuance. As Of the accompanying common stock warrants, warrants to purchase an aggregate of November 9, 2023 7,299,270 shares had an expiration date of April 5, 2025, warrants to purchase an aggregate of 1,851,852 shares had an expiration date of

common stock that are April 18, 2025, warrants to expire in April 2025 purchase an aggregate of 7,299,270 shares had an expiration date of October 5, 2028, and warrants to purchase 7,851,852 an aggregate of 1,851,852 shares had an expiration date of October 18, 2028. As of May 7, 2024, all of the pre-funded warrants have been exercised, all of the accompanying common stock warrants expiring on April 5, 2025 have been exercised, and accompanying common stock warrants to purchase 1,299,270 shares expiring on October 5, 2028 have been exercised. Warrants to purchase 1,851,852 shares of common stock that are to expire in October 2028 on April 18, 2025, warrants to purchase 6,000,000 shares of common stock that are to expire on October 5, 2028 and warrants to purchase 1,851,852 shares of common stock that are to expire on October 18, 2028 remained outstanding.

On April 11, 2022, we issued and sold in a private placement, or the April 2022 Private Placement, (i) an aggregate of 4,580,526 shares of our common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 24,379,673 shares of our common stock. Each share of our common stock was sold at a price of $1.90, and each pre-funded warrant was sold at a price of $1.899 per warrant share, for gross proceeds of approximately $55.0 million. Each pre-funded warrant has an exercise price of $0.001 per share, is became exercisable immediately upon issuance and will be exercisable until the pre-funded warrant is exercised in full. As of November 9, 2023 May 7, 2024,

pre-funded warrants to purchase 21,379,673 17,282,760 shares of common stock that we issued and sold in the April 2022 Private Placement remained outstanding.

On September 27, 2022, we issued and sold 14,252,670 shares of our common stock and, in lieu of common stock to certain investors, pre-funded warrants to purchase 14,247,330 shares of common stock in a public offering, or the September 2022 Offering, at a public offering price of $1.93 per share of common stock and $1.929 per pre-funded warrant pursuant to an underwriting agreement, or the Underwriting Agreement, with SVB Securities, Stifel, Nicolaus & Company, Incorporated and Oppenheimer & Co. Inc., as representatives of the several underwriters, or the Underwriters. Each pre-funded warrant has an exercise price of $0.001 per share, is became exercisable immediately upon issuance and will be exercisable until the pre-funded warrant is exercised in full. Under the terms of the Underwriting Agreement, we agreed not to issue and sell additional shares until after November 21, 2022 except in certain circumstances, including the issuance and sale of additional shares pursuant to the Underwriting Agreement. Under the terms of the Underwriting Agreement, we granted the Underwriters an option, or the Option, exercisable for 30 days, to purchase up to an additional 4,275,000 shares of common stock, or the Additional Shares, at the public offering price of $1.93 per share. The Underwriters partially exercised the Option to purchase 1,600,428 Additional Shares, which shares were issued and sold on October 25, 2022. The September 2022 Offering, including the initial closing on September 27,

2022 and the Option closing on October 25, 2022, resulted in aggregate gross proceeds to us of approximately $58.1 million. As of November 9, 2023 May 7, 2024, all of the pre-funded warrants to purchase 13,270,983 shares of common stock that we issued and sold in the September 2022 Offering remained outstanding.

On May 9, 2023, we paid the remaining amount due under the loan and security agreement, or the SVB Loan Agreement, that we originally entered into with Silicon Valley Bank, or SVB, in August 2020, resulting in the full extinguishment of the term loan thereunder, or the SVB Term Loan. The total payoff amount was $6.5 million, consisting of the remaining principal amount due of $5.2 million, the final payment fee of $1.2 million, and $0.1 million of accrued interest and prepayment premium. In August 2020, we entered into the SVB Loan Agreement with SVB, pursuant to which SVB provided the SVB Term Loan to us in the original principal amount of $14.0 million. On the first business day of each month commencing on March 1, 2022, we were required to repay the SVB Term Loan in 24 consecutive installments of principal plus monthly payments of accrued interest. All outstanding principal and accrued and unpaid interest under the SVB Term Loan and all other outstanding obligations with respect to the SVB Term Loan were due and payable in full on February 1, 2024. The SVB Loan Agreement permitted voluntary prepayment of all, but not less than all, of the SVB Term Loan, subject to a prepayment premium. For further discussion of the SVB Term Loan, see "—Liquidity and Capital Resources."

As of September 30, 2023 March 31, 2024, we had cash, cash equivalents and marketable securities of $88.9 million $72.8 million. We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements for at least 12 months from the date of issuance of the Condensed Consolidated Financial Statements included in this Quarterly Report on Form 10-Q.

We expect to incur substantial expenditures in the foreseeable future as we advance Haduvio through clinical development, the regulatory approval process and, if approved, commercial launch activities. Specifically, in the near term, we expect to incur substantial expenses relating to the next trials we are conducting and plan to conduct for Haduvio including our Phase 2b CORAL clinical trial for the treatment of chronic cough in IPF, our Phase 2a RIVER clinical trial of Haduvio for the treatment of refractory chronic cough, RCC, our planned Phase 1b respiratory physiology clinical trial in patients with IPF of varying disease severity and the second part of our HAP study to determine compare the abuse potential of oral nalbuphine ER relative to IV butorphanol.

We will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from sales of Haduvio, if ever, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies or other strategic transactions. Adequate funding may not be available to us on acceptable terms or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development and commercialization of Haduvio for one or more indications or delay our efforts to expand our product pipeline.

Components of Operating Results

Operating Expenses

Research and Development Expenses

For the periods presented, all of our research and development expenses consist of expenses incurred in connection with the development of Haduvio. These expenses include personnel-related costs, including stock-based compensation, consulting costs,

contract manufacturing costs and fees paid to contract research organizations, or CROs, to conduct certain research and development activities on our behalf. We do not allocate all of our costs by each indication for which we are developing Haduvio, as a significant amount of our development activities broadly support all indications. In addition, several of our departments support our Haduvio drug candidate development program and we do not identify internal costs for each potential indication.

We expect our research and development expenses to increase over the next few years as we pursue our development program, pursue regulatory approval of Haduvio in the U.S., Europe and other jurisdictions outside the U.S. and prepare for a possible commercial launch of Haduvio. Predicting the timing or the cost to conduct our Haduvio development program and prepare for a possible commercial launch of Haduvio is difficult and delays may occur because of many factors including factors outside of our control. For example, if the FDA or other regulatory authorities were to require us to conduct clinical trials beyond those that we currently anticipate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend

significant additional financial resources and time on our development program. Furthermore, we are unable to predict when or if Haduvio will receive regulatory approval in the U.S. or elsewhere with any certainty.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, including stock-based compensation for personnel in executive, finance, commercial and other administrative functions; professional fees for legal, consulting and accounting services; as well as rent and other general operating expenses not otherwise classified as research and development expenses.

We anticipate that our general and administrative expenses will increase as a result of increased personnel costs, including stock-based compensation and expanded infrastructure.

Other Income (Expense), Net

Interest Income, Net

Interest income, net consists of interest earned primarily on our cash, cash equivalents and marketable securities as well as accretion of discounts/amortization of premiums on purchases of marketable securities.

Other Income (Expense), Net

Other income, net consists of income related to an consists of foreign currency transaction gains and losses as well asemployee retention tax credit under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, foreign currency transaction gains and losses as well as an immaterial effect from early extinguishment of debt in connection with us paying the remaining amounts due under the SVB Loan Agreement. Act.

Interest Expense

In August 2020, we entered into Interest expense consists of the interest expense associated with our finance lease along with the SVB Loan Agreement pursuant to which we borrowed $14.0 million under the SVB Term Loan. In connection with the SVB

Term Loan, we recognized interest expense which included amortization of deferred financing charges, accretion of loan discount-financing costs, accrual of the final payment fee, amortization of the term loan discount-interest and the stated interest on the SVB Term Loan. Prior to the Third Amendment to the SVB Loan Agreement that we entered into with SVB in April 2022, or the Third Amendment, the SVB Term Loan bore interest at a floating rate per annum equal to the greater of (A) the prime rate plus 1.00% and (B) 4.25%. If SVB received evidence satisfactory to it that we had (i) received positive data for the Phase 2b/3 PRISM trial sufficient to advance Haduvio into a second Phase 3 clinical trial for prurigo nodularis and (ii) raised sufficient financing to fund such Phase 3 clinical trial and our operations, which we refer to together as the Phase 3 Event, the interest rate under the SVB Term Loan would have been adjusted to a floating rate equal to the greater of (A) the prime rate plus 3.00% and (B) 6.25%.

Under the Third Amendment, SVB agreed that amounts outstanding under the SVB Loan Agreement would accrue interest at a floating per annum rate equal to (i) the greater of (A) the prime rate plus 1.00% and (B) 4.25%, prior to raising $45.0 million in net proceeds from the sale of equity securities, which we refer to as the 2022 Equity Event, and (ii) upon and after the occurrence of the 2022 Equity Event, the greater of (A) the prime rate plus 3.00% and (B) 6.25%. The closing of the April 2022 Private Placement constituted the 2022 Equity Event.

The SVB Term Loan required interest-only payments until March 2022. Commencing on March 1, 2022, we were required to repay the SVB Term Loan in 24 consecutive installments of principal plus monthly payments of accrued interest. All outstanding principal and accrued and unpaid interest under the SVB Term Loan and all other outstanding obligations with respect to the SVB Term Loan were due and payable in full on February 1, 2024. On May 9, 2023, we paid the remaining amount due under the SVB Loan Agreement, resulting in the full extinguishment of the SVB Term Loan. The total payoff amount was $6.5 million, consisting of the remaining principal amount due of $5.2 million, the final payment fee of $1.2 million, and $0.1 million of accrued interest and prepayment premium.

Change in Fair Value of Term Loan Derivative Liability

Before it was amended by the Third Amendment, the SVB Loan Agreement provided that upon the occurrence of the Phase 3 Event, as described below, the interest rate on the SVB Term Loan would increase by 2.00%. This contingent interest rate increase represented a free-standing financial instrument. Accordingly, we accounted for the contingent interest rate increase as a derivative under Accounting Standards Codification, or ASC, 815, *Derivatives and Hedging* and therefore, we recorded a term loan derivative liability for the contingent interest rate increase at its fair value. We adjusted this liability to fair value at each reporting date it remained outstanding. We recognized changes in the fair value of this term loan derivative in our statements of comprehensive loss as a component of other income (expense), net.

Results of Operations

Comparison of the Three Months Ended September 30, 2023 March 31, 2024 and 2022 2023

The following table summarizes our results of operations for the periods indicated (in thousands):

	Three Months Ended September 30,			Three Months Ended March 31,		
	2023	2022	Change	2024	2023	Change
Operating expenses:						

Research and development	$ 6,323	$ 5,769	$ 554	$ 8,804	$ 5,000	$ 3,804
General and administrative	2,722	2,636	86	3,102	2,563	539
Total operating expenses	9,045	8,405	640	11,906	7,563	4,343
Loss from operations	(9,045)	(8,405)	(640)	(11,906)	(7,563)	(4,343)
Other income (expense):						
Interest income, net	1,183	424	759	998	1,221	(223)
Other income, net	154	—	154			
Other (expense) income, net				(1)	165	(166)
Interest expense	(3)	(292)	289	(1)	(231)	230
Total other income, net	1,334	132	1,202	996	1,155	(159)
Loss before income taxes	(7,711)	(8,273)	562	(10,910)	(6,408)	(4,502)
Income tax benefit	13	7	6	8	7	1
Net loss	$ (7,698)	$ (8,266)	$ 568	$ (10,902)	$ (6,401)	$ (4,501)

Operating Expenses

Research and Development Expenses

The following table summarizes our research and development expenses for the periods indicated (in thousands):

	Three Months Ended September 30,			Three Months Ended March 31,		
	2023	2022	Change	2024	2023	Change
Clinical development expenses	$ 3,799	$ 4,126	$ (327)	$ 7,128	$ 3,410	$ 3,718
Personnel and related expenses	1,112	851	271	1,275	1,241	34
Consultant services in support of clinical development	948	550	398			
Stock-based compensation expenses				298	213	85
Other research and development expenses	243	44	199	103	136	(33)

Stock-based compensation expenses	211	198	13			
Total research and development expenses	6,32 $ 3	5,76 $ 9	$ 554	$ 8,804	$ 5,000	$ 3,804

Research and development expenses for the three months ended September 30, 2023 March 31, 2024 increased to $6.3 million $8.8 million from $5.8 million $5.0 million for the corresponding period in 2022, 2023, primarily due to increased startup costs clinical development expenses for our Phase 2b CORAL trial, our Phase 2a RIVER trial, and consultant services associated with our chronic cough programs as well as an increase in personnel-related expenses. HAP study. These increases were partially offset by a decline in decreased clinical development expenses related to for our completed Phase 2b/3 PRISM trial and our Phase 2 CANAL because dosing in the open-label extension portion of the PRISM trial as well as decreased purchases completed in the first quarter of clinical trial supplies, among other factors. 2023.

General and Administrative Expenses

General and administrative expenses for the three months ended September 30, 2023 were $2.7 million, compared March 31, 2024 increased to $3.1 million from $2.6 million for the corresponding period in 2022. 2023, primarily due to increases in information technology and finance staffing and activities as well as professional fees.

Other Income, Net

Other income, net for the three months ended September 30, 2023 March 31, 2024 was $1.3 million $1.0 million compared to other income, net of $0.1 million $1.2 million for the corresponding period in 2022. 2023. The change was primarily due to an increase a decrease in interest income of $0.8 million $0.2 million due to higher lower cash equivalent and marketable securities balances and higher interest rate yields and reduced interest expense due to balances. In addition, during the early payoff of the SVB Term Loan in May 2023.

Comparison of the Nine Months Ended September 30, 2023 and 2022

The following table summarizes our results of operations for the periods indicated (in thousands):

	Nine Months Ended September 30,		
	2023	2022	Change
Operating expenses:			
Research and development	$ 17,165	$ 15,517	$ 1,648
General and administrative	7,825	7,733	92
Total operating expenses	24,990	23,250	1,740
Loss from operations	(24,990)	(23,250)	(1,740)
Other income (expense):			
Interest income, net	3,611	623	2,988
Other income, net	472	—	472
Interest expense	(387)	(889)	502
Change in fair value of term loan derivative liability	—	(147)	147

Total other income (expense), net	3,696	(413)	4,109
Loss before income taxes	(21,294)	(23,663)	2,369
Income tax benefit	50	16	34
Net loss	$ (21,244)	$ (23,647)	$ 2,403

Operating Expenses

Research and Development Expenses

The following table summarizes our research and development expenses for the periods indicated (in thousands):

	Nine Months Ended September 30,		
	2023	2022	Change
Clinical development expenses	$ 9,616	$ 10,005	$ (389)
Personnel and related expenses	3,589	3,044	545
Consultant services in support of clinical development	2,702	974	1,728
Stock-based compensation expenses	657	631	26
Other research and development expenses	601	863	(262)
Total research and development expenses	$ 17,165	$ 15,517	$ 1,648

Research and development expenses for the nine three months ended September 30, 2023 increased to $17.2 million from $15.5 million for the corresponding period in 2022, primarily due to increased startup costs and consultant services associated with our chronic cough programs as well as an increase in personnel-related expenses. These increases were partially offset by a decline in clinical development expenses related to our completed Phase 2b/3 PRISM trial and our Phase 2 CANAL trial as well as decreased purchases of clinical trial supplies, among other factors.

General and Administrative Expenses

General and administrative expenses for the nine months ended September 30, 2023 were $7.8 million March 31, 2023, compared to $7.7 million for the corresponding period in 2022.

Other Income (Expense), Net

Other income (expense), net for the nine months ended September 30, 2023 was $3.7 million compared to other expense, net of $0.4 million for the corresponding period in 2022. The change was primarily due to an increase in interest income of $3.0 million due to higher cash equivalent and marketable securities balances and higher interest rate yields. Contributing to the increase we recorded $0.2 million in other income, (expense), net, was $0.4 million in other income that we recorded in the 2023 period related to a tax credits credit against employment taxes for certain previous periods provided under the CARES Act. No income was recorded related to tax credits under the CARES Act as well as $0.5 million in 2024. These decreases were partially offset by lower interest expense of $0.2 million due to the early payoff of the SVB Term Loan in May 2023.

Liquidity and Capital Resources

Since our inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. Prior to the completion of our IPO, and concurrent private placement in May 2019, we financed our operations primarily through private placements of our preferred stock and convertible notes as well as borrowings under a our prior

term loan. From inception to our IPO, we raised an aggregate of $102.2 million in gross proceeds from sales of our preferred stock and convertible notes and borrowed $15.0 million under a prior term loan.

In May 2019, we issued and sold 5,500,000 shares of common stock in our IPO and 1,500,000 shares of common stock in a concurrent private placement, in each case at an offering price of $10.00 per share, for combined net proceeds of $62.1 million after deducting aggregate underwriting discounts and commissions and private placement agent fees of $4.9 million and other offering expenses of $3.0 million.

In June 2020, we entered into the ATM Sales Agreement, under which we were able to issue and sell shares of common stock, from time to time, having an aggregate offering price of up to $12.0 million. In May 2022, we and SVB Securities amended the ATM Sales Agreement to increase the maximum aggregate offering price of common stock that we are were able to issue and sell from time to time under the ATM Sales Agreement by $50.0 million, from $12.0 million to up to $62.0 million. Sales of common stock under the ATM Sales Agreement were able to be made by any method that was deemed an “at-the-market” offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. We were not obligated to make any sales of our common stock under the ATM Sales Agreement. We began making sales pursuant to the ATM Sales Agreement in July 2020 and through September 30, 2023 August 15, 2023, the date of termination of the ATM Sales Agreement, we had issued and sold an aggregate of 4,333,394 shares of common stock for gross proceeds of $12.7 million, before deducting estimated commissions and allocated fees of $1.0 million.

In June 2023, we filed with the SEC the Shelf Registration Statement, which allows us to offer and sell up to $200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The Shelf Registration Statement was filed to replace our prior universal shelf registration statement on Form S-3 and was declared effective on August 15, 2023. Further, in June 2023, we entered into the New 2023 ATM Sales Agreement with Leerink Partners, under which we may issue and sell shares of common stock, from time to time by any method that is deemed an “at-the-market” offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. We are not obligated to make any sales of our common stock under the New 2023 ATM Sales Agreement. We filed a prospectus under the Shelf Registration Statement for the offer and sale of shares of our common stock having an aggregate offering price of up to $75.0 million pursuant to the New 2023 ATM Sales Agreement. In accordance with the terms of the New 2023 ATM Sales Agreement, the ATM Sales Agreement terminated upon effectiveness of the Shelf Registration Statement, at which point we were no longer able to issue and sell shares of our common stock under the ATM Sales Agreement. As of September 30, 2023 March 31, 2024, we had not made any sales pursuant to the New 2023 ATM Sales Agreement.

On June 18, 2021 Subsequent to March 31, 2024, and through May 7, 2024, we entered into the LPC Purchase Agreement with Lincoln Park for an equity line financing. The LPC Purchase Agreement provided that, subject to the terms issued and conditions set forth therein, we had the right, but not the obligation, to sell to Lincoln Park and Lincoln Park was obligated to purchase up to $15.0 million of sold 1,474,926 shares of common

stock at our sole discretion, over a 24-month period commencing on July 23, 2021. We filed a registration statement on Form S-1 covering the resale for gross proceeds of shares $5.0 million, before deducting estimated commissions and allocated fees of common stock that are issued to Lincoln Park $0.2 million under the LPC Purchase Agreement, which was declared effective on July 14, 2021. We issued 170,088 shares of our common stock to Lincoln Park as consideration for its commitment to purchase shares of our common stock under the LPC Purchase Agreement. As of July 23, 2023, no shares had been sold to Lincoln Park and the LPC Purchase Agreement terminated by its terms.

SVB Loan Agreement

On May 9, 2023, we paid the remaining amount due under the SVB Loan Agreement, resulting in the full extinguishment of the SVB Term Loan. The total payoff amount was $6.5 million, consisting of the remaining principal amount due of $5.2 million, the final payment fee of $1.2 million, and $0.1 million of accrued interest and prepayment premium.

In August 2020, we entered into the SVB Loan Agreement with SVB, pursuant to which SVB provided the SVB Term Loan in the original principal amount of $14.0 million. Prior to the Third Amendment, the SVB Term Loan bore interest at a floating rate per annum equal to the greater of (A) the prime rate plus 1.00% and (B) 4.25%. If SVB received evidence satisfactory to it that we had (i) received positive data for the Phase 2b/3 PRISM trial, sufficient to advance Haduvio into a second Phase 3 clinical trial for prurigo nodularis and (ii) raised sufficient financing to fund such Phase 3 clinical trial and our operations, the interest rate under the SVB Term Loan would have been adjusted to a floating rate equal to the greater of (A) the prime rate plus 3.00% and (B) 6.25%. Commencing on March 1, 2022 and on the first business day of each month thereafter, we were required to repay the SVB Term Loan in 24 consecutive installments of principal plus monthly payments of accrued interest. All outstanding principal and accrued and unpaid interest under the SVB Term Loan and all other outstanding obligations with respect to the SVB Term Loan were due and payable in full on February 1, 2024. The SVB Loan Agreement permitted voluntary prepayment of all, but not less than all, of the SVB Term Loan, subject to a prepayment premium. Such prepayment premium would have been 3.00% of the principal amount of the SVB Term Loan if prepaid prior to the first anniversary of the date on which we entered into the SVB Term Loan, or the Effective Date, 2.00% of the principal amount of the SVB Term Loan if prepaid on or after the first anniversary of the Effective Date, but prior to the second anniversary of the Effective Date and 1.00% of the principal amount of the SVB Term Loan if prepaid on or after the second anniversary of the Effective Date but prior to February 1, 2024. Upon repayment in full of the SVB Term Loan, we were required to pay a final payment fee equal to $1.2 million.

On July 6, 2021, we and SVB entered into the First Amendment to the SVB Loan Agreement, or the First Amendment. The First Amendment modified the conditions under which we were required to cash collateralize outstanding amounts owed to SVB under the SVB Loan Agreement. Under the First Amendment, if we failed to receive positive data in our Phase 2b/3 PRISM trial or, prior to June 30, 2022, failed to raise sufficient net proceeds from the sale of equity securities to finance our planned second Phase 3

clinical trial of Haduvio for prurigo nodularis and our ongoing operations, each of which we refer to as a Milestone Condition, we would have been required to deposit unrestricted and unencumbered cash equal to 100% of all outstanding amounts owed to SVB in a cash collateral account with SVB, which could have been used by SVB to prepay the SVB Term Loan at any time. In addition, the First Amendment provided that if we failed to maintain at least $20.0 million in unrestricted and unencumbered cash in our accounts with SVB, or the Minimum Required Cash, at any time prior to the satisfaction of all the Milestone Conditions, we would have been required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement. We would also

have been required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement if we did not raise at least $15.0 million in net proceeds from the sale of equity securities during the period from June 1, 2021 through October 31, 2021. We satisfied this equity funding condition through a combination of equity issuances under our 2023 ATM Sales Agreement and the proceeds from the October 2021 Private Placements.

On April 6, 2022, we entered into the Third Amendment to the SVB Loan Agreement. The Third Amendment principally modified the conditions under which we were required to cash collateralize all outstanding amounts owed to SVB under the SVB Loan Agreement. Under the terms of the Third Amendment, upon the closing of the April 2022 Private Placement, our obligations to achieve the Milestone Conditions and maintain the Minimum Required Cash terminated and the sole remaining cash collateralization requirement under the SVB Loan Agreement was the requirement that we receive positive final data by December 31, 2022 from either our Phase 2b/3 PRISM trial of Haduvio for prurigo nodularis or our Phase 2 CANAL trial of Haduvio for the treatment of chronic cough in IPF. On August 3, 2022, SVB confirmed that the reported data from the Phase 2b/3 PRISM trial satisfied the requirement for positive data and that the cash collateralization requirements of the SVB Loan Agreement were no longer in effect.

In addition, the Third Amendment modified the interest rate on the principal amount outstanding under the SVB Loan Agreement, as discussed above under "—Components of Operating Results—Operating Expenses—Interest Expense."

Cash Flows

The following table summarizes our cash flows for each of the periods presented below (in thousands):

	Nine Months Ended September 30,		
	2023	2022	Change
Net cash used in operating activities	$ (25,351)	$ (21,844)	$ (3,507)
Net cash provided by (used in) investing activities	46,583	(59,067)	105,650
Net cash (used in) provided by financing activities	(7,856)	110,655	(118,511)
Net increase in cash and cash equivalents	$ 13,376	$ 29,744	$ (16,368)

	Three Months Ended March 31,		
	2024	2023	Change
Net cash used in operating activities	$ (10,467)	$ (8,197)	$ (2,270)
Net cash (used in) provided by investing activities	(8,091)	8,962	(17,053)
Net cash used in financing activities	(28)	(1,703)	1,675
Net decrease in cash and cash equivalents	$ (18,586)	$ (938)	$ (17,648)

Operating Activities

During the nine three months ended September 30, 2023 March 31, 2024, operating activities used $25.4 million $10.5 million of net cash, principally resulting from our net loss of $21.2 million $10.9 million and net changes in our operating assets and liabilities of $4.6 million $0.1 million, partially offset by net non-cash charges of $0.5 million. The non-cash charges consisted primarily of stock-based compensation expense of $1.7 million, $0.3 million change in value of our operating lease right-of-use assets and $0.2 million of accretion/accrual of term loan discounts and debt issuance costs, which were partially offset by $1.8

million of accretion of our available-for-sale marketable securities. Changes in our operating assets and liabilities consisted of a $2.9 million increase $0.9 million decrease in accrued expenses and other liabilities partially offset by a $0.6 million decrease in prepaid expenses and other current assets and a $1.7 million decrease $0.3 million increase in accounts payable. The increase decrease in accrued expenses and other liabilities was primarily due to a decrease in accrued compensation and benefits. The decrease in prepaid expenses and other current assets was primarily due to an increase a decrease in prepayments related to our corporate insurance as well as our clinical trial work performed by our CROs as well as an increase in prepayments of our corporate insurance policies. CROs. The decrease in accounts payable was primarily due to the timing of vendor invoices. The non-cash charges consisted primarily of stock-based compensation expense of $0.7 million and $0.1 million change in value of our operating lease right-of-use assets and liabilities, partially offset by $0.4 million of accretion of our available-for-sale marketable securities.

During the nine three months ended September 30, 2022 March 31, 2023, operating activities used $21.8 million $8.2 million of net cash, resulting from our net loss of $23.6 million $6.4 million and net changes in our operating assets and liabilities of less than $0.1 million, partially offset by non-cash charges of $2.3 million $1.8 million. The non-cash charges consisted primarily of stock-based compensation expense of $1.8 million and $0.4 million of accretion/accrual of term loan discounts and debt issuance costs, offset by $0.3 million of accretion of our available-for-sale marketable securities. Changes in our operating assets and liabilities consisted of a $0.6 million $0.9 million decrease in accounts payable, and a $0.5 million $0.8 million increase in prepaid expenses and other current assets, partially offset by and a $0.7 million increase $0.1 million decrease in accrued expenses and other liabilities. The decrease in accounts payable was primarily due to the timing of vendor invoices. The increase in prepaid expenses and other current assets was primarily due to an increase in prepayments of related to our corporate insurance policies clinical trial work performed by our CROs as well as an increase in interest income receivable related to our marketable securities. The increase decrease in accrued expenses and other liabilities was primarily due to increased accruals for research,development and clinical trial work performed by our CROs and increased accruals for consulting and professional fees partially offset by a decrease in accrued compensation and benefits. The non-cash charges consisted primarily of stock-based compensation expense of $0.6 million and $0.1 million of accretion/accrual of term loan discounts and debt issuance costs, offset by $0.7 million of accretion of our available-for-sale marketable securities.

Investing Activities

During the nine three months ended September 30, 2023 March 31, 2024, net cash used in investing activities was $8.1 million, primarily related to $30.3 million of purchases of available-for-sale marketable securities, partially offset by $22.2 million of proceeds from maturities of available-for-sale marketable securities.

During the three months ended March 31, 2023, net cash provided by investing activities was $46.6 million $9.0 million, consisting of $55.7 million primarily related to $18.0 million of proceeds from maturities of available-for-sale marketable securities, partially offset by $9.0 million of purchases of available-for-sale marketable securities.

During the nine months ended September 30, 2022, net cash used in investing activities was $59.1 million, primarily related to securities and $0.1 million of purchases of available-for-sale marketable securities, partially offset by proceeds from maturities of available-for-sale marketable securities. property, equipment and leasehold improvements.

Financing Activities

During the nine three months ended September 30, 2023 March 31, 2024, net cash used in financing activities was $7.9 million less than $0.1 million, primarily consisting of repayments of $9.4 million payments on the SVB Term Loan including payment of the final payment fee and prepayment premium, both associated with the payoff of the SVB Term Loan and payments of offering costs of $0.2 million. These cash outflows were our finance lease, partially offset by gross cash proceeds of $1.7 million, net of commissions from sales of our common stock under the ATM Sales Agreement and $0.1 million of cash proceeds from the exercise of stock options and sales under our 2019 Employee Stock Purchase Plan. options.

During the nine three months ended September 30, 2022 March 31, 2023, net cash provided by used in financing activities was $110.7 million $1.7 million, primarily consisting of net cash proceeds from our April 2022 Private Placement and our September 2022 Offering repayments of $103.0 million, cash proceeds of $11.8 million from $1.8 million on the exercise of warrants and SVB Term Loan, partially offset by cash proceeds from the exercise of stock options of $0.1 million, partially offset by repayments of $4.1 million on the SVB Term Loan and payments of offering costs of $0.2 million.

Funding Requirements

We expect to incur substantial expenditures in the foreseeable future as we advance Haduvio through clinical development, the regulatory approval process and, if approved, commercial launch activities. Specifically, in the near term, we expect to incur substantial expenses relating to:

- the next trials we plan to conduct for our Phase 2b CORAL clinical trial of Haduvio for the treatment of chronic cough in IPF
- our Phase 2a RIVER clinical trial of Haduvio for the treatment of refractory chronic cough; RCC;
- our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respiratory physiology in patients with IPF of varying disease severity; and
- the second part of our HAP study. study to compare the abuse potential of oral nalbuphine to IV butorphanol.

We expect to continue to incur costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses.

We will need substantial additional funding to support our continuing operations. Until such time as we can generate significant revenue from sales of Haduvio, if ever, we expect to finance our operations through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms or at all. Our future funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of Haduvio, including the next our Phase 2b CORAL clinical trials trial of Haduvio for the treatment of chronic cough in IPF, our Phase 2a RIVER clinical trial in refractory chronic cough and RCC, the second part of our HAP study, and our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respiratory physiology in patients with IPF of varying disease severity, as well as trials for any future product candidates;
- the number and characteristics of indications for which we seek to develop Haduvio or any future product candidates and their respective development requirements;
- the outcome, timing and costs of clinical and nonclinical trials and of seeking regulatory approvals, including the costs of

supportive clinical studies such as our HAP study and a potential Thorough QT study;

- the costs associated with the manufacture of necessary quantities of Haduvio or any future product candidate for clinical development in connection with regulatory submissions;
- the costs of commercialization activities for Haduvio for the treatment of chronic cough in IPF or refractory chronic cough o for the treatment of prurigo nodularis and RCC or for any future product candidates that receive marketing approval, if any, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approvals, revenue, if any, received from commercial sales of Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC or for the treatment of prurigo nodularis, or from any future product candidates;
- our ability to identify potential collaborators for Haduvio for the treatment of prurigo nodularis or for the treatment of chronic cough in IPF or refractory chronic cough RCC or for any future product candidates, and the terms and timing of any collaboration agreement that we may establish for the development and any commercialization of such product candidates
- the extent to which we acquire or in-license rights to other potential product candidates or technologies and the terms and timing of any such acquisition or licensing arrangements;
- our potential obligation to make milestone payments to Endo Pharmaceuticals Inc., or Endo, which would become due upo the successful completion of the first Phase 3 clinical trial of a licensed product candidate and the marketing approval of a licensed product in the United States, as well as our potential obligations to pay Endo royalties on the net sales of the product;

- our headcount growth and associated costs as we expand our research and development activities and medical affairs activities and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining, expanding and protecting our intellectual property rights and defending against intellectual property-related claims;
- the effect of competing technologies and market developments;
- our ability to establish and maintain healthcare coverage and adequate reimbursement for our products; and
- the costs of operating as a public company.

We believe that our existing cash, cash equivalents and marketable securities, will enable us to fund our operating expenses and capital expenditure requirements into 2026. Our current plans do not take into account the cost of any additional clinical trials for the treatment of prurigo nodularis.

We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong and we could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing and financing may not be available to us on acceptable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We do not have any committed external source of funds. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources to complete the clinical development and commercialization of Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC or for the treatment of prurigo nodularis or any other indication. If we raise additional funds by issuing equity securities, our stockholders may experience dilution. Any debt financing into which we enter would result in fixed payment obligations and may involve agreements

that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, granting liens over our assets, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect

our management's ability to oversee the development of our product candidates. Any debt financing that we seek or additional equity that we raise may contain terms that could adversely affect our common stockholders.

If we are unable to raise sufficient capital as and when needed, we may be required to delay, reduce or abandon our product development programs or commercialization efforts. If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Contractual Obligations and Commitments

A significant portion of our development activities are outsourced to third parties under agreements, including with CROs and contract manufacturers in connection with the production of clinical trial materials. The contracts are cancelable at any time by us, generally upon 60 days' prior written notice to the CRO, and therefore we believe that our non-cancelable obligations under these agreements are not material. For information related to our future commitments relating to our lease and licensing agreements, see Note 5, "Leases" and Note 11, "Collaborative and Licensing Agreements" of our Condensed Consolidated Financial Statements.

Critical Accounting Policies and Use of Estimates

Our Condensed Consolidated Financial Statements have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these Condensed Consolidated Financial Statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the Condensed Consolidated Financial Statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in the Notes to our financial statements, we believe that the critical accounting policies, which include those policy related to research and development expenses stock-based compensation expense, income taxes, warrants and fair value measurements and which are that is described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Use of Estimates" in our Annual Report on Form 10-K for the year ended December 31, 2022 December 31, 2023, are is the most important to understanding and evaluating our reported financial results. During the nine three months ended September 30, 2023 March 31, 2024, there were no material changes to our critical accounting policies.

Recently Adopted Accounting Pronouncements

There have been no new pronouncements adopted during the nine months ended September 30, 2023.

Recently Issued Accounting Pronouncements

There have been no new pronouncements issued during the nine months ended September 30, 2023 which could be expected to materially impact our Condensed Consolidated Financial Statements.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

Not Applicable.

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, evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as of September 30, 2023 March 31, 2024. Our disclosure controls and procedures are designed to ensure that information we are required to disclose in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures, and is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Because of the inherent limitations in all control systems, no evaluation of controls and procedures can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected. Based on the evaluation of our disclosure controls and procedures as of September 30, 2023 March 31, 2024, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended September 30, 2023 March 31, 2024 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

We are not subject to any material legal proceedings.

Item 1A. Risk Factors.

Our business is subject to numerous risks. The following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in this Quarterly Report on Form 10-Q and other filings with the Securities and Exchange Commission, or SEC, press releases, communications with investors and oral

statements. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception, expect to incur significant and increasing losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred significant annual net losses every year since our inception. We expect to continue to incur significant and increasing net losses for at least the next several years. Our net losses were $21.2 million $10.9 million and $29.2 million $29.1 million for the nine three months ended September 30, 2023 March 31, 2024 and for the year ended December 31, 2022 December 31, 2023, respectively. As of September 30, 2023 March 31, 2024, we had an accumulated deficit of $231.3 million $250.0 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through private placements of our convertible preferred stock and convertible notes prior to our initial public offering, or IPO, proceeds from our IPO, sales of our common stock and warrants to purchase our common stock, and proceeds borrowings from term loans. We have devoted substantially all our financial resources and efforts to the clinical development of our product candidate Haduvio and related activities. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials of Haduvio, including the next trials we plan to conduct for our Phase 2b CORAL clinical trial of Haduvio for the treatment of chronic cough in idiopathic pulmonary fibrosis, or IPF, our Phase 2a RIVER clinical trial of Haduvio for the treatment of refractory chronic cough, or RCC, and the second part of our human abuse potential, or HAP, study; study, and our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respirator physiology in patients with IPF of varying disease severity;
- complete other development work required for the filing of a new drug application, or NDA, with the U.S. Food and Drug Administration, or FDA, and the filing of marketing authorization applications, or MAAs, with the European Medicines Agen or EMA, and the Medicines and Healthcare Products Regulatory Agency in the United Kingdom, or MHRA, or other government agencies, for Haduvio;

- seek regulatory and marketing approvals for Haduvio for the treatment of chronic cough in IPF, or refractory chronic cough RCC and/or for the treatment of prurigo nodularis or for any future product candidate that successfully completes clinical trials, if any;
- negotiate and execute pediatric development plans and complete any post-approval commitments;
- establish sales, marketing, distribution and other commercial infrastructure to commercialize any products for which we ma obtain marketing approval;

- require the manufacture of larger quantities of Haduvio or any future product candidate for clinical development and, potentially, commercialization;
- acquire or in-license rights to other potential product candidates or technologies;
- initiate and conduct research, preclinical and clinical development efforts for any future product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, regulatory and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts and to help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our development program for Haduvio and for any future product candidates.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are able to obtain marketing approval for and successfully commercialize Haduvio or any future product candidate. Successful commercialization will require achievement of key milestones, including completing clinical trials of Haduvio or any future product candidate, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for any such product from private insurance or government payors. For example, in order to successfully commercialize Haduvio for the treatment of prurigo nodularis, chronic cough in IPF, we are may be required, at a minimum, to successfully complete an two additional Phase 3 clinical trial trials prior to submitting an NDA and MAA to regulatory authorities to obtain marketing approval. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues and if or when we might achieve profitability. We may never succeed in these activities and, even if we do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our

ability to raise capital, expand our business, maintain our development efforts, develop a pipeline of product candidates or continue our operations.

We have a limited operating history and no products approved for commercial sale, which may make it difficult to evaluate the prospects for our future success and viability.

We were founded and commenced operations in 2011. Our operations to date have been limited to financing and staffing our company and conducting preclinical and clinical development of Haduvio. We have not yet demonstrated an ability to successfully complete clinical development of any product candidates, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third-party to do so on our behalf or conduct sales and marketing activities necessary for successful commercialization of any products. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by clinical-stage biopharmaceutical companies such as ours. Any predictions you make about

our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. If we obtain marketing approval for Haduvio or any future product candidate, we will need to transition from a company focused on clinical development to a company capable of supporting commercial activities. We may not be successful in effectuating such a transition.

We expect our financial condition and operating results will continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding and if we are unable to raise sufficient capital when needed on acceptable terms or at all, we could be forced to delay, reduce or abandon our product development programs or commercialization efforts.

Developing pharmaceutical products, including conducting preclinical and nonclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We have consumed substantial amounts of cash since our inception. For example, in the nine three months ended September 30, 2023 March 31, 2024 and the year ended December 31, 2022 December 31, 2023, we used net cash of $25.4 million $10.5 million and $28.2 million $31.7 million, respectively, in our operating activities, substantially all of which related to development activities for Haduvio. As of September 30, 2023 March 31, 2024, our cash, cash equivalents and marketable securities were $88.9 million $72.8 million. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we continue to develop Haduvio, including as we:

- conduct the next trials we plan to conduct for our Phase 2b CORAL clinical trial of Haduvio for the treatment of chronic cou in IPF;
- conduct our Phase 2a RIVER clinical trial of Haduvio for the treatment of refractory chronic cough; RCC;
- conduct our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respiratory physiology in patients with IPF o varying disease severity; and
- conduct the second part of our HAP study to further characterize compare the abuse potential of oral nalbuphine ER. to intravenous, or IV, butorphanol.

In addition, we may incur additional expenses:

- if we determine to conduct an additional clinical trial of Haduvio for the treatment of prurigo nodularis; and
- if we acquire or in-license rights to other potential product candidates or technologies and seek regulatory and marketing approvals for Haduvio or any future product candidate that successfully completes clinical trials.

In addition, if we obtain marketing approval for Haduvio or any future product candidate, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. For instance, we currently intend to commercialize Haduvio in the U.S. ourselves by developing a focused, specialty sales, marketing and distribution organization. Furthermore, we expect to continue to incur significant costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise sufficient capital when needed on acceptable terms or at all, we may be forced to delay, reduce or abandon our development programs or any future commercialization efforts.

We plan to use our existing cash, cash equivalents and marketable securities to fund the development of Haduvio and for working capital and other general corporate purposes. We will be required to expend significant funds to advance the development of Haduvio in multiple indications, as well as any future product candidates we may seek to develop. Our existing cash, cash equivalents and marketable securities will not be sufficient to complete development of Haduvio for the treatment of chronic cough in IPF, for refractory chronic cough RCC or for prurigo nodularis, or for any other condition or of any future product candidate. We do not have any committed external source of funds. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

We believe that our existing cash, cash equivalents and marketable securities will enable us to fund our operating expenses and capital expenditure requirements into 2026. Our current plans do not take into account the cost of any additional clinical trials for the treatment of prurigo nodularis.

We have based our estimates as to how long we expect we will be able to fund our operations on assumptions that may prove to be wrong and we could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing. However, such a financing may not be available to us on acceptable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy.

Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate and we may need to seek additional funds sooner than planned. Our future funding requirements, both short-term and long-term, will depend on many factors including:

- the scope, progress, timing, costs and results of clinical trials of Haduvio, including the next our Phase 2b CORAL clinical trials trial of Haduvio for the treatment of chronic cough in IPF, our Phase 2a RIVER clinical trial in refractory chronic cough and RCC, the second part of our HAP study, and our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respiratory physiology in patients with IPF of varying disease severity, as well as trials for any future product candidates;
- the number and characteristics of indications for which we seek to develop Haduvio or any future product candidates and their respective development requirements;
- the outcome, timing and costs of clinical and nonclinical trials and of seeking regulatory approvals, including the costs of supportive clinical studies such as our HAP study and a potential Thorough QT, or TQT, study;
- the costs associated with the manufacture of necessary quantities of Haduvio or any future product candidate for clinical development in connection with regulatory submissions;

- the costs of commercialization activities for Haduvio for the treatment of chronic cough in IPF and refractory chronic cough RCC or for any future product candidates that receive marketing approval, if any, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

- subject to receipt of marketing approvals, revenue, if any, received from commercial sales of Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC or for the treatment of prurigo nodularis, or from any future product candidates;
- our ability to identify potential collaborators for Haduvio for the treatment of prurigo nodularis or for the treatment of chronic cough in IPF or refractory chronic cough RCC or for any future product candidates, and the terms and timing of any collaboration agreement that we may establish for the development and any commercialization of such product candidates
- the extent to which we acquire or in-license rights to other potential product candidates or technologies and the terms and timing of any such acquisition or licensing arrangements;
- our potential obligation to make milestone payments to Endo Pharmaceuticals Inc., or Endo, which would become due upo the successful completion of the first Phase 3 clinical trial of a licensed product candidate and the marketing approval of a licensed product in the United States, as well as our potential obligations to pay Endo royalties on the net sales of the product;
- our headcount growth and associated costs as we expand our research and development activities and medical affairs activities and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining, expanding and protecting our intellectual property rights and defending against intellectual property-related claims;
- the effect of competing technologies and market developments;
- our ability to establish and maintain healthcare coverage and adequate reimbursement for our products; and
- the costs of operating as a public company.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our product candidates.

We expect our expenses to increase substantially in connection with our planned operations, particularly as we:

- conduct the next our Phase 2b CORAL clinical trials we plan to conduct for trial of Haduvio for the treatment of chronic coug in IPF;
- conduct our Phase 2a RIVER clinical trial of Haduvio for the treatment of refractory chronic cough; and RCC;
- conduct our planned Phase 1b clinical trial to evaluate the effect of Haduvio on respiratory physiology in patients with IPF c varying disease severity; and

- conduct the second part two of our HAP study to further characterize compare the abusive abuse potential of oral nalbuphir ER. to IV butorphanol.

Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources to fund these expenses. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder.

Debt financing, if available, would result in fixed payment obligations and may involve agreements that include grants of security interests on our assets and restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, granting liens over our assets, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business.

Securing financing could also require a substantial amount of time from our management and may divert a disproportionate amount of their attention away from daily activities, which may adversely affect our management's ability to oversee the development of Haduvio or that of any future product candidates. If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

Risks Related to the Development and Commercialization of Haduvio and Any Future Product Candidates

We are dependent on the successful development and commercialization of Haduvio, our sole product candidate. If we are unable to complete the clinical development of, obtain marketing approval for or successfully commercialize Haduvio or if we experience significant delays in doing so, our business would be substantially harmed.

We currently have no products approved for sale and are investing substantially all our efforts and financial resources to fund the development and commercialization of Haduvio for the treatment of chronic cough in IPF and refractory chronic cough and for the treatment of prurigo nodularis. RCC. Our prospects are dependent on our ability to develop, obtain marketing approval for and successfully

commercialize Haduvio in one or more indications as we currently have no other product candidates under development. We may acquire or in-license rights to other potential product candidates or technologies in the future, but we are currently not developing any other product candidates.

Our most advanced programs are the development of Haduvio for the treatment of chronic cough in IPF and refractory chronic cough and for the treatment of prurigo nodularis. RCC. As a result, if our efforts to develop and commercialize Haduvio for the treatment of chronic cough in IPF or refractory chronic cough or for the treatment of prurigo nodularis RCC are unsuccessful or we experience significant delays in doing so, our business could also be substantially harmed.

The success of Haduvio for the treatment of chronic cough in IPF and refractory chronic cough and for the treatment of prurigo nodularis RCC will depend on several factors, including the following:

- initiating and successfully recruiting, enrolling and retaining subjects patients in and completing additional clinical and nonclinical trials of Haduvio, including the additional clinical trials we are conducting and plan to conduct for the treatment c chronic cough in IPF which are subject to the submission and clearance by the FDA of an IND, and refractory chronic cough; RCC;
- completing the analysis of the open-label extension portion second part of our Phase 2b/3 PRISM trial and determining the next steps for the prurigo nodularis program after discussions with the FDA; HAP study;
- completing other supportive clinical studies such as potential studies of physical dependence and Thorough QT;
- completing the second part of our HAP study; TQT;
- demonstrating safety, tolerability and efficacy profiles that are satisfactory to the FDA, EMA, MHRA and other comparable regulatory authorities for marketing approval;

- receiving timely marketing approvals from applicable regulatory authorities;
- managing any required post-marketing approval commitments to applicable regulatory authorities;
- establishing and maintaining arrangements with our third-party supplier of drug substance for Haduvio;
- establishing and maintaining arrangements with third-party manufacturers of Haduvio, including developing, validating and maintaining a commercially viable manufacturing process that is compliant with current good manufacturing practices, or cGMPs;
- obtaining, maintaining and protecting our patents, trade secrets and regulatory exclusivity in the U.S. and other countries;
- establishing a focused, specialty sales organization in the U.S. and successfully launching commercial sales following any marketing approval;
- obtaining commercial acceptance of our products, if approved, by patients, the medical community and third-party payors a obtaining and maintaining healthcare coverage and adequate reimbursement;
- maintaining an acceptable safety profile following any marketing approval; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including the clinical development and regulatory approval process; potential threats to our intellectual property rights; and the manufacturing, marketing and sales efforts, respectively, of any current or future third-party contractors. If we are unable to develop, receive marketing approval for and successfully commercialize Haduvio or if we experience delays as a result of any of these factors or otherwise, our business would be substantially harmed.

Our approach to the development and commercialization of Haduvio to treat chronic cough is unproven.

We are currently focused on the development and commercialization of Haduvio for the treatment of chronic cough in IPF and refractory chronic cough. RCC. Haduvio is an oral extended-release formulation of nalbuphine, the active drug ingredient in Haduvio, which is a mixed κ-opioid receptor agonist and μ-opioid receptor antagonist that has been approved and marketed as an injectable for pain indications for more than 20 years in the U.S. and Europe. Nalbuphine is currently not commercially available in an oral dosage form, such as Haduvio. While we believe that nalbuphine's dual mechanism of action, which targets both the central and peripheral nervous systems, makes Haduvio a promising potential therapy for the treatment of chronic cough and that Haduvio has the potential to be safe and well-tolerated, nalbuphine has not been approved in any indications other than pain and balance balanced anesthesia. Additionally, Haduvio has not been approved in any indication. No therapies have been approved in the U.S. or Europe for the treatment of chronic cough in IPF and no therapies have been approved in the U.S. or outside the U.S. (with the exception of Japan and Switzerland) for the treatment of refractory chronic cough. RCC. We can provide no assurance that Haduvio or any other future product candidate that we may seek to develop for chronic cough indications will be effective or safe, obtain regulatory approval or be commercially successful.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome.

We are not permitted to commercialize, market, promote or sell any product candidate in the U.S. without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA and MHRA, impose similar requirements. We must complete extensive clinical trials to demonstrate the safety and efficacy of Haduvio and any future product candidate in humans and complete required regulatory submissions before we will be able to obtain these approvals. We may never receive such approvals.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. The clinical development of Haduvio and any future product candidate is susceptible to the risk of failure at any stage of product development and we may experience numerous unforeseen events during or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of Haduvio or any future product candidate, including:

- clinical trials may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to restructure clinical trials, conduct additional clinical and nonclinical trials or abandon product development programs;
- we may experience delays in obtaining authorization to commence a clinical trial from regulators, clinical sites and institutional review boards;
- the number of subjects patients required for clinical trials may be larger than we anticipate, as we experienced with the increase of the target number of enrolled subjects patients for our Phase 2b/3 PRISM trial from 240 to 360 subjects patients as a result of the sample size re-estimation analysis;
- subject patient enrollment in clinical trials may be slower than we anticipate or participants may discontinue their participatio in these clinical trials at a higher rate than we anticipate, as we experienced in our Phase 2b/3 PRISM trial of Haduvio for th treatment of prurigo nodularis;
- the cost of planned clinical trials may be greater than we anticipate, such as if we are required to add additional sites, increase the target number of enrolled subjects patients or use additional incentive strategies to address site activation and enrollment;
- our clinical trials trial sites may not have adequate staff and resources to support our trials on a timely basis;
- our third-party contractors, including any that may be manufacturing a product candidate or drug substance or conducting clinical trials on our behalf, may deviate from applicable trial protocols, fail to comply with regulatory requirements or fail to meet their contractual obligations to us in a timely manner or at all;
- 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 protoc with prospective trial sites;
- subjects patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with applicable clinical trial protocols, resulting in the need to drop the subjects patients from the clinical trial, increase the neede enrollment size for the clinical trial or extend the clinical trial's duration;
- we may have to delay, suspend or terminate clinical trials for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of a product candidate;

- 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 their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or produc candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our clinical trial designs or our interpretation of dat from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplie
- the supply or quality of drug substance for our product candidates or the manufactured product candidate or other material or drug substances necessary to conduct clinical trials of the product candidate may be insufficient, inadequate or not available at an acceptable cost or we may experience interruptions in supply, such as the difficulties we have had in

obtaining supply of IV butorphanol, the comparator drug in our HAP study;

- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change or the landscape of available, approved therapies could change in a manner rendering our clinical data insufficient to obtain marketing approvals; and
- the FDA or comparable foreign regulatory authorities may refuse to accept for substantive review any NDA, MAA or other comparable foreign regulatory application that we submit for a product candidate or may conclude after review of our data that our application is insufficient to obtain marketing approval of a product candidate.

In addition to the above, the COVID-19 pandemic previously adversely affected our clinical trial operations worldwide, and other outbreaks of infectious disease could in the future adversely affect our clinical trial operations worldwide, including our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to infectious diseases. The COVID-19 pandemic resulted in delays in our clinical trials due to prioritization of hospital and medical resources toward the pandemic, restrictions in travel, potential unwillingness of patients to enroll in trials or the inability of patients to comply with clinical trial protocols where quarantines or travel restrictions impeded patient movement or interrupted healthcare services. Furthermore, the response to any future outbreak of infectious disease may redirect resources of regulators in a way that would adversely impact our ability to progress regulatory approvals. In addition, we may face impediments to regulatory meetings and approvals relating to our clinical trials due to measures intended to limit in-person interactions. In the future, we may experience adverse impacts on our clinical trial activities, business operations, financial condition, and prospects as a result of outbreaks of infectious disease, among other factors.

If we are required to conduct additional clinical trials or other testing of Haduvio or any future product candidate beyond the trials and testing that we contemplate, we are unable to successfully and timely complete clinical trials or other testing of Haduvio or any future product candidate, the results of these trials or tests are unfavorable, uncertain or are only modestly favorable or there are unacceptable safety concerns associated with the product candidate, we may:

- incur additional unplanned costs, which may exceed the resources that we have available or are able to obtain on reasonal terms;
- experience delays in obtaining marketing approval for the applicable product candidate for several years or more, which

could shorten the periods during which we may have the exclusive right to commercialize the product candidate or allow competitors to bring products to market before us;

- fail to obtain marketing approval at all;
- obtain marketing approval for indications or patient populations that are not as broad as we originally intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or significant safety warnings including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. For example, in December 2022, with the passage of the Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase Phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

Similarly, the regulatory landscape related to clinical trials in the E.U. recently evolved. The E.U. Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the E.U. Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate clinical trial application, or CTA, to be submitted in each member state, Member State of the E.U., or E.U. Member State, to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application to all member states Member States concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, Member State, leading to a single

decision per member state. Member State. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states Member States concerned, and a separate assessment by each member state Member State with respect to specific requirements related to its own territory, including ethics rules. Each member state's Member State's decision is communicated to the sponsor via the centralized E.U. portal. Once the CTA is approved, clinical study development may proceed. If we are not able to address these changes in existing requirements or the adoption of new requirements or policies governing clinical trials or there are difficulties with the implementation of the CTR process, our development plans may be impacted.

Our failure to successfully and timely complete clinical trials of Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC or for the treatment of prurigo nodularis or of any future product candidate and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any such product candidates would significantly harm our business and could result in the loss or impairment of our ability to generate revenues and effectuate our business strategy.

Our clinical trials may fail to demonstrate adequately the safety and efficacy of Haduvio or any future product candidates, which would likely prevent or delay regulatory approval and commercialization.

Before obtaining regulatory approvals for the commercial sale of Haduvio or any future product candidate we must demonstrate through lengthy, complex and expensive clinical trials that the product candidate is both safe and effective for use in the target indication. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. It is possible that even if Haduvio or any future product candidate has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. For example, our Phase 2 clinical trial of Haduvio for the treatment of prurigo nodularis failed to meet its primary endpoint and the number of subjects who discontinued treatment prior to the end of the trial had a substantial impact on the results. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of Haduvio or any future product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of, or intolerability caused by, Haduvio or any future product candidate or mistakenly believe that Haduvio or any future product candidate is toxic or not well tolerated when that is not the case after the clinical evaluation is completed. Many pharmaceutical and biotechnology companies have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we cannot be certain that we will not face setbacks as we continue our clinical development of Haduvio and develop any other product candidates. It is also possible that any of our development programs could be placed on full or partial clinical hold by regulatory authorities at any point, which would delay and possibly prevent further development of those programs.

In addition, even if the clinical trials we plan are successfully completed and Haduvio or any future product candidate achieves its specified endpoints in such trials, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we are able to submit product candidates for marketing approval.

Use of patient-reported outcome assessments, or PROs, in our clinical trials and high placebo response rates may delay or impair the development of Haduvio or adversely impact our clinical trials.

Although the primary endpoint in our future clinical trials of Haduvio for the treatment of chronic cough in IPF and refractory chronic cough RCC will be measured using an objective cough monitor, we have PRO instruments as secondary endpoints that may need to validate a supportive PRO instrument of the primary endpoint. endpoints. There is not currently a validated PRO instrument that has been accepted for chronic cough indications.

In addition, due to the difficulty of objectively measuring pruritus, the assessment of pruritus in clinical trials typically involves the use of PROs. Our clinical trials evaluating the efficacy of Haduvio in pruritus indications, including our Phase 2b/3 PRISM trial, have used PROs as primary endpoints. For example, the primary endpoint of our Phase 2b/3 PRISM trial was the proportion of patients achieving at least a 4-point improvement from baseline with respect to their worst itch at week 14 as measured by the Worst Itch Numerical Rating Scale, or WI-NRS, scores, which is a patient-reported assessment on an 11-point scale from 0 to 10 of the severity of the worst itch experienced in the last 24 hours. PROs have an important role in the development and regulatory approval of treatments for pruritus. However, PROs involve patients' subjective assessments of efficacy, and this subjectivity can increase the uncertainty of clinical trial outcomes assessing pruritus. Such assessments can be influenced by a number of factors

and can vary widely from day to day for any particular patient and from patient to patient and site to site within a clinical trial, leading to high variability in PRO measurements.

In addition, PROs have historically been observed to have high placebo group response rates. We observed this in some of our clinical trials of Haduvio. The variability of PRO measures may be greater than other measures used for clinical trial assessments, and that variability can complicate clinical trial design, adversely impact the ability of a trial to show a statistically significant improvement and generally adversely impact a clinical development program by introducing additional uncertainties.

The variability of PRO measures and related high placebo response rates have adversely impacted clinical results of other therapies being tested and could adversely impact our clinical development of Haduvio. The FDA could also require changes in the PROs we are currently using or indicate that the PROs we are using are insufficient for demonstrating efficacy, potentially delaying clinical development of Haduvio, increasing our costs and making additional clinical trials necessary.

If we experience delays or difficulties in the enrollment of subjects patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for Haduvio or any future product candidate if we are unable to locate and enroll a sufficient number of eligible subjects patients to participate in clinical trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of our clinical trials and is affected by many factors, including:

- the size and nature of the eligible patient population;
- the severity of the disease under investigation;

- the proximity of eligible patients to clinical sites;
- patient referral practices of physicians;
- the eligibility criteria for the clinical trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relat to other available therapies, including any new drugs that may be approved for the indications under investigation.

In particular, the successful completion of our clinical development program for Haduvio for the treatment of chronic cough in IPF and refractory chronic cough RCC and for the treatment of prurigo nodularis is dependent upon our ability to enroll a sufficient number of subjects patients with these severe conditions. We experienced delays and difficulties in the enrollment of subjects patients in our clinical trials, including our Phase 2 CANAL trial and our Phase 2b/3 PRISM trial, which delayed the completion of our trials.

Other companies are conducting clinical trials or have announced plans for future clinical trials that are seeking or are likely to seek to enroll patients with IPF, refractory chronic cough RCC or prurigo nodularis, and patients are generally only able to enroll in a single trial at a time. No therapies have been approved in the U.S. or Europe for the treatment of chronic cough in IPF and no therapies have been approved in the U.S. or outside the U.S. (with the exception of Japan and Switzerland) for the treatment of refractory chronic cough. RCC. However, patients with these conditions, as well as their physicians, may be reluctant to forgo, discontinue or otherwise alter their use of the therapeutic approaches they currently use in order to participate in our clinical trials. For example, patients may use Dupixent (dupilumab), an injectable prescription medicine, that was approved by the FDA for the treatment of prurigo nodularis in September 2022 or various treatments off-label for the treatment of prurigo nodularis, such as antihistamines or gabapentin; these patients and their physicians may be reluctant to forgo, discontinue or otherwise alter their use of Dupixent or any off-label therapeutic approaches to participate in our clinical trials.

In response to the COVID-19 pandemic, the FDA issued numerous guidance documents and took other actions to facilitate research and development of new drug products. Although the public health emergency declarations related to COVID-19 ended on May 11, 2023, the FDA retained a number of COVID-19 related policies. It is unclear how, if at all, these policies will impact our efforts to develop and commercialize our product candidates.

Any inability to enroll a sufficient number of subjects patients for our clinical trials could result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for Haduvio or any future product candidate, delay or halt the development of and approval processes for such product candidate and jeopardize our ability to commence sales of and generate revenues from such product candidate, any of which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

Adverse events or undesirable side effects caused by, or other unexpected properties of, Haduvio or any future product candidate may be identified during development and could delay or prevent the marketing approval or limit the use of Haduvio or any future product candidate.

Adverse events or undesirable side effects caused by or other unexpected properties of, Haduvio or any future product candidate could cause us, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of such product candidate and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. We cannot be certain that serious adverse events or SAEs, will not occur in future clinical trials, which could cause the FDA or comparable foreign regulatory authorities to interrupt, delay or halt clinical trials of such product candidate, approve a more restrictive label than we desire or delay or deny regulatory approval.

In addition, Haduvio, as a mixed κ-opioid receptor agonist and μ-opioid receptor antagonist, may be susceptible to side effects associated with drugs having either of those mechanisms of action. κ-opioid receptor agonists have been associated with poorly tolerated psychiatric side effects, such as feelings of emotional and mental discomfort or dysphoria and hallucinations, at high doses. While we believe that the dual κ-opioid receptor agonist and μ-opioid receptor antagonist mechanism of action of nalbuphine reduces the likelihood of such psychiatric side effects, we have observed mild psychiatric side effects, including a few reported cases of mild euphoria, somnolence and feeling relaxed or feeling “high,” in clinical trials of Haduvio to date. μ-opioid receptor antagonists have the potential to precipitate withdrawal effects in patients, including drug addicts. To support our planned submission of an NDA to the FDA for Haduvio, due to the association of opioids with endocrine dysfunction, we may be required to conduct a clinical trial of Haduvio to evaluate potential endocrine side effects. We cannot be certain that any of these side effects often associated with opioids, or other side effects, will not be observed or observed at more severe levels in the future or that the FDA will not require additional trials or impose more severe labeling restrictions due to these side effects or other concerns. Such

drug-related side effects could also affect patient recruitment or the ability of enrolled subjects patients to complete a trial or result in potential product liability claims.

In our clinical trials of Haduvio for the treatment of prurigo nodularis, the most frequently reported treatment emergent adverse events associated with Haduvio were nausea, fatigue, dizziness, vomiting, headache, anxiety, depression, constipation and

somnolence. In our Phase 2 CANAL trial of Haduvio for the treatment of chronic cough in IPF, the most frequently reported treatment emergent adverse events associated with Haduvio were nausea, fatigue, dizziness, vomiting, headache, constipation and somnolence.

If Haduvio or any future product candidate is associated with adverse events or undesirable side effects or demonstrates unexpected properties, we may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that have initially shown promise in clinical or earlier stage testing were later discovered to cause undesirable or unexpected side effects or raised other safety issues that delayed or prevented further development of the compound.

The drug label for nalbuphine, the active ingredient in Haduvio, carries an opioid class label warning for serious, life-threatening or fatal respiratory depression.

μ-opioid receptor antagonists such Opioids as nalbuphine a class are associated with respiratory depression. The drug label for nalbuphine, the active ingredient in Haduvio, carries an opioid class label warning for serious, life-threatening or fatal respiratory depression and Haduvio, if approved for marketing in any indication, will likely carry a similar opioid class label. We intend to conduct a Phase 1b study to evaluate the effect of Haduvio on respiratory physiology in patients with IPF of varying disease severity. We cannot be certain that respiratory depression will not be observed or that the FDA will not require additional trials or impose more severe labeling restrictions related to respiratory depression. If there is a safety signal in the Phase 1b study, it could affect our ability to conduct a trial in this patient population.

Many currently approved μ-opioid products are subject to restrictive marketing and distribution regulations which, if applied to Haduvio, could potentially restrict its use and harm our ability to generate profits.

Many currently approved μ-opioid receptor agonists require a Risk Evaluation and Mitigation Strategy, or REMS, as part of their approval by the FDA. REMS programs may require medication guides for patients, special communication plans to healthcare professionals or elements to assure safe use, such as restricted distribution methods, patient registries and/or other risk minimization tools. While Haduvio has a μ-antagonist mechanism of action and has been well-tolerated in clinical trials to date, we have observed a few cases of mild euphoria, somnolence and feeling relaxed or feeling “high,” which are characteristics that have led to misuse, abuse and addiction of μ-opioids. We are conducting a HAP study to further characterize compare the abuse

potential of oral nalbuphine ER. to IV butorphanol. If the results of the HAP study suggest that Haduvio may carry risks of misuse, abuse or addiction or even if the trial indicates that Haduvio does not carry such risks, the FDA may require us to implement a REMS program in connection with any commercialization of Haduvio. We cannot predict whether a REMS program would be required as part of FDA approval of Haduvio and, if required, what requirements it might entail. Any limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensation of Haduvio, if approved. If a REMS program is required, depending on the extent of the REMS requirements, the program might significantly increase our costs to commercialize Haduvio. Furthermore, risks of Haduvio that are not adequately addressed through a proposed REMS program for Haduvio may also prevent or delay any approval for commercialization.

In addition, the parenteral formulation of nalbuphine is currently not scheduled as a controlled substance under the federal Controlled Substances Act of 1970 or the regulations of the U.S. Drug Enforcement Agency, or the DEA, in the U.S. It is possible that, based on the results of our HAP study, adverse events in our clinical trials or for other reasons, the DEA could determine that Haduvio, which is an oral, extended-release formulation, should be classified as a controlled substance. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the U.S. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and carrying the greater level of regulatory control and Schedule V substances considered to present the lowest relative risk of abuse among such substances and, accordingly, the lowest level of regulatory control. Various states also independently regulate controlled substances. Though state-controlled substance laws often mirror federal law, because the states are separate jurisdictions, they may separately regulate drugs as well. While some states automatically classify a drug when the DEA does so, in other states there must be rulemaking or a legislative action. Regulatory authorities in foreign jurisdictions may also determine to classify Haduvio as a controlled substance under different, but potentially no less burdensome, regulations.

If Haduvio is classified as a controlled substance, the level of regulation would depend on how it is scheduled and we and our suppliers, manufacturers, contractors, distributors and any future customers would be required to obtain and maintain any applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with any applicable state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. Also, if Haduvio is classified as a controlled substance, there is a risk that such regulations could limit its supply for use in clinical trials and, in the future, limit our ability to produce and distribute Haduvio in the volume needed to meet potential commercial demand.

Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, record keeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs

and the expense associated with development and commercialization of product candidates, including controlled substances. The DEA and some states conduct periodic inspections of registered establishments that handle controlled substances. If Haduvio is classified as a controlled substance, failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing Haduvio and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some

circumstances, violations could lead to criminal proceedings. Because of the restrictive nature of these regulations, if Haduvio is classified as a controlled substance, depending on how it is scheduled, its commercial prospects could be limited.

Results of preclinical studies and clinical trials may not be predictive of results of later clinical trials.

The outcome of preclinical studies and clinical trials may not be predictive of the success of later clinical trials and preliminary or interim results of clinical trials do not necessarily predict final results. For instance, Haduvio or any future product candidate may fail to show the desired safety and efficacy in future clinical trials despite demonstrating positive results in preclinical studies or earlier clinical trials. The results of our Phase 2 CANAL trial for the treatment of chronic cough in IPF may not be predictive of the results of future trials of Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC, and the results of our Phase 2b/3 PRISM trial of Haduvio

for the treatment of prurigo nodularis may not be predictive of the results of any future clinical trial in prurigo nodularis. Many pharmaceutical and biotechnology companies have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier stages of clinical development and we could face similar setbacks. Similarly, the design of a clinical trial can determine whether its results will support marketing approval of a product and adjustments in the design of a clinical trial may not be possible once the clinical trial has commenced.

We have limited experience in designing pivotal clinical trials and flaws in the design of a clinical trial could result in significant delays in completing the clinical trial or may require us to abandon the clinical trial altogether or conduct additional clinical trials. Preclinical and clinical data are also often susceptible to varying interpretations and analyses. Many pharmaceutical and biotechnology companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for those product candidates. Even if we believe that the results of clinical trials for Haduvio or any future product candidate warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of the product candidate.

In addition, some of our data for Haduvio for the treatment of cough and prurigo nodularis is drawn from *post hoc* analyses of data subsets from the Phase 2 CANAL trial and a Phase 2 trial in prurigo nodularis. While we believe these data may be useful in informing the design of future Phase 3 clinical trials for Haduvio, *post hoc* analyses performed after unmasking trial results can result in the introduction of bias and may not be predictive of success in Phase 3 clinical trials.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of patient populations, changes in and adherence to dosing regimens and other clinical trial protocols, as well as the rate of discontinuation among clinical trial participants. If we fail to receive positive results in clinical trials of Haduvio or any future product candidate, the development timeline and regulatory approval and commercialization prospects for those product candidates and, correspondingly, our business and financial prospects would be negatively impacted.

Even if Haduvio or any future product candidate receives marketing approval, we or others may later discover that the product is less effective than previously believed or that it causes undesirable side effects that were not previously

identified, which could compromise our ability to market the product.

Clinical trials are conducted in carefully defined sets of patients who have agreed to participate in clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we or others discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of or the manufacturing processes for, the product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distributio to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and

- our reputation may suffer.

Any of these events could harm our business and operations and could negatively impact our stock price.

Even if Haduvio or any future product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case the market opportunity for Haduvio may be smaller than we estimate and we may not generate significant revenues or become profitable.

We have never commercialized a product and even if Haduvio or any future product candidate is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market and may be reluctant to prescribe opioid-based therapies due to perceived risks of misuse, abuse and addiction. Further, patients often acclimate to their current therapies and do not want to switch unless their physicians recommend changing products or they are required to switch therapies due to lack of reimbursement for existing therapies.

Efforts to educate the medical community and third-party payors on the benefits of Haduvio or any future product candidate may require significant resources and may not be successful. If Haduvio or any future product candidate is approved but does not

achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of Haduvio or any future product candidate, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential and perceived advantages of the product compared to other therapies;
- the prevalence and severity of any side effects;
- the potential that the DEA could determine that Haduvio should be classified as a controlled substance;
- the clinical indications for which the product is approved;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability to offer the product for sale at competitive prices;
- the product's convenience and ease of administration;
- the willingness of the target patient population to try and of physicians to prescribe the product;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;
- the strength of sales, marketing and distribution support for the product;
- the approval of other new products for the same indications;
- the timing of market introduction of the product as well as competitive products;
- adverse publicity about the product or favorable publicity about competitive products;
- potential product liability claims;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-part payors.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates 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 intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. For example, we currently intend to focus our resources on the development of Haduvio for certain indications. However, the development of Haduvio for these indications may ultimately prove to be unsuccessful or less successful than another product candidate or other indications that we might have chosen to pursue with our limited resources.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable product candidates. 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 the product candidate.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing Haduvio or any future product candidates if and when they are approved.

We do not currently have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. If Haduvio receives marketing approval from the FDA for chronic cough in IPF, we plan to market and commercialize Haduvio in the U.S. with our own focused, specialty sales organization targeting pulmonologists who specialize in IPF. We would not If Haduvio receives marketing approval from the FDA for other larger chronic conditions, such as RCC or prurigo nodularis, we may plan to market and commercialize Haduvio for other larger conditions such as refractory chronic cough in the U.S. with our own focused, specialty sales organization, or prurigo nodularis. Instead, we would plan to seek to enter into a strategic alliance for commercialization for such indication or indications. We also expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Haduvio outside the U.S.

We plan to build focused capabilities to commercialize development programs for certain indications where we believe that medical specialists are sufficiently concentrated to allow us to effectively promote products with a specialty sales team. The

development of sales, marketing and distribution capabilities will require substantial resources, will be time-consuming and could delay any product launch. We could prematurely or unnecessarily incur commercialization costs if the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason. This may be costly, and our business and financial prospects could be significantly affected if we could not retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the U.S. that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain an adequate sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

In certain indications and markets, we may seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize Haduvio or any future product candidate. We may also seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be substantially lower than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable

to us. In addition, we may have little or no control over such third parties and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any product candidate that receives marketing approval.

We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do.

The development and commercialization of new products is highly competitive. We expect that we will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to Haduvio or any future product candidate that we may seek to develop or commercialize. Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective, have fewer or more tolerable side effects or are more convenient or less costly than Haduvio or any future product candidate we may develop, which could render any product candidates obsolete and noncompetitive. Our competitors also may obtain FDA or other marketing approval for their products before we are able to obtain approval for ours, which could result in competitors establishing a strong market position before we are able to enter the applicable market.

If Haduvio is approved for the treatment of chronic cough in IPF, we expect that it may compete with product candidates currently in clinical development for the treatment of chronic cough in IPF, such as orvepitant, a NK1 receptor antagonist, which is being developed by Nerre Therapeutics, inhaled IMID, ME-015, a reactive oxygen species scavenger, which is being developed by Vicore, Melius Pharma, BI 1839100, which is being developed by Boehringer Ingelheim, and ifenprodil, a NMDA receptor antagonist, which is being developed by Algernon Pharmaceuticals. In addition, it is possible that product candidates currently in development for the treatment of IPF could, if approved, reduce the need for therapies to treat chronic cough in IPF. We expect that Haduvio might also compete with other product

candidates currently in development, or submitted for approval to the FDA, for the treatment of refractory chronic cough RCC and unexplained chronic cough that might be used off-label to treat chronic cough in IPF.

If Haduvio is approved for the treatment of refractory chronic cough, RCC, we expect that it may compete with product candidates currently in clinical development for the treatment of refractory chronic cough RCC such as gefapixant, a P2X3 antagonist, which is being developed by Merck, however, in December of 2023 the FDA issued a complete response letter to Merck which concluded that Merck's application did not meet substantial evidence of effectiveness for treating RCC and unexplained chronic cough. On December 20, 2023, Merck announced that it is reviewing the FDA's feedback to determine next steps. Other product candidates that are currently in development for the treatment of RCC include camlipixant, a P2X3 antagonist, which is being developed by GSK plc, sivopixant, which is being developed by Shionogi, ADX-629, which is being developed by Alderya, NTX-1175, a charged sodium channel blocker, which is being developed by Nocion, GDC-6599, a TRPA1 antagonist, which is being developed by Genentech, ifenprodil, a NMDA receptor antagonist, which is being developed by Algernon Pharmaceuticals, AX-8, a TRPM8 antagonist, which is being developed by Axalbion, and GABAB PAM, a GABA agonist, which is being developed by Addex Therapeutics.

We also expect that Haduvio would compete with a number of therapeutics that are used off-label to treat chronic cough, including opioids, proton-pump inhibitors, and neuromodulators.

If Haduvio is approved for the treatment of prurigo nodularis, we expect that it would compete with Dupixent (dupilumab), an injectable prescription medicine which was jointly developed by Sanofi and Regeneron, which is approved in the U.S., E.U., Japan, and which was approved by the FDA China for the treatment of adults with moderate-to-severe prurigo nodularis in September 2022. Sanofi has announced its plans to make regulatory submissions around the world for this indication. nodularis. We also expect that Haduvio would compete with a number of therapeutics that are used off-label to treat prurigo nodularis, including anti-itch creams and emollients, oral janus kinase, or JAK, receptor inhibitors, and oral or injectable antihistamines. Patients may also try gabapentin and Lyrica (pregabalin), which are prescription medicines approved for the treatment of seizures and neuropathic pain, naltrexone and UVB light therapy. We also expect that Haduvio might compete with product candidates currently in clinical development in this indication, including nemolizumab, an anti-interleukin-31 receptor A humanized monoclonal antibody being developed by Galderma; vixarelimab, a monoclonal antibody targeting oncostatin M receptor beta being developed by Kiniksa Pharmaceuticals; abrocitinib, an oral small molecule targeting the janus kinase 1, or JAK1, receptor being developed by Pfizer Inc.; povorcitinib, an oral small molecule targeting the JAK 1, receptor being developed by Incyte; ruxolitinib cream, a topical therapy targeting the JAK 1/JAK 2 receptor being developed by Incyte; M1880C, a topical non-steroidal anti-inflammatory drug, or NSAID, being developed by Maruho; and CDX-0159, barzolvolimab (CDX-0159), a humanized monoclonal antibody targeting the KIT receptor being developed by Celldex Therapeutics. In addition, a number of other product candidates are currently in clinical development to treat

other pruritic conditions and Haduvio, if approved for the treatment of prurigo nodularis could face competition from these product candidates, including difelikefalin, an oral kappa opioid receptor agonist being developed by Cara Therapeutics that is initiating Phase 3 clinical trials for chronic pruritus in patients with atopic dermatitis, and in Phase 2 clinical trials for chronic kidney disease, chronic liver disease and notalgia paresthetica.

Many of our competitors and potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and commercializing approved products than we do. Mergers and acquisitions in the pharmaceutical biotechnology and biotechnology pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These companies also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials.

Even if we are able to commercialize a product candidate, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of any product we develop will depend substantially, both in the U.S. and other countries, on the extent to which the costs of the product will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement are not available or reimbursement is available only to limited

levels, we may not be able to successfully commercialize that product. Even if coverage is provided for the product, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a return on our investments. In the U.S., no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of any product we commercialize to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we may obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if those product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability to commercialize any product candidate will depend in part on the

extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the U.S. and other countries. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability to sell products profitably. These payors may not view our products, if any, as cost-effective and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us to decrease the price we might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

The commercial potential of any products we are able to commercialize depends in part on reimbursement by government health administration authorities, private health insurers and other organizations. If we are unable to obtain coverage or reimbursement for those products at the levels anticipated, our financial condition could be harmed. Additionally, if new compounds currently in development by potential competitors obtain marketing approval, there may be downward pressure on reimbursement levels for therapies in our target indications, which could have a negative impact on our ability to achieve and maintain profitability.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the

product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new therapies and are challenging the prices charged for new products. We cannot be sure that coverage will be available for any product candidate that we commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. An inability to promptly obtain coverage and adequate payment rates

from both government-funded and private payors for any of our product candidates for which we obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits could divert our resources, cause us to incur substantial liabilities and limit commercialization of any products that we may develop or in-license.

We face an inherent risk of product liability claims as a result of our clinical trials, despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we commercialize any product that we may develop. For example, 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. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any products that we may develop or in-license;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend resulting litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we maintain product and clinical trial liability insurance of at least $7.0 million in the aggregate, our insurance coverage may not fully cover potential liabilities that we may incur. The cost of any product or clinical trial liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we commercialize any product that receives marketing approval. If we are unable to maintain sufficient insurance coverage at an

acceptable cost or otherwise protect against potential clinical trial liability or product liability claims, the development and commercial production and

sale of Haduvio or any future product candidate could be prevented or inhibited, which could harm our business, financial condition, results of operations and prospects.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials. If they do not perform satisfactorily, our business could be harmed.

We do not independently conduct clinical trials of our product candidate. We rely on and expect to continue to rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of Haduvio and any future product candidate that we may develop. These third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new CRO begins work on a clinical trial. As a result, delays would likely occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable approved protocol, as well as applicable legal, regulatory and scientific standards. Moreover, the FDA and/or other regulatory authorities require us to comply with standards, commonly referred to as current Good Clinical Practices, or cGCPs, 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 clinical trial participants are protected. The FDA and other regulatory authorities enforce these cGCPs through periodic inspections of clinical trial sponsors, principal investigators, clinical trial sites and institutional review boards. If we or our third-party contractors fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA and other regulatory authorities may require us to perform additional clinical trials before approving the applicable product candidate, which would delay the marketing approval process. We cannot be certain that, upon inspection, the FDA and other regulatory authorities will determine that any of our clinical trials complies with cGCPs. Similar regulatory requirements apply outside the U.S., including the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use, or ICH. We are also required to register our clinical trials and post the results of our completed clinical trials on a government-sponsored database, ClinicalTrials.gov, and other registries within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees and except for remedies available to us under our agreements with our contractors, we cannot control whether they devote sufficient time, skill and resources to our

ongoing development programs. Additionally, these third parties may have relationships with other commercial entities, including potential competitors, for which they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. Third parties may not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our protocols. For example, we have terminated clinical investigators from our previous clinical trials due to suspected non-compliance with regulatory requirements. If the third parties on which we rely do not carry out their duties, meet their deadlines or comply with regulatory requirements, we will not be able to, or may be delayed in our efforts to, successfully commercialize Haduvio or any future product candidate. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and we may not be able to generate revenues or become profitable.

We contract with third parties for the manufacture, storage, packaging and distribution of Haduvio and other drug product for clinical trials, including a single supplier for the active ingredient in Haduvio and expect to continue to rely on third parties for these services in connection with our future development and commercialization efforts for Haduvio and any future product candidates.

We currently have no manufacturing facilities and a relatively small number of personnel with sufficient experience to oversee the manufacturing process. We rely and plan to continue to rely, on contract manufacturers and other third-party contractors to manufacture, store, package and distribute both drug substance and drug product for our clinical trials. If any of our product candidates receive regulatory approval, we plan to continue to rely upon contract manufacturers and, potentially, collaboration partners, to manufacture commercial quantities of such products. We may be unable to establish any further agreements with contract manufacturers or any other third-party contractors or may fail to do so on acceptable terms or when needed. Even if we are able to establish agreements with such third-party contractors, reliance on third-party contractors entails additional risks, including:

- manufacturing delays if our third-party contractors experience supply chain-related delays, prioritize the supply of other companies' products over Haduvio or any other drug product needed for our clinical trials or any future product candidates, such as IV butorphanol for our HAP study, or otherwise fail to satisfactorily perform according to the terms of the agreemer between us and them or if unforeseen events in the manufacturing process arise;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient us;
- the possible breach by third-party contractors of our agreements with them;

- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug c placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

We do not have long-term supply agreements with any of our contract manufacturers. If any of our existing manufacturers should become unavailable to us for any reason or fail to supply us with the ordered quantities, we may incur delays in identifying or qualifying replacement manufacturers or in obtaining replacement supply. Any performance failure on the part of our contract

manufacturers or the other third-party contractors that we use to store and distribute drug substance and drug product could be disruptive to our operations and delay clinical development or marketing approval of Haduvio or any future product candidates of ours or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

We also rely, and plan to continue to rely, on a single supplier, Mallinckrodt, for nalbuphine hydrochloride drug substance. We do not have agreements in place with Mallinckrodt that guarantee supply quantities or pricing. In October 2020, Mallinckrodt and certain of its subsidiaries filed for bankruptcy protection in the U.S. Bankruptcy Court for the District of Delaware, or the Bankruptcy Court. In February 2022, the Bankruptcy Court approved a settlement of Mallinckrodt's opioid litigation and broader chapter 11 reorganization plan, which was also subject to approval by Irish authorities. On April 27, 2022, the High Court of Ireland confirmed the scheme of arrangement between Mallinckrodt, its creditors and its members under Irish law and ordered that the scheme of arrangement would become effective on the same date that the chapter 11 reorganization plan becomes effective. On June 16, 2022, Mallinckrodt announced that it had completed its reorganization process, emerged from chapter 11 bankruptcy proceedings and completed the Irish examinership proceedings. In August 2023, Mallinckrodt again filed for bankruptcy protection in the Bankruptcy Court and is seeking sought that court's approval of a second chapter 11 reorganization plan. On October 10, 2023, the Bankruptcy Court confirmed Mallinckrodt's plan of reorganization. On November 14, 2023, Mallinckrodt expects to complete its second bankruptcy in the fourth quarter of 2023. emerged from bankruptcy. It is currently uncertain what impact, if any, Mallinckrodt's bankruptcy filings and the associated reorganization plans may have on its ability to continue supplying nalbuphine hydrochloride drug substance to us. Any significant delay in acquisition, increase in cost or decrease in availability of nalbuphine hydrochloride drug substance could considerably delay the manufacture of Haduvio, which could adversely impact the timing of our current and planned clinical trials and potential regulatory approval and commercialization of Haduvio. Although we are evaluating alternate sources of supply that could satisfy our clinical and commercial requirements for nalbuphine drug substance, we have not qualified any alternate sources and cannot assure you that we would be able to establish relationships with any such sources in a timely fashion, on commercially reasonable terms or at all.

If Haduvio or any future product candidates are approved by any regulatory agency, we will need to enter into agreements with third-party contract manufacturers for the commercial production and distribution of those products. In addition, we may face competition for access to manufacturing facilities as there may be a limited number of contract manufacturers operating under cGMPs

that are able to manufacture any such product. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, in a timely manner or at all, which could delay our commercialization efforts.

Third-party manufacturers are required to comply with cGMPs and similar regulatory requirements outside the U.S., such as the ICH. Facilities used by our third-party manufacturers must be approved by the FDA after we submit an NDA and before potential approval of the applicable product candidate. Similar regulations apply to manufacturers of product candidates for use or sale in foreign countries. We do not control the manufacturing process and are completely dependent on our third-party manufacturers for compliance with the applicable regulatory requirements for the manufacture of Haduvio. We expect that we would be similarly dependent on third-party manufacturers of Haduvio at commercial scale or any future product candidate. If our

manufacturers cannot successfully manufacture drug substance or drug product that conforms to our specifications or the strict regulatory requirements of the FDA and any applicable foreign regulatory authority, they will not be able to secure the applicable approval for their manufacturing facilities. If these facilities are not approved for commercial manufacture, we may need to find alternative manufacturing facilities, which could result in delays in obtaining approval for the applicable product candidate and any future commercialization efforts.

In addition, our manufacturers are subject to ongoing periodic inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements both prior to and following the receipt of marketing approval for any product candidate. Some of these inspections may be unannounced. Failure by any of our manufacturers to comply with applicable cGMPs or other regulatory requirements could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspensions or withdrawals of approvals, operating restrictions, seizures or recalls of product candidates, interruptions in supply and criminal prosecutions, any of which could significantly impact the available supplies of Haduvio or any future product candidate and harm our business, financial condition and results of operations.

Our current and anticipated future dependence upon others for the manufacture of Haduvio, any other drug product needed for our clinical trials or any future product candidate may harm our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We may seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

While we have not entered into any collaborations to date, we may seek to establish one or more collaborations for the development and commercialization of Haduvio or any future product candidate. Potential collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies, biotechnology companies and academic research institutions. If Haduvio receives marketing approval from the FDA for chronic cough in IPF, we plan to market and commercialize Haduvio in the U.S. with our own focused, specialty sales organization targeting pulmonologists who specialize in IPF. We would not If Haduvio receives marketing approval from the FDA for other larger chronic conditions, such as RCC or prurigo nodularis, we may plan to market and commercialize Haduvio for other larger conditions such as refractory chronic cough in the U.S. with our own focused, specialty sales organization, or prurigo nodularis. Instead, we would plan to seek to enter into a strategic alliance for commercialization for such indication or indications. We also expect to utilize a variety of collaboration, distribution and other marketing arrangements with one or more third parties to commercialize Haduvio outside the U.S.

We face significant competition in seeking appropriate collaborators. There have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Whether we reach a definitive agreement for a 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. Those factors may include the potential differentiation of our product candidates from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and existing or potential competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than a collaboration with us. Any collaboration agreements

that we enter into in the future may also contain restrictions on our ability to enter into other potential collaborations or to develop specified product candidates. We may not be able to negotiate collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay the potential commercialization of such product candidate, 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 increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

If we establish one or more collaborations, all the risks relating to product development, regulatory approval and commercialization described in this Quarterly Report on Form 10-Q would also apply to the activities of any such future collaborators.

If we enter into collaborations with third parties for the development or commercialization of Haduvio or any future product candidate, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We may seek to enter into collaborations with third parties for the development or commercialization of Haduvio or any future product candidate. If we enter into any such collaborations, we would have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of any such product candidates. Our ability to generate revenues from these arrangements would depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving a product candidate would pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of the product candidates under the collaboration 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 or external factors, such as an acquisition of the collaborator, that divert resources or create competing priorities;
- collaborators may be involved in a business combination and could decide to delay, diminish or terminate the development commercialization of any product candidate licensed by us;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testir

- collaborators could independently develop or develop with third parties, products that compete directly or indirectly with the product candidates under the collaboration;
- collaborators with marketing and distribution rights to one or more products 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 product candidates, might lead to additional responsibilities for us with respect to 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 or misappropriate our intellectual property or other proprietary information;
- collaborators may engage in misconduct or other improper activities, including non-compliance with regulatory standards a requirements;
- disputes may arise between the collaborators and us regarding ownership of or other rights in the intellectual property generated in the course of the collaborations; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further developme or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are critical to our business or owe damages to the licensor of such intellectual property.

We are party to an exclusive license agreement with Endo Pharmaceuticals Inc. under which we have licensed certain patent rights and know-how to develop and commercialize products incorporating nalbuphine hydrochloride in any formulation, including an extended-release formulation such as Haduvio. We may in the future seek additional licenses from others to develop and commercialize additional product candidates or technologies. These licenses may not provide exclusive rights to use the relevant intellectual property in all desired fields of use and in all territories in which we may wish to develop or commercialize product candidates in the future. It is also possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all.

Our existing license agreements impose and we expect that future license agreements will impose, various diligence, development and commercialization, milestone payment, royalty and other obligations on us. If we fail to comply with our material obligations under these agreements or if we are subject to a bankruptcy event, the licensor may have the right to terminate the license

or convert the license to a non-exclusive license, in which event we may be required to negotiate a new or reinstated license with less favorable terms or would not be able to exclusively market or market at all, products covered by the license. Any termination of our license agreements could have a material adverse impact on our business.

Disputes may also arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our activities or product candidates may infringe the intellectual property of the licensor that is not subje to the licensing agreement;
- the sublicensing of patent and other rights under any collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship or ownership of inventions and know-how resulting from joint creation or use of intellectual property by licensors and us; and
- the priority of invention of any patented technology.

If disputes over intellectual property that we license prevent or impair our ability to maintain those license arrangements on acceptable terms or at all, we may be unable to successfully develop and commercialize any affected product candidates.

If we are unable to obtain and maintain sufficient patent protection for Haduvio or any future product candidate and the disease indications for which we are developing or may in the future develop, Haduvio or if the scope of the patent protection is not sufficiently broad, competitors could develop and commercialize products similar or identical to such product candidate and our ability to successfully commercialize such product candidate may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the U.S. and other countries with respect to Haduvio and any future product candidates and their use for indications for which we are developing or may develop, them in the future. If we do not adequately protect our intellectual property rights, competitors may erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we have licensed exclusive rights under patents, prosecuted additional patents and filed patent applications in the U.S. and other countries related to methods of use and formulations of Haduvio. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner or at all.

Agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented and may not be able to secure, maintain or successfully enforce necessary or desirable patent protection from those patent rights. We may not have primary control over patent prosecution and maintenance for certain of the patents and patent applications we may license and therefore cannot guarantee that these patents and applications will be prosecuted in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors or other responsible third parties have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope or patent term adjustments, or PTA. If we, our licensors or any future partners, collaborators, licensors or licensees fail to establish, maintain or protect such patents and other intellectual property

rights, such rights may be reduced or eliminated. If our licensors or any future partners, collaborators, licensors or licensees disagree or do not fully cooperate with us as to the prosecution, maintenance or enforcement of any patent rights, those patent rights could be compromised. We, our licensors and any future partners, collaborators, licensors and licensees may also fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the U.S. or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which in recent years have been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the U.S., the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications or that we were the first to file for patent protection of such inventions. Similarly, we cannot be certain that parties from whom we do or may license or purchase patent rights were the first to make relevant claimed inventions or were the first to file for patent protection

for them. If third parties have filed patent applications on inventions claimed in our patents or applications on or before March 15, 2013, an interference proceeding in the U.S. can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding in the U.S. can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the U.S. and other countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or to other patent offices around the world. Alternatively or additionally, we may become involved in post-grant review procedures, oppositions, derivation proceedings, reexaminations, inter partes review or interference proceedings, in the U.S. or other countries, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenge may result in loss of exclusivity 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 products or product candidates or limit the duration of the patent protection of Haduvio or any future product candidates of ours. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents

protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. As a result, the inventorship or ownership of our intellectual property may be challenged in the future.

Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the U.S. For example, patent laws in various jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than U.S. law does.

Issued patents that we have, may obtain or license may not 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 patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with any products that we are able to develop and commercialize. Alternatively, our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications, or ANDAs, to the FDA claiming that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable or find that competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Pursuant to the terms of our license agreements with third parties, we have the right, but not the obligation, to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we pursue such enforcement or defense, we will require the cooperation of our licensors and cannot guarantee that we would receive it and on what terms. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

If we are unable to protect the confidentiality of our trade secrets, the value of our products could be negatively impacted and our business would be harmed.

In addition to the protection afforded by patents, we also rely on trade secret protection for certain aspects of our intellectual property. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees

and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

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Our competitors may infringe our patents, trademarks, copyrights 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 and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable or both. In any patent infringement proceeding, there is a risk that a court will decide that one of our patents is invalid or unenforceable, in whole or in part and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

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Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. 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 litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years and require

substantial resources. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time-consuming, its outcome would be uncertain and it could prevent or delay us from developing or commercializing Haduvio or any future product candidate.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell products without infringing the intellectual property and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds and methods of use for the treatment of the disease indications for which we are developing or may in the future develop, Haduvio or any future product candidate. If any third-party patents or patent applications are found to cover Haduvio or any future product candidate or their methods of use, we may not be free to manufacture or market the product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries and we may become party to or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our Haduvio or any future product candidates, including interference proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to Haduvio or any future product candidate. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that Haduvio or any future product candidate may be accused of infringing. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the relevant patent claims are invalid or unenforceable and we may not be able to do this. Proving invalidity is difficult. For example, in the U.S., proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third-party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. 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; alternatively or additionally, it could include terms that impede or eliminate our ability to compete successfully in the commercial marketplace. 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 Haduvio or any future product candidate or force us to cease some of our business operations,

which could 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.

Changes to the patent law in the U.S. and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Recent patent reform legislation in the U.S., including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs. The America Invents Act was signed into law on September 16, 2011 and many of the substantive changes became effective on March 16, 2013. The America Invents Act reformed U.S. patent law in part by changing the U.S. patent system from a “first to invent” system to a “first inventor to file” system, expanding the definition of prior art and developing a post-grant review system. This legislation changes U.S. patent law in a way that may weaken our ability to obtain patent protection in the U.S. for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the U.S., including post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with an effective filing date of March 16, 2013 or later, a petition for post-grant

review can be filed by a third party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas inter partes review proceedings can only raise grounds of invalidity based on lack of novelty or obviousness using published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third-party to have a U.S. patent invalidated in a USPTO post-grant review or inter partes review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third-party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. Additionally, there have been recent proposals for additional changes to the patent laws of the U.S. and other countries that, if adopted, could impact our ability to enforce our patents. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S.

Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, recent decisions, including by the U.S. Court of Appeals for the Federal Circuit, raise questions regarding the award of PTA for patents in families where related patents have issued without PTA. Thus, it cannot be said with certainty how PTA will/will not be viewed in the future and whether patent expiration dates may be impacted.

Further, in Europe, a new unitary patent system took effect June 1, 2023, which significantly impacts European patents, including those granted before the introduction of such a system. Under the unitary patent system, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or the UPC. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. Patents granted before the implementation of the UPC have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC will be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who are signatories to the UPC. We cannot predict with certainty the long-term effects of any potential changes.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive and our intellectual property rights in some countries outside the U.S. are less extensive than those in the U.S. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products. Our competitors may export otherwise infringing products to territories where we have no patent protection or where we may obtain patent protection, but where patent enforcement is not as strong as that in the U.S. and our issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the U.S. and Europe do not afford intellectual property protection to the same extent as the laws of the U.S. and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the U.S. and Europe.

In addition, geo-political geopolitical actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications and the maintenance, enforcement or defense of our issued patents. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or

prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and

into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings 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. Furthermore, while we intend to protect our intellectual property rights in major markets for any products that we are able to develop, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market any such products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property or claiming ownership of what we regard as our own intellectual property.

Many of our employees and our licensors' employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure, non-competition and non-solicitation agreements or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third-party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third-party and we could be required to obtain a license from such third-party to commercialize Haduvio or any future product candidate. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or

against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the U.S. in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, the failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering Haduvio or any future product candidate, our competitive position would be adversely affected.

If we are unable to obtain licenses from third parties on commercially reasonable terms, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize Haduvio or any future product candidate, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation in connection with any sales we make. Even

if we are able to obtain a license, it may be non-exclusive, which could enable our competitors to obtain access to the same technologies licensed to us.

Risks Related to Regulatory Approval and Other Legal Compliance Matters

If the FDA does not conclude that Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC or for the treatment of prurigo nodularis, or any other development program, satisfies the requirements under Section 505(b)

(2) of the FDCA or if the requirements for such programs are not as we expect, the approval pathway for these programs will likely take significantly longer, cost significantly more and entail significantly greater complications and risks than anticipated and in any case may not be successful.

We have completed our Phase 2b/3 PRISM trial intend to pursue FDA approval of Haduvio for the treatment of prurigo nodularis and we believe we will need to conduct an additional Phase 3 clinical trial of Haduvio for the treatment of prurigo nodularis chronic cough in IPF under the FDA's Section 505(b)(2) regulatory pathway. The Drug Price Competition and Patent Term Restoration Act of 1984 or the Hatch-Waxman Act, added Section 505(b)(2) to the FDCA. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies that were not conducted by or for the sponsor and for which the sponsor has not received a right of reference, which could expedite the development program for Haduvio by potentially decreasing the amount of preclinical and clinical data that we would need to generate in order to obtain FDA approval. However, while we believe that Haduvio is a reformulation of an existing drug and, therefore, its active moiety will not be treated as a new chemical entity, or NCE, the submission of an NDA under the Section 505(b)(2) regulatory pathway does not preclude the FDA from determining that Haduvio contains an active moiety that is an NCE and, therefore, is not eligible for review under such regulatory pathway.

If the FDA does not allow us to pursue the Section 505(b)(2) or similar regulatory pathway as anticipated, we may need to conduct additional preclinical experiments and clinical trials, provide additional data and information and meet additional standards for regulatory approval. If this were to occur, the time and financial resources required to obtain FDA approval for Haduvio for the treatment of prurigo nodularis chronic cough in IPF and any future product candidates and complications and risks associated with these product candidates, would likely increase significantly. Moreover, our inability to pursue the Section 505(b)(2) regulatory pathway could result in new competitive products reaching the market more quickly than our product candidates, which would likely harm our competitive position and prospects. Even if we are allowed to pursue the Section 505(b)(2) regulatory pathway, our product candidates may not receive the requisite approvals for commercialization.

In addition, notwithstanding the approval of a number of products by the FDA under Section 505(b)(2) over the last few years, certain competitors and others have objected to the FDA's interpretation of Section 505(b)(2). If the FDA's interpretation of Section 505(b)(2) is successfully challenged, the FDA may be required to change its 505(b)(2) policies and practices, which could delay or even prevent the FDA from approving any NDA that we submit under Section 505(b)(2). In addition, the pharmaceutical industry is highly competitive and Section 505(b)(2) NDAs are subject to special requirements designed to protect the patent rights of sponsors of previously approved drugs that are referenced in a Section 505(b)(2) NDA. These requirements may give rise to patent litigation and mandatory delays in approval of our potential future NDAs for up to 30 months depending on the outcome of any litigation. It is not uncommon for a manufacturer of an approved product to file a citizen petition with the FDA seeking to delay approval of or impose additional approval requirements for, pending competing products. If successful, such petitions can significantly delay or even prevent, the approval of the new product. However, even if the FDA ultimately denies such a petition, the FDA may substantially delay approval while it considers and responds to the petition. In addition, even if we are able to utilize the Section 505(b)(2) regulatory pathway for our product candidates, there is no guarantee this would ultimately lead to faster product development or earlier approval.

Moreover, even if our product candidates are approved under the Section 505(b)(2) pathway, the approval may be subject to limitations on the indicated uses for which the products may be marketed or to other conditions of approval or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of Haduvio or any future product candidate. As a result, we cannot predict when or if and in which territories, we will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We are not permitted to market Haduvio or any other product candidate in the U.S. until we receive approval of an NDA from the FDA or in other countries until we receive marketing approval from the applicable regulatory authorities outside the U.S. We have not submitted an application for or received marketing approval for any product candidate in the U.S. or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the U.S. and other countries, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. 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. Securing marketing approval also requires the submission of information about the product

manufacturing process to and inspection of manufacturing facilities by, the relevant regulatory authorities. The FDA or other regulatory authorities may determine that Haduvio or any future product candidate is not safe and effective, only moderately effective or has undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use. 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.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and

may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. 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.

The FDA may also require that NDA submissions for our product candidates include pediatric data. Under the Pediatric Research Equity Act, an NDA, BLA or supplement to an NDA or BLA for certain drugs and biological products must contain data to assess the safety and effectiveness of the drug or biological product in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective, unless the sponsor receives a

deferral or waiver from the FDA. The applicable legislation in the E.U. also requires sponsors to either conduct clinical trials in a pediatric population in accordance with a Pediatric Investigation Plan approved by the Pediatric Committee of the European Medicines Agency, or EMA, or to obtain a waiver or deferral from the conduct of these studies by this Committee. For any of our product candidates for which we are seeking regulatory approval in the U.S. or the E.U., we cannot guarantee that we will be able to obtain a waiver or alternatively complete any required studies and other requirements in a timely manner, or at all, which could result in associated reputational harm and subject us to enforcement action.

Any delay in obtaining or failure to obtain required approvals and clearances could negatively impact our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

We have conducted, are conducting and intend in the future to conduct clinical trials for Haduvio and may conduct clinical trials for any future product candidates, at sites outside the U.S. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the U.S. could subject us to additional delays and expense.

We have conducted, are conducting and intend in the future to conduct clinical trials for Haduvio, and may conduct clinical trials for any future product candidates, at trial sites that are located outside the U.S. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of these data is subject to certain conditions imposed by the FDA.

The FDA will not accept foreign study data as support for an application for marketing approval unless the study satisfies certain conditions. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with cGCPs. The FDA must be able to validate the data from the trial, including, if necessary, through an onsite inspection. The trial population must also have a similar profile to the U.S. population and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the U.S. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the U.S. If the FDA does not accept the data from any trial that we conduct outside the U.S., it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of Haduvio or the applicable future product candidate.

In addition, the conduct of clinical trials outside the U.S. could have a significant adverse impact on us. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange rate fluctuations; and
- diminished protection of intellectual property in some countries.

Failure to obtain marketing approval in foreign jurisdictions would prevent Haduvio or any future product candidate from being marketed in other countries. Any marketing approval we are granted in the U.S. would not assure marketing approval in foreign jurisdictions.

In order to market and sell products in the E.U. and other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The 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 marketing approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., a product must be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the U.S. 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 U.S. does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize any products in any market. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of any product candidates in any country. In addition, if we fail to obtain the non-U.S. approvals required to market products outside the U.S. or if we fail to comply with applicable non-U.S. regulatory requirements, our target markets will be reduced and our ability to realize the full market potential of Haduvio or any future product candidate will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, Further, we could face heightened risks with respect to seeking obtaining marketing approval authorization in the United Kingdom U.K. as a result of the withdrawal of the United Kingdom U.K. from the E.U., commonly referred to as Brexit. The United Kingdom U.K. is no longer part of the European Single Market and European Union E.U. Customs Union. As of January 1, 2021, the MHRA became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas under the terms of the Northern Ireland will continue to be Protocol, Northern Ireland is currently subject to European Union rules E.U. rules. The U.K. and E.U. have however agreed to the Windsor Framework which fundamentally changes the existing system under the Northern Ireland Protocol. Protocol, including with respect to the regulation of medicinal products in the U.K. Once implemented, the changes introduced by the Windsor Framework will see the MHRA be responsible for approving all medicinal products destined for the U.K. market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland.

In addition, foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the E.U. pharmaceutical legislation is currently undergoing a complete review process, in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. The MHRA will rely European Commission's proposal for revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory data protection, revising the eligibility for expedited pathways, etc.) was published on April 26, 2023. The proposed revisions remain to be agreed and adopted by the European Parliament and European Council and the proposals may therefore be substantially revised before adoption, which is not anticipated before early 2026. The revisions may however have a significant impact on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval pharmaceutical industry and our business in the United Kingdom for our product candidates, which could significantly and materially harm our business. long term.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the U.S., including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the U.S.

A Fast Track designation, grant of Priority Review status or Breakthrough Therapy status by the FDA is not assured and, in any event, may not actually lead to a faster development or regulatory review or approval process and, moreover, would not assure FDA approval of Haduvio or any future product candidate.

We may be eligible for Fast Track designation, Priority Review or Breakthrough Therapy status for specific indications for the product candidates we may develop. If a product candidate is intended for the treatment of a serious or life-threatening disease or condition and the product candidate demonstrates the potential to address unmet medical needs for this disease or condition, the product candidate sponsor may apply for FDA Fast Track designation. If a product candidate offers major advances in treatment, the product candidate sponsor may apply for FDA Priority Review status. Additionally, a product candidate may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for such designation or status, the FDA could decide not to grant it. We have received Fast Track designation for the program to develop Haduvio for the treatment of itch in patients with prurigo nodularis, however this designation or any future Fast Track designation for a different indication, Priority Review or Breakthrough Therapy status designation, may not result in our experiencing a faster development process, review or approval compared to conventional FDA procedures and there is no assurance that the product candidate will be approved by the FDA.

We may seek PRIME Designation in the E.U. for Haduvio but we might not receive such designations and, even if we do, such designations may not lead to a faster development or regulatory review or approval process.

In the E.U., we may seek PRIME designation for Haduvio in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the E.U. or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the E.U. and the sponsor intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims.

The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables a sponsor to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to

conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

Even if we obtain marketing approvals for a product, the terms of approvals and ongoing regulation of such product may limit how we manufacture and market the product, which could impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We would therefore be required to comply with requirements concerning advertising and promotion for any product for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we receive marketing approval for one or more products, we and our contract manufacturers will continue to expend time, money and effort in a number of areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

Any regulatory approval to market Haduvio in the U.S. will be limited by indication. If we fail to comply or are found to be in violation of FDA regulations restricting the promotion of Haduvio for unapproved uses, we could be subject to criminal penalties, substantial fines or other sanctions and damage awards.

If our clinical trials are successful, we intend to seek approval to market Haduvio for the treatment of chronic cough in IPF or refractory chronic cough RCC or for the treatment of prurigo nodularis. If we obtain regulatory approval to market Haduvio with an indication statement for the treatment of chronic cough in IPF or refractory chronic cough, RCC, we expect to be prohibited from marketing Haduvio using any promotional claims relating to treatment of cough generally. If we obtain regulatory approval to market Haduvio with an indication statement for the treatment of prurigo nodularis, we expect to be prohibited from marketing Haduvio using any promotional claims relating to treatment of pruritus generally. Marketing of Haduvio may also be limited by regulatory authorities based on use as a monotherapy or adjuvant, concomitant medications, severity of pruritus and other factors.

The regulations relating to the promotion of products for unapproved uses are complex and subject to substantial interpretation by the FDA, EMA, MHRA and other government agencies. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. While we have conducted, or may in the future conduct, clinical trials to evaluate the use of Haduvio to treat cough conditions other than

chronic cough in IPF and pruritic conditions other than prurigo nodularis, Haduvio cannot be promoted for uses other than uses approved in the labeling by the FDA, EMA, MHRA or other applicable regulatory authorities. Physicians may nevertheless prescribe Haduvio off-label to their patients in a manner that is inconsistent with the approved label. We intend to implement compliance and training programs designed to ensure that our sales and marketing practices comply with applicable regulations. Notwithstanding these programs, the FDA or other government agencies may allege or find that our practices constitute prohibited promotion of Haduvio for unapproved uses. We also cannot be sure that our employees will comply with company policies and applicable regulations regarding the promotion of products for unapproved uses.

Notwithstanding the regulatory restrictions on off-label promotion, the FDA and other regulatory authorities allow companies to engage in truthful, non-misleading, and non-promotional scientific communications concerning their products in certain circumstances. For example, in October 2023, the FDA published draft guidance outlining the agency's non-binding policies governing the distribution of scientific information on unapproved uses to healthcare providers. This draft guidance calls for such communications to be truthful, non-misleading, factual, and unbiased and include all information necessary for healthcare providers to interpret the strengths and weaknesses and validity and utility of the information about the unapproved use. In addition, under some relatively recent guidance from the FDA and the Pre-Approval Information Exchange Act, or PIE Act, signed into law as part of the Consolidated Appropriations Act of 2023, companies may also promote information that is consistent with the prescribing information and proactively speak to formulary committee members of payors regarding data for an unapproved drug or unapproved uses of an approved drug. We may engage in these discussions and communicate with healthcare providers, payors and other constituencies in compliance with all applicable laws, regulatory guidance and industry best practices. We will need to carefully navigate the FDA's various regulations, guidance and policies, along with recently enacted legislation, to ensure compliance with restrictions governing promotion of our products.

In recent years, a significant number of pharmaceutical and biotechnology companies have been the target of inquiries and investigations by various federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys' Offices, the Office of Inspector General of the Department of Health and Human Services, or the HHS, the FDA, the Federal Trade Commission, or the FTC, and various state Attorneys General offices. These investigations have alleged violations of various federal and state laws and regulations, including claims asserting antitrust violations, violations of the FDCA, the False Claims Act, the Prescription Drug Marketing Act and anti-kickback laws and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. Many of these investigations originate as "*qui tam*" actions under the False Claims Act. Under the False Claims Act, any individual can bring a claim on behalf of the government alleging that a person or entity has presented a false claim or caused a false claim to be submitted to the government for payment. The person bringing a *qui tam* suit is entitled to a share of any recovery or settlement. *Qui tam* suits, also commonly referred to as "whistleblower suits," are often brought by current or former employees. In a *qui tam* suit, the government must decide whether to intervene and prosecute the case. If it declines, the individual may pursue the case alone.

If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects and reputation.

Any product for which we obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with any such product following approval.

Any product for which we obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control,

quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product 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 the requirement to implement a REMS.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market any product for an indication that is not approved, we may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with any product for which we may obtain marketing approval and its manufacturers or manufacturing processes or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such product, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of the product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the product from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;

- recall of the product;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of the product;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

Finally, our ability to develop and market new drug products may be impacted by ongoing litigation challenging the FDA's approval of mifepristone. Specifically, on April 7, 2023, the U.S. District Court for the Northern District of Texas stayed the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various conditions adopted under a REMS. In reaching that decision, the district court made a number of findings that may negatively impact the development, approval and distribution of drug products in the U.S. Among other determinations, the district court held that plaintiffs were likely to prevail in their claim that the FDA had acted arbitrarily and capriciously in approving mifepristone without sufficiently considering evidence bearing on whether the drug was safe to use under the conditions identified in its labeling. Further, the district court read the standing requirements governing litigation in federal court as permitting a plaintiff to bring a lawsuit against the FDA in connection with its decision to approve an NDA or establish requirements under a REMS based on a showing that the plaintiff or its members would be harmed to the extent that the FDA's drug approval decision effectively compelled the plaintiffs to provide care for patients suffering adverse events caused by a given drug.

On April 12, 2023, the district court decision was stayed, in part, by the U.S. Court of Appeals for the Fifth Circuit. Thereafter, on April 21, 2023, the U.S. Supreme Court entered a stay of the district court's decision, in its entirety, pending disposition of the appeal of the district court decision in the Court of Appeals for the Fifth Circuit and the disposition of any petition for a writ of certiorari to the Supreme Court. The Court of Appeals for the Fifth Circuit held oral argument in the case on May 17, 2023 and, on August 16, 2023, issued its decision. The court declined to order the removal of mifepristone from the market, finding that a challenge to the FDA's initial approval in 2000 is barred by the statute of limitations. But the Court of Appeals did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone that FDA authorized in 2016 and 2021 were arbitrary and capricious. On September 8, 2023, the Justice Department and a manufacturer of mifepristone filed petitions for a writ of certiorari, requesting that asked the U.S. Supreme Court to review the Court of Appeals' decision. On December 13, 2023, the Supreme Court granted these petitions for writ of certiorari for the Court of Appeals' decision and on March 26, 2024, the Supreme Court heard oral arguments for the case.

Similar restrictions apply to the approval of our products in the E.U. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These

include: compliance with the E.U.'s stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the E.U.

and are also subject to E.U. Member State laws. The failure to comply with these and other E.U. requirements can also lead to significant penalties and sanctions.

Inadequate funding for the FDA, the SEC and other national government agencies, including from government shutdowns or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC, and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA, EMA and other agencies may also slow the time necessary for new product candidates drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several in recent years, including in 2018 and 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

In addition, in response disruptions may result that are similar to the COVID-19 pandemic. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As In the event of early 2022, a similar public health emergency in the FDA has resumed inspections of domestic and foreign facilities to ensure timely reviews of applications for medical products. However, future, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required. extended. Regulatory authorities outside the U.S. have adopted or United States facing similar circumstances may adopt similar restrictions or other policy measures in response to a similar public health emergency and may also experience delays in their regulatory activities.

If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize Haduvio or any future product candidate and may affect the prices we may obtain.

In the U.S. and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing

approval of Haduvio or any future product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval. We expect that current laws, as well as other 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 may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief and Economic Security Act, or the CARES Act. These Medicare sequester reductions were suspended and reduced through the end of June 2022, with the full 2% cut resuming thereafter.

The American Taxpayer Relief Act of 2012, among other things, 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. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts for Jobs Act, or TCJA, in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in June 2021, the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court dismissed this action a lawsuit challenging the constitutionality of the

ACA after finding that the plaintiffs do not have standing to challenge bring the constitutionality of the ACA. litigation. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden revoked those Orders and issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care and consider actions that will protect and strengthen that access. Under this

Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related

to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

Current and future legislative efforts may limit the prices for our products, if and when they are licensed for marketing and that could materially impact our ability to generate revenues.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, Health and Human Services, or HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently That regulation was challenged in a lawsuit by the subject Pharmaceutical Research and Manufacturers of ongoing litigation, America, or PhRMA, but at least six the case was dismissed by a federal district court in February 2023 after the court found that PhRMA did not have standing to sue HHS. Nine states (Vermont, Colorado, (Colorado, Florida, Maine, New Hampshire, New Mexico, North Dakota, Texas, Vermont and New Hampshire) Wisconsin) have passed laws allowing for the importation of drugs from Canada with Canada. Certain of these states have submitted Section 804 Importation Program proposals and are awaiting FDA approval. On January 5, 2023, the intent of developing SIPs FDA approved Florida's plan for review and approval by the FDA. Canadian drug importation.

Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The final rule would eliminate the current also creates a new safe harbor for Medicare drug rebates price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and create new manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors for beneficiary point-of-sale discounts were delayed and pharmacy benefit manager, or PBM, service fees. It originally was set to go into effect recent legislation imposed a moratorium on January 1, 2022, but with passage implementation of the rule until January 1, 2026. The Inflation Reduction Act has been of 2022, or the IRA, further delayed by Congress implementation of this rule to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. To address these costs, the Order directs the Department of Health and Human Services, or HHS to create a plan within 45 days to combat "excessive pricing of prescription drugs and enhance domestic pharmaceutical supply chains, to reduce the prices paid by the federal government for such drugs, and to address the recurrent problem of price gouging." Thereafter, on September 9, 2021, HHS released its plan to reduce drug prices. The key features of that plan are to: (a) make drug prices more affordable and equitable for all consumers and throughout the health care system by supporting drug price negotiations with manufacturers; (b) improve and promote competition throughout the prescription drug industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on 55

On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

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Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish

a maximum price for these products in price negotiations, we would be fully at risk of government action if our products are the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also further heighten the risk that we would not be able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products have been on the market for nine years.

Further, the legislation subjects patients drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at $2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications.

A On June 6, 2023, Merck & Co. filed a lawsuit against the HHS and CMS asserting that, among other things, the IRA's Drug Price Negotiation Program for Medicare constitutes an uncompensated taking in violation of the Fifth Amendment of the Constitution. Subsequently, a number of other parties, including the U.S. Chamber of Commerce, Bristol Myers Squibb Company, the PhRMA, Astellas, Novo Nordisk, Janssen Pharmaceuticals, Novartis, AstraZeneca and Boehringer Ingelheim, also filed lawsuits have been filed challenging in various courts with similar constitutional claims against the IRA. HHS and CMS. We expect that litigation challenging involving these and other provisions of the IRA will continue, with unpredictable and uncertain results. Accordingly, while it is currently unclear how the IRA will be effectuated, we cannot predict with certainty what impact any federal or state health reforms will have on us, but such changes could impose new or more stringent regulatory requirements on our activities or result in reduced reimbursement for our products, any of which could adversely affect our business, results of operations and financial condition.

In the E.U., similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In markets outside of the U.S. and the E.U., reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the E.U., the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. 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 materially harmed.

Any relationships we may have with customers, healthcare providers and professionals and third-party payors, among others, will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we are able to obtain marketing approval. Any arrangements we have with healthcare providers, third-party payors and customers will subject us to broadly applicable fraud and abuse and other healthcare laws and regulations. The laws and regulations may constrain the business or financial arrangements and relationships through which we conduct clinical research, market, sell and distribute any products for which we obtain marketing approval. These include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration (including any kickback, bribe or rebate), directly or indirectly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for or the purchase, lease or order of a good, facility, item or service for which payment may be made under a federal healthcare program such as Medicare and Medicaid.

False Claims Laws. The federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions against individuals or entities for, among other things, knowingly presenting or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties.

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing a scheme or making materially false statements in connection with the delivery of or payment for health care benefits, items or services. Additionally, HIPAA, as amended by the Health Information Technology for Economic and

Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates that perform certain functions or activities that involve the use or disclosure of protected health information on their behalf, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information.

Transparency Requirements. The federal Physician Payments Sunshine Act 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, with specific exceptions, to report annually to CMS information related to payments or transfers of value made to physicians, other healthcare providers and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.

Analogous State and Foreign Laws. Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and

require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that any business arrangements we have with third parties and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the E.U. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of E.U. Member States. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain E.U. Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual E.U. Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the E.U. Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The collection, use, disclosure, transfer or other processing of personal data, including personal health data, of individuals in the E.U. is governed by the General Data Protection Regulation, or GDPR. The GDPR became effective on May 25, 2018. It imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data; obtaining consent of individuals; providing notice to individuals regarding data processing activities; responding to data subject requests; taking certain measures when engaging third-party processors; notifying data subjects and regulators of data breaches; and implementing safeguards to protect the security and confidentiality of personal data. The GDPR imposes strict rules on the transfer of personal data to countries outside the E.U., including the U.S. Failure to comply with the requirements of the GDPR may result in fines of up to 20 million euros or four percent of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages. The GDPR increases our responsibility and

potential liability in relation to personal data that we process and we may be required to change our business practices or put in place additional mechanisms ensuring compliance with the GDPR. This may be onerous and adversely affect our business, financial condition, results of operations and

prospects and despite our efforts, there is a risk that we may be subject to fines, litigation and reputational harm in connection with our European activities.

Additionally, in In October 2022, President Biden signed an executive order to implement the E.U.-U.S. Data Privacy Framework, which would serve as a replacement to the E.U.-U.S. Privacy Shield. The European Union initiated the process to adopt an adequacy decision for the E.U.-U.S. Data Privacy Framework in December 2022 and the European Commission adopted the adequacy decision on July 10, 2023. The adequacy decision will permit U.S. companies who self-certify to the E.U.-U.S. Data Privacy Framework to rely on it as a valid data transfer mechanism for data transfers from the E.U. to the U.S. However, some privacy advocacy groups have already suggested that they will be challenging the E.U.-U.S. Data Privacy Framework. If these challenges are successful, they may not only impact the E.U.-U.S. Data Privacy Framework, but also further limit the viability of the standard contractual clauses and other data transfer mechanisms. The uncertainty around this issue has the potential to impact any future business we may have at the international level.

Similar actions are either in place or under way in the U.S. There are a broad variety of data protection laws that are applicable to our activities and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The FTC and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the FTC has been particularly focused on the unpermitted processing of health and genetic data through its recent enforcement actions and is expanding the types of privacy violations that it interprets to be “unfair” under Section 5 of the Federal Trade Commission Act, as well as the types of activities it views to trigger the Health Breach Notification Rule (which the FTC also has the authority to enforce). The agency is also in the process of developing rules related to commercial surveillance and data security that may impact our business. We will need to account for the FTC’s evolving rules and guidance for proper privacy and data security practices in order to mitigate our risk for a potential enforcement action, which may be costly. If we are subject to a potential FTC enforcement action, we may be subject to a settlement order that requires us to adhere to very specific privacy and data security practices, which may impact our business. We may also be required to pay fines as part of a settlement (depending on the nature of the alleged violations). If we violate any consent order that we reach with the FTC, we may be subject to additional fines and compliance requirements.

In addition, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information

has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. These obligations may be applicable to some or all of our business activities now or in the future.

If we are unable to properly protect the privacy and security of protected health information, we could be found to have breached our contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

New laws also are being considered at the state level. For example, Most prominently, in California, the California Consumer Privacy Protection Act, or the CCPA, which went into effect on January 1, 2020, created similar risks and obligations as those created amended by GDPR, though the CCPA does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Additionally, as of January 1, 2023, the California Privacy Rights Act, or the CPRA, significantly modified which went into effect on January 1, 2023, establishes a privacy framework for covered businesses by creating an expansive definition of personal information, establishing data privacy rights for consumers and employees in the State of California, imposing special rules on the collection of consumer data from minors, and creating a potentially severe statutory damages framework for violations of the CCPA including by expanding consumers' rights with respect and for businesses that fail to certain sensitive personal information. implement reasonable security procedures and practices to prevent data breaches. The CPRA also creates created a new state agency that will be is vested with authority to implement and enforce the CCPA and the CPRA. While clinical trial data is currently exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope.

In addition to California, at least eleven other states have passed comprehensive privacy laws similar to the CCPA and CPRA. These laws are either in effect or will go into effect sometime before the end of 2026. Like the CCPA and CPRA, these laws create obligations related to the processing of personal information, as well as special obligations for the processing of "sensitive" data (which includes health data in some cases). Some of the provisions of these laws may apply to our business activities. There are also states that are strongly considering or have already passed comprehensive privacy laws during the 2023 legislative sessions that will go into effect in 2024 and beyond, including New Hampshire and New Jersey. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. There are also states that are specifically regulating health information that may affect our business. For example, Washington state passed a health privacy law in 2023 that will regulate the collection and sharing of health information, and the law also has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data and additional states (including Vermont) are considering such legislation for 2024. These laws may impact our business activities, including our identification of research patients, relationships with business partners and ultimately the marketing and distribution of our products.

Accordingly, any failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have

violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the U.S. and require us to develop and implement costly compliance programs.

If we further expand our operations outside the U.S., we will need to dedicate additional resources to comply with U.S. laws regarding international operations and the laws and regulations in each jurisdiction in which we operate and plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the company, including international subsidiaries and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry because in many countries, hospitals are operated by the government and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Further, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the E.U. The provision of benefits or advantages to physicians is also governed by the national anti-bribery laws, such as the U.K. Bribery Act 2010. Infringement of

these laws could result in substantial fines and imprisonment. Payments made to physicians in certain E.U. Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician’s employer, his or her competent professional organization and/or the regulatory authorities of the individual E.U. Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the E.U. Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

If we expand our presence outside of the U.S., it will require us to dedicate additional resources to comply with these laws and these laws may preclude us from developing, manufacturing or selling certain products and product candidates outside of the

U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from workplace and other work-related accidents, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental, health and safety laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Our business and operations would suffer in the event of system failures.

Our computer systems, as well as those of our CROs and other third-party contractors and consultants, are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, sabotage, natural disasters (including hurricanes), terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business and development programs. programs, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of preclinical studies or clinical trial data from completed, ongoing or planned trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce data. To the extent any disruption or security breach were to result in a loss of or damage to our data or applications or inappropriate disclosure of personal, confidential or proprietary information, we could also incur liability, our competitive position could be harmed and the development of Haduvio or

any future product candidate could be significantly delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

In the ordinary course of our business, we directly or indirectly collect and store sensitive data, including intellectual property, confidential information, preclinical and clinical trial data, proprietary business information, personal data and personally identifiable health information of our clinical trial subjects patients and employees, in our data centers and on our networks or on those of third parties. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be vulnerable to attacks by hackers or internal bad actors or breached due to employee error, a technical vulnerability, malfeasance or other disruptions. Additionally, the risk of a security breach or disruption through cyber-attacks has generally increased as the number, intensity and sophistication of attempted attacks from around the world have increased. Although, to our knowledge, we have not experienced any such material security breach to date, any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information and significant regulatory penalties and such an event could disrupt our operations, damage our reputation and cause a loss of confidence in us and our ability to conduct clinical trials, which could adversely affect our reputation and delay our clinical development of our product candidates.

If the FDA EMA, MHRA or other comparable foreign regulatory authorities approve generic versions of any of our small molecule investigational future products that receive marketing approval through the NDA pathway, or such authorities do not grant our such future products appropriate periods of data exclusivity before approving generic versions of those products, the sales of our products, if approved, our sales could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a “reference listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of ANDAs in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the sponsor applicant generally must show that its product has

the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labelling labeling as the reference listed reference-listed drug and that the generic version is bioequivalent to the reference listed reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed reference-listed drug is typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. Specifically, in cases where such exclusivity has been granted, an ANDA may not be submitted to the FDA until the expiration of five years unless the submission is accompanied

by a Paragraph IV certification that a patent covering the reference listed reference-listed drug is either invalid or will not be infringed by the generic product, in which case the sponsor applicant may submit its application four years following approval of the reference listed reference-listed drug. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical trials, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application.

Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if our products product candidates are approved, even if we still have patent protection for such products. product candidates. Competition that our products could any such product candidates of ours may face from generic versions of our such products could materially and adversely affect impact our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made may make in those product candidates.

Artificial intelligence presents risks and challenges that can impact our business including by posing security risks to our confidential information, proprietary information and personal data.

Issues in the use of artificial intelligence, combined with an uncertain regulatory environment, may result in reputational harm, liability or other adverse consequences to our business operations. As with many technological innovations, artificial intelligence presents risks and challenges that could impact our business. Our vendors may incorporate generative artificial intelligence tools into their offerings without disclosing this use to us, and the providers of these generative artificial intelligence tools may not meet existing or rapidly evolving regulatory or industry standards with respect to privacy and data protection and may inhibit our or our vendors' ability to maintain an adequate level of service and experience. If any of our vendors experiences an actual or perceived breach or privacy or security incident because of the use of generative artificial intelligence, we may lose valuable intellectual property and confidential information and our reputation and the public perception of the effectiveness of our security measures could be harmed. Further, bad actors around the world use increasingly sophisticated methods, including the use of artificial intelligence, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these outcomes could damage our reputation, result in the loss of valuable property and information, and adversely impact our business.

Risks Related to Employee Matters and Managing our Growth

Our future success depends on our ability to retain our executive team and to attract, retain and motivate qualified personnel.

We are highly dependent on Jennifer Good, our President and Chief Executive Officer; Thomas Sciascia, M.D., our Chief Scientific Officer; and David Clark, M.D., MRCP, our Chief Medical Officer; as well as the other principal members of our management and scientific teams. Although we have a formal employment agreements agreement with Ms. Good and offer letter agreements with Dr. Sciascia and Dr. Clark, these agreements do not prevent them from terminating their employment with us at any time. Except as otherwise required by law, all members of our executive team are employed "at will," meaning that they may terminate their employment with us at any time with or without notice and for any reason or no reason. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified scientific, clinical, manufacturing and sales and marketing personnel. Our industry has experienced a high rate of turnover of such personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key 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 marketing 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 these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize Haduvio or any future product candidate will be limited.

If we expand our organization, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of September 30, 2023 March 31, 2024, we had 25 employees. We may experience significant growth in the number of our employees and the scope of our operations. For example, if any product candidate appears likely to receive marketing approval, we expect to significantly expand our sales, marketing and distribution capabilities to support the potential commercialization of the product candidate. Our management may need to devote a significant amount of its attention to managing these growth activities. Due to our limited financial resources and the limited experience of our management team in managing a company with such growth, we may not be able to effectively manage the expansion of our operations, retain key employees or identify, recruit and train additional qualified personnel. Our inability to manage the expansion of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Any significant growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of Haduvio for additional indications or the development of additional product candidates. If we are unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may be unable to implement our business strategy, including the successful commercialization of any product candidate.

Our employees, independent contractors and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors and consultants may engage in fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable non-U.S. regulatory

authorities, to provide accurate information to the FDA or comparable non-U.S. regulatory authorities, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities, to report financial information or data

accurately or to disclose unauthorized activities to us. Such misconduct could also involve the improper use 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 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, standards 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 results of operations, including the imposition of significant criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm and requirements to curtail or restructure our operations.

Risks Related to Our Common Stock

An active trading market for our common stock may not be sustainable.

Our shares of common stock began trading on the Nasdaq Global Market, or Nasdaq, on May 7, 2019. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price for our common stock and thereby affect the ability of our stockholders to sell their shares. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

If we fail to comply with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted. 61

Our common stock is currently listed for trading on Nasdaq. We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share, or risk delisting, which would have a material adverse effect on our business. A delisting of our common stock from Nasdaq could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities.

On January 10, 2022, we received a deficiency letter from the Listing Qualifications Department, or the Staff, of Nasdaq notifying us that, for the prior 30 consecutive business days, the bid price for our common stock had closed below the $1.00 per share minimum bid price requirement for continued inclusion on Nasdaq pursuant to Nasdaq Listing Rule 5450(a)(1), or the Bid Price Requirement.

In accordance with Nasdaq Listing Rule 5810(c)(3)(A), or the Compliance Period Rule, we were provided a period of 180 calendar days, or until July 11, 2022, or the Compliance Date, to regain compliance with the Bid Price Requirement. If, at any time before the Compliance Date, the bid price for our common stock closed at $1.00 or more for a minimum of 10 consecutive business days as required under the Compliance Period Rule, the Staff would provide written notification to us that we had regained compliance with the Bid Price Requirement, unless the Staff chose to exercise its discretion to extend this ten-day period pursuant to Nasdaq Listing Rule 5810(c)(3)(H).

On March 16, 2022, we received a letter from the Staff indicating that we had regained compliance with the Bid Price Requirement as of such date.

Although we were able to regain compliance with the Bid Price Requirement within the manner and time period prescribed by Nasdaq, there can be no assurance that we will be able to maintain compliance with the Bid Price Requirement or other Nasdaq continued listing requirements in the future or that we will be able to regain compliance with respect to any future deficiencies. If we fail to satisfy the Nasdaq Global Market's continued listing requirements, we may submit an application to transfer to the Nasdaq Capital Market, which generally has lower financial requirements for initial listing, in an effort to avoid delisting. However, we may not be able to satisfy the initial listing requirements for the Nasdaq Capital Market and may therefore not be able to transfer our listing to the Nasdaq Capital Market. A transfer of our listing to the Nasdaq Capital Market could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

The trading price of our common stock is highly volatile, which could result in substantial losses for purchasers of our common stock.

The trading price of our common stock is highly volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The trading price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of Haduvio or any future product candidates;
- the success of existing or new competitive products or technologies;
- regulatory actions with respect to Haduvio or any future product candidates or competitors' products and product candidate
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property rights;
- recruitment or departure of key personnel;
- expenses related to any of our development programs;
- results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimated financial results or development timelines;
- announcements or expectations of additional financing efforts;

- sales of our common stock by us, our insiders or other stockholders;
- expiration of market stand-off or lock-up agreements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- recommendations and changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems in the U.S. and other countries;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including recent adverse changes in the domestic and international financial markets and the impacts of inflation and government action in response thereto;
- our ability to maintain our listing on the Nasdaq Global Market;
- our ability to continue as a going concern; and
- other factors and considerations described in this “Risk Factors” section.

In addition, inflation and interest rate increases and other factors have negatively affected, and may in the future negatively affect, the stock market and investor sentiment. The price and volatility of our common stock may be disproportionately affected as investors may favor traditional profit-making industries and companies during such times of market uncertainty and instability.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against public companies following declines in the trading prices of their securities. This risk is especially relevant for us because companies in the life sciences space have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and our resources, which could harm our business.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, the trading price and volume of our shares could decline.

The trading market for our common stock will likely depend in part on the research and reports that securities or industry analysts publish about us and our business. We do not have any control over these analysts. There can be no assurance that analysts

will cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, the trading price of our shares would likely decline. In addition, if one or more analysts cease coverage of us or fail to regularly publish

reports on us, we could lose visibility in the financial markets, which could cause the trading price and volume of our shares to decline.

Future sales of shares of our common stock, including by us, employees and significant stockholders, could negatively affect our stock price.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales or the perception in the market that the holders of a large number of shares of our common stock intend to sell their shares, could reduce the trading price of our common stock.

All of our outstanding shares of common stock may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent that such shares have already been registered under the Securities Act and are held by non-affiliates of ours.

Moreover, holders of a substantial number of shares of our common stock have rights, subject to specified limitations and conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

In addition, we have registered all shares of common stock that we may issue under our equity compensation plans. These shares can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates. If these additional shares are sold or if it is perceived in the market that they will be sold, in the public market, the trading price of our common stock could decline.

In June 2023, we filed with the SEC a universal shelf registration statement on Form S-3, or the Shelf Registration Statement, which allows us to offer and sell up to $200.0 million of common stock, preferred stock, debt securities, units and/or warrants from time to time pursuant to one or more offerings at prices and terms to be determined at the time of sale. The Shelf Registration Statement was filed to replace our prior universal shelf registration statement on Form S-3, or the Prior Shelf Registration Statement. The Shelf Registration Statement was declared effective on August 15, 2023. In June 2023, we entered into a new sales agreement, or the New 2023 ATM Sales Agreement, with Leerink Partners and filed a prospectus under our Shelf Registration Statement for the offer and sale of shares of our common stock having an aggregate offering price of up to $75.0 million pursuant to the New 2023 ATM Sales Agreement. In accordance with the terms of the New 2023 ATM Sales Agreement, the our prior ATM Sales Agreement sales agreement terminated upon effectiveness of the Shelf Registration Statement, at which point we were no longer able to issue and sell shares of our common stock under the our prior ATM Sales Agreement. sales agreement. From time to time, we may offer and sell under the New 2023 ATM Sales Agreement common stock registered under the Shelf Registration Statement pursuant to one or more “at-the-market” offerings. The extent to which we utilize the New 2023 ATM Sales Agreement as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, general market conditions and the extent to which we are able to secure funds from other sources.

On October 5, 2021, we issued to a single investor in a private placement, or the Initial Private Placement Investor, (i) 2,373,201 shares of our common stock and accompanying warrants to purchase an aggregate of 4,746,402 shares of our common stock, and (ii) pre-funded warrants to purchase up to an aggregate of 4,926,069 shares of our common stock and accompanying warrants to purchase an aggregate of 9,852,138 shares of our common stock. Under the terms of the pre-funded warrants and the accompanying common stock warrants, we may not effect the exercise of any such warrant, and the Initial Private Placement Investor will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of common stock beneficially owned by the Initial Private Placement Investor, together with its affiliates, would exceed 4.99%, for the accompanying common stock warrants, or 9.99%, for the pre-funded warrants, of the number of shares of common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at the Initial Private Placement

Investor's election upon 61 days' notice to us, subject to the terms of such warrants, provided that such percentage may in no event exceed 9.99%. We refer to such percentage limitations as the Initial Private Placement Beneficial Ownership Limitations. We filed a registration statement on Form S-3, or the Initial Private Placement Form S-3, covering the resale of up to 21,897,810 shares of common stock, comprised of the 2,373,201 shares of common stock issued outright and the 19,524,609 shares of common stock issuable upon exercise of the warrants, which was declared effective in October 2021. While the Initial Private Placement Form S-3 covers the resale of the number of shares of common stock issued or issuable to the Initial Private Placement Investor without giving effect to the Initial Private Placement Beneficial Ownership Limitations, the Initial Private Placement Investor may not exercise, and subsequently resell the underlying shares of common stock of, any portion of the warrants to the extent such exercise would result in the Initial Private Placement Investor exceeding the applicable Initial Private Placement Beneficial Ownership Limitation. The Initial Private Placement Investor may resell all, some or none of the shares of common stock registered pursuant to the Initial Private Placement Form S-3 at any time or in its discretion, subject to the Initial Private Placement Beneficial Ownership Limitations. As of November 9, 2023 May 7, 2024, warrants issued to the Initial Private Placement Investor to purchase 6,000,000 shares of common stock remained outstanding.

Similarly, on October 18, 2021, we issued to New Enterprise Associates 16, L.P., or NEA, in a private placement, 1,851,852 shares of our common stock and accompanying warrants to purchase an aggregate of 3,703,704 shares of our common stock. We filed a registration statement on Form S-3, or the Second Private Placement Form S-3, covering the resale of 5,555,556 shares of common stock, comprised of the 1,851,852 shares of common stock and the 3,703,704 shares of common stock issuable upon exercise of the warrants, which was declared effective in November 2021. NEA will be able to resell all, some or none of the shares of common stock

registered pursuant to the Second Private Placement Form S-3 at any time or in its discretion. As of November 9, 2023 May 7, 2024, all of the warrants issued to NEA remained outstanding.

Similarly, on April 11, 2022, we issued to several purchasers in a private placement, or the April 2022 Private Placement, (i) an aggregate of 4,580,526 shares of our common stock and (ii) pre-funded warrants to purchase an aggregate of 24,379,673 shares of our common stock. Under the terms of the pre-funded warrants, we may not effect the exercise of any such warrant, and a purchaser will

not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of common stock beneficially owned by such purchaser (together with its affiliates, any other persons acting as a group together with such purchaser or any of such purchaser's affiliates, and any other persons whose beneficial ownership of common stock would or could be aggregated with such purchaser's for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 9.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at such purchaser's election upon 61 days' notice to us subject to the terms of such warrants, provided that such

percentage may in no event exceed 19.99%. We refer to such percentage limitations as the 2022 Private Placement Beneficial Ownership Limitations. We filed a registration statement on Form S-3, or the Third Private Placement Form S-3, covering the resale of 28,960,199 shares of common stock, comprised of the 4,580,526 shares of common stock and the 24,379,673 shares of common stock issuable upon exercise of the warrants, which was declared effective in May 2022. While the Third Private Placement Form S-3 covers the resale of the number of shares of common stock issued or issuable to the purchasers without giving effect to the 2022 Private Placement Beneficial Ownership Limitations, a purchaser may not exercise, and subsequently resell the underlying shares of common stock of, any portion of the warrants to the extent such exercise would result in such purchaser exceeding the applicable 2022 Private Placement Beneficial Ownership Limitation. The purchasers will be able to resell all, some or none of the shares of common stock registered pursuant to the Third Private Placement Form S-3 at any time or in their discretion, subject to the 2022 Private Placement Beneficial Ownership Limitations. As of November 9, 2023 May 7, 2024, pre-funded warrants that we issued and sold in the April 2022 Private Placement to purchase 21,379,673 17,282,760 shares of common stock remained outstanding.

Finally, on September 27, 2022, we issued in the September 2022 Offering and sold an aggregate of 14,252,670 shares of our common stock, and, in lieu of common stock to certain investors, pre-funded warrants to purchase 14,247,330 shares of common stock. stock, in a public offering, or the September 2022 Offering. Under the terms of the pre-funded warrants, we may not effect the exercise of any such warrant, and a purchaser will not be entitled to exercise any portion of any such warrant, if, upon giving effect to such exercise, the aggregate number of shares of common stock beneficially owned by such purchaser (together with its affiliates, any other persons acting as a group together with such purchaser or any of such purchaser's affiliates, and any other persons whose beneficial ownership of common stock would or could be aggregated with such purchaser's for purposes of Section 13(d) or Section 16 of the Exchange Act) would exceed 9.99% of the number of shares of common stock outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of such warrant, which percentage may be increased or decreased at such purchaser's election upon 61 days' notice to us subject to the terms of such warrants, provided that such percentage may in no event exceed 19.99%. We refer to such percentage limitations as the September 2022 Offering Beneficial Ownership Limitations. The shares of common stock and the pre-funded warrants were issued pursuant to a prospectus supplement dated September 22, 2022 to the Prior Shelf Registration Statement. A purchaser may not exercise, and subsequently resell the underlying shares of common stock of, any portion of the pre-funded warrants to the extent such exercise would result in such purchaser exceeding the applicable September 2022 Offering Beneficial Ownership Limitation. The purchasers will be able to resell all, some or none of the shares of common stock registered pursuant to the Prior Shelf Registration Statement at any time or in their discretion, subject to the September 2022 Offering Beneficial Ownership Limitations. As of November 9, 2023 May 7, 2024, all of the pre-funded warrants that we issued to purchasers and sold in the September 2022 Offering to purchase 13,270,983 shares of common stock remained outstanding.

Sales of substantial amounts of shares of our common stock or other securities by our stockholders, by us under the Shelf Registration Statement, whether pursuant to the New 2023 ATM Sales Agreement or otherwise, by the private placement investors pursuant to the Initial Private Placement Form S-3, the Second Private Placement Form S-3 or the Third Private Placement Form S-3 or through any other means could also lower the market price of our common stock, make it more difficult for you to sell your shares at a price that you desire and impair our ability to raise capital through the sale of equity or equity-related securities.

The number of shares of common stock underlying our outstanding warrants is significant in relation to our currently outstanding common stock, which could have a negative effect on the market price of our common stock and make it more difficult for us to raise funds through future equity offerings. In addition, in connection with any merger, consolidation or sale of all or substantially all of our assets, holders of our outstanding warrants would be entitled to

receive consideration in excess of their reported beneficial ownership of our common stock and this could adversely impact the consideration our other stockholders would receive.

As part of our October 2021 Private Placements, private placements, we issued to the Initial Private Placement Investor warrants to purchase an aggregate of 14,598,540 shares of our common stock at an exercise price of $1.37 per share, and pre-funded warrants to purchase up to an aggregate of 4,926,069 shares of our common stock at an exercise price of $0.001 per share, which as of February 10, 2022, had been exercised in full. Of the common stock warrants issued to the Initial Private Placement Investor at an exercise price of $1.37 per share, warrants to purchase an aggregate of 7,299,270 shares will expire on April 5, 2025 and warrants to purchase an aggregate of 7,299,270 shares will expire on October 5, 2028. In addition, we issued to NEA warrants to purchase an aggregate of 3,703,704 shares of our common stock at an exercise price of $1.37 per share. Of the common stock warrants issued to NEA, warrants to purchase an aggregate of 1,851,852 shares of our common stock will expire on April 18, 2025 and warrants to purchase an aggregate of 1,851,852 shares of our common stock will expire on October 18, 2028. We issued pre-funded warrants to purchase up to an aggregate of

24,379,673 shares of our common stock to the purchasers in the April 2022 Private Placement. Placement, of which pre-funded warrants to purchase 17,282,760 shares of common stock remained outstanding of as May 7, 2024. Finally, we issued pre-funded warrants to purchase up to an aggregate of 14,247,330 shares of our common stock at an exercise price of $0.001 per share to certain purchasers in the September 2022 Offering. Offering, of which pre-funded warrants to purchase 13,270,983 shares of common stock remained outstanding as of May 7, 2024.

As discussed above, the common stock warrants issued to the Initial Private Placement Investor are subject to the Initial Investor Beneficial Ownership Limitations, the pre-funded warrants issued to the purchasers in the April 2022 Private Placement are subject to the 2022 Private Placement Beneficial Ownership Limitations and the pre-funded warrants issued to certain purchasers in the

September 2022 Offering are subject to the September 2022 Offering Beneficial Ownership Limitations. Although the Initial Private Placement Investor's warrants are subject to the Initial Investor Beneficial Ownership Limitations, the pre-funded warrants issued to the purchasers in the April 2022 Private Placement are subject to the 2022 Private Placement Beneficial Ownership Limitations and the pre-funded warrants issued to the purchasers in the September 2022 Offering are subject to the September 2022 Offering Beneficial Ownership Limitations, upon exercise in full of the warrants, the shares issuable upon exercise would represent a significant portion of our outstanding common stock. As a result, the Initial Private Placement Investor, NEA and the other purchasers in the April 2022 Private Placement and the September 2022 Offering may be able to exert substantial influence over our business. The concentration of voting power resulting from the exercise of the warrants could delay, defer or prevent a change of control, entrench our management and our board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and the Initial Private Placement Investor, NEA, the purchasers in the April 2022 Private

Placement and/or the purchasers in the September 2022 Offering on the other hand, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters. In addition, sales of these shares could cause the market price of our common stock to decline significantly.

Furthermore, in the event of a sale of our company, whether by merger, sale of all or substantially all of our assets or otherwise, the holders of warrants would be entitled to receive, with respect to each share of common stock issuable upon exercise of the warrants then held by them and, and in the case of the Initial Private Placement Investor, without regard to the Beneficial Ownership Limitations, the same amount and kind of securities, cash or property as they would have been entitled to receive if such securities had been converted into or exercised for shares of our common stock immediately prior to such sale of our company. Although the Initial Private Placement Investor's beneficial ownership of our common stock is reported as 9.99% as a result of the application of the Beneficial Ownership Limitations, in the event of a sale of our company, the Initial Private Placement Investor would receive sale consideration without regard to the Beneficial Ownership Limitations. In such a sale, the Initial Private Placement Investor would be entitled to receive a significantly larger portion of the total proceeds distributable to the holders of our securities than is represented by its reported beneficial ownership of our common stock. In addition, pursuant to the terms of the common stock warrants issued to both the Initial Private Placement Investor and NEA in our October 2021 Private Placements, in specified circumstances upon a fundamental transaction by us, such warrant holders may have the right to require us to repurchase their common stock warrants at their fair value using a Black Scholes option pricing formula. As a result, in the event of a sale of our company, the Initial Private Placement Investor and NEA may be entitled to receive a significantly larger portion of the total proceeds distributable to our stockholders than they would if they exercised the warrants immediately prior to the transaction, and our stockholders could receive significantly less than they otherwise would in such a transaction.

Given the amount and terms of these warrants, we may find it more difficult to raise additional equity capital on favorable terms or at all while these warrants are outstanding.

Ownership of our common stock is concentrated among our executive officers and directors and their affiliates, who have significant influence over our business, which may prevent new investors from influencing significant corporate decisions.

Our executive officers and directors and their respective affiliates, beneficially own, in the aggregate, shares representing approximately 35.8% 24.6% of our common stock as of November 9, 2023 May 7, 2024. As a result, our executive officers and directors and their affiliates acting together may be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management or the board of directors; or
- impede a merger, consolidation, takeover, sale, other business combination or other significant corporate transaction involving us that other stockholders may desire.

Some of these persons or entities may have interests different than yours. For example, certain of these stockholders may have purchased their shares at prices substantially below the prices you paid for your shares or may have held their shares for a longer period, and they may be more interested in selling our company to an acquirer or they may want us to pursue strategies that deviate from your interests.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on appreciation in the price of our common stock, if any, for any return on their investment.

We have never declared or paid cash dividends on our capital stock and we do not intend to do so in the foreseeable future. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our product pipeline and business. As a result, future appreciation, if any, in the market value of our common stock will be your sole source of gain for the foreseeable future. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

We are an "emerging growth company" and a "smaller reporting company" and the reduced disclosure requirements applicable to us may make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years, or until December 31, 2024. For so long as we remain an emerging growth company, we are permitted and plan to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements and not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of SOX Section 404 and reduced disclosure obligations regarding executive compensation. If some investors find our common stock less attractive as a result of our reliance on these exemptions, the trading market for our common stock may be less active and our stock price may be more volatile.

We incur increased costs as a result of operating as a public company and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company and particularly after we are no longer an "emerging growth company" or a "smaller reporting company," we incur and will continue to incur, significant legal, accounting, investor relations and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Stock Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We may need to hire additional accounting, finance and other personnel in connection with our efforts to comply with the requirements of being a public company and our management and other personnel devote a substantial amount of time in complying with these requirements, which could negatively impact our financial results. Current and changing laws, rules and regulations relating to corporate governance and public disclosure may increase our legal and financial compliance costs and

make some activities more time-consuming and costly. For example, the rules and regulations applicable to us as a public company have made it and we expect that they may continue to make it, more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are evaluating these rules and regulations and cannot currently predict or estimate the additional costs we may incur or the timing of such costs. In addition, these laws, rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We have invested in and intend to continue to invest in, resources to comply with evolving laws, rules and regulations and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, rules and regulations, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

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, or the Exchange Act, the Sarbanes-Oxley Act of 2002 and the rules and regulations of the Nasdaq Stock Market. The Sarbanes-Oxley Act of 2002 requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. Pursuant to SOX Section 404, we are required to furnish annual reports by our management on our internal control over financial reporting. However, while we remain an emerging growth company or a smaller reporting company with less than $100 million in annual revenue, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with SOX Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude that our internal control over financial reporting is effective. If we are unable to comply with the requirements of SOX Section 404 in a timely manner

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or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the trading price of our common stock could decline and we could be subject to sanctions or investigations by the Nasdaq Stock Market, the SEC or other regulatory authorities.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2022 December 31, 2023, we had federal and state net operating loss carryforwards of $178.4 million $186.9 million and federal research and development tax credit carryforwards of $5.4 million $6.2 million, which if not utilized generally will begin to expire in 2031 and 2032, respectively. These net operating loss and research and development tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In general, under Section Sections 382

and 383 of the Internal Revenue Code of 1986, as amended, or the IRC, and corresponding provisions of state law, a corporation that undergoes an “ownership change,” generally defined as a

greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three year period, is subject to limitations on its ability to utilize its pre-change net operating losses loss and research and development tax credit carryforwards to offset future taxable income. We previously completed a Section 382 analysis, and due to multiple historical ownership changes, all of our net operating loss carryforwards as of December 31, 2022, and research and development tax credits are were subject to limitation. If a further ownership change occurs, our ability to use our tax attributes might be further limited. In addition to potential Section 382 limitations, there are other factors that might limit the availability of our tax attributes. For example, we have not conducted a detailed research and development tax credit analysis to document whether our historical business activities qualify to support our research and development credit carryforwards. A detailed study could result in adjustment to our research and development credit carryforwards.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. As described below in “Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition,” the Tax Cuts and Jobs Act, or the Tax Act, as amended by the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our net operating losses and other tax attributes.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Act, which significantly reformed the IRC. The Tax Act, among other things, as amended by the CARES Act, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), and the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for such losses arising in taxable years ending after December 31, 2017 (though any such NOLs may be carried forward indefinitely), . In addition, beginning in 2022, the imposition Tax Act eliminated the option to deduct research and development expenditures currently and generally requires corporations to capitalize and amortize them over five years or 15 years in the case of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on expenditures attributable to foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time and the modification or repeal of many business deductions and credits. research.

As In addition to the CARES Act, as part of Congress's response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, economic relief legislation was enacted on March 18, 2020 in 2020 and the CARES Act was enacted on March 27, 2020. Both contain numerous 2021 containing tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application The IRA was also signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded companies. The 1% excise tax generally applies to any acquisition of stock by a publicly traded company (or certain of its affiliates) from a stockholder of the 80%-of-income limitation on the use of net operating losses, which was enacted as part company in exchange for money or other property (other than stock of the Tax Act. It also provides company itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that net operating losses arising in any taxable year beginning after December 31, 2017 and before January 1, 2021, are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income. not traditional stock repurchases.

Regulatory guidance under the Tax Act, the FFCR Act IRA, and the CARES Act such additional legislation is and continues to be forthcoming and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the FFCR Act or the CARES Act. IRA, and such additional legislation.

Provisions in our organizational documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the trading price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our

stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that ca be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend repeal certain provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits an “interested stockholder,” which is either a person who owns at least 15% of our outstanding voting stock or an affiliate or associate who owned at least 15% of our outstanding voting stock at any time within the prior three years, from engaging in a business combination with us for a period of three years after the date of the transaction in which the person became an “interested stockholder” unless the business combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by or beneficial to, our stockholders. This 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.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders and that the federal district courts of the U.S. are the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These choice of forum provisions could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company, (2) any action asserting a claim of breach of fiduciary duty owed by any director, officer, other employee or stockholder of our company to us or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws or governed by the internal affairs doctrine. Our certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Neither of these choice of forum provisions would affect suits brought to enforce any liability or duty created by the Exchange Act or the rules and regulations thereunder, jurisdiction over which is exclusively vested by statute in the U.S. federal courts or any other claim for which U.S. federal courts have exclusive jurisdiction.

These choice of forum provisions may limit a stockholder’s ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

If we fail to comply with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

Our common stock is currently listed for trading on Nasdaq. We must satisfy Nasdaq's continued listing requirements, including, among other things, a minimum closing bid price of $1.00 per share, Bid Price Requirement, or risk delisting, which would have a material adverse effect on our business. A delisting of our common stock from Nasdaq could materially reduce the liquidity of our common stock and result in a corresponding material reduction in the price of our common stock. In addition, delisting could harm our ability to raise capital through alternative financing sources on terms acceptable to us, or at all, and may result in the potential loss of confidence by investors, suppliers, customers and employees and fewer business development opportunities.

There can be no assurance that we will be able to maintain compliance with the Bid Price Requirement or other Nasdaq continued listing requirements in the future or that we will be able to regain compliance with respect to any future deficiencies. If we fail to satisfy the Nasdaq Global Market's continued listing requirements, we may submit an application to transfer to the Nasdaq Capital Market, which generally has lower financial requirements for initial listing, in an effort to avoid delisting. However, we may not be able to satisfy the initial listing requirements for the Nasdaq Capital Market and may therefore not be able to transfer our listing to the Nasdaq Capital Market. A transfer of our listing to the Nasdaq Capital Market could adversely affect the liquidity of our common stock. Any such event could make it more difficult to dispose of, or obtain accurate quotations for the price of, our common stock, and there also would likely be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. We may also face other material adverse consequences in such event, such as negative publicity, a decreased ability to obtain additional financing, diminished investor and/or employee confidence, and the loss of business development opportunities, some or all of which may contribute to a further decline in our stock price.

Item 5. Other Information.

(c) Director and Officer Trading Arrangements

None of our directors or officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement (as defined in Item 408(c) of Regulation S-K) during the three months ended March 31, 2024.

Item 6. Exhibits.

Exhibit Number	Description
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) or 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) or 15d-14(a) under the Securities Exchange

31.2*	Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Filed herewith.

75 ** Furnished herewith.

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.

TREVI THERAPEUTICS, INC.

Date: November 9, 2023 May 7, 2024

By: /s/ Jennifer L. Good

Jennifer L. Good
President and Chief Executive Officer
(Principal Executive Officer)

By: /s/ Lisa Delfini

Lisa Delfini
Chief Financial Officer
(Principal Financial Officer)

Exhibit 31.1

CERTIFICATION PURSUANT TO RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Jennifer L. Good, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Trevi 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(s) 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(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

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

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

Date: November 9, 2023 May 7, 2024

By: /s/ Jennifer L. Good

Jennifer L. Good

President and Chief Executive Officer

(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Lisa Delfini, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Trevi 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(s) 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(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

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

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

Date: November 9, 2023 May 7, 2024

By: /s/ Lisa Delfini

Lisa Delfini

Chief Financial Officer

(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION 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 Trevi Therapeutics, Inc. (the "Company") for the period ended September 30, 2023 March 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jennifer L. Good, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to her knowledge:

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

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

Date: November 9, 2023 May 7, 2024

By: /s/ Jennifer L. Good

Jennifer L. Good

President and Chief Executive Officer

(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION 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 Trevi Therapeutics, Inc. (the "Company") for the period ended September 30, 2023 March 31, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Lisa Delfini, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to her knowledge:

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

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

Date: November 9, 2023 May 7, 2024

By: /s/ Lisa Delfini

Lisa Delfini

Chief Financial Officer

(Principal Financial Officer)

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