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, 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: 001-40657

Omega Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**81-3247585**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
140 First Street Suite 501 Cambridge, MA	**02141**
(Address of principal executive offices)	**(Zip Code)**

(617) 949-4360

(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	OMGA	The Nasdaq Global Select Market

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, 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 8, 2024, the registrant had 55,366,213 shares of common stock, $0.001 par value per share, outstanding.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q, or Quarterly Report, contains forward-looking statements. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). All statements other than statements of historical facts contained in this Quarterly Report, including statements regarding our future results of operations and financial position, the sufficiency of our cash and cash equivalents to fund our operating expenses and capital expenditure requirements, our ability to continue as a going concern, business strategy, product candidate development, prospective products, product candidate approvals, research and development activities and costs, future revenue, the timing and likelihood of success of our business plans, plans and objectives of management, future results and timing of clinical trials, treatment potential of our product candidates, and the market potential of our product candidates are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential," "would" or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements contain these words. The forward-looking statements in this Quarterly Report are only predictions and are based largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Quarterly Report and are subject to a number of known and unknown risks, uncertainties and assumptions, including those described under Part II, Item 1A. "Risk Factors" in this Quarterly Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

SUMMARY RISK FACTORS

Our business is subject to numerous risks and uncertainties, including those described in Part II, Item 1A. “Risk Factors” in this Quarterly Report on Form 10-Q. You should carefully consider these risks and uncertainties when investing in our common stock. The principal risks and uncertainties affecting our business include the following:

- Our product candidates are based on a novel technology, which makes it difficult to predict the time and cost of preclinical and clinical development and of subsequently obtaining regulatory approval, if at all.
- No epigenomic controllers have been approved in this potentially new class of medicines, and may never be approved as a result of efforts by others or us. mRNA drug development has substantial development and regulatory risks due to the novel and unprecedented nature of this new category of medicines.
- We have a limited operating history and no history of successfully developing or commercializing any approved product candidates, which may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.
- We have incurred significant losses since inception and expect to incur significant additional losses for the foreseeable future.
- We require substantial additional financing, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce, or terminate our product development.
- Volatility in capital markets and general economic conditions in the United States may be a significant obstacle to raising required funds. This and other factors raise substantial doubt about the Company's ability to continue as a going concern.
- We have invested, and expect to continue to invest, in research and development efforts that further enhance the OMEGA platform. Such investments may affect our operating results, and, if the return on these investments is lower or develops more slowly than we expect, our revenue and operating results may suffer.
- Preclinical development is uncertain, especially for a new class of medicines such as epigenomic controllers, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance into the clinic, any of which may have a material adverse impact on our platform or our business.
- Our product candidate, OTX-2002, was cleared by the United States Food and Drug Administration to advance to clinical development. Clinical development of OTX-2002 may be delayed or terminated, and we may never obtain regulatory approval of OTX-2002, which may have a material adverse impact on our platform or our business. Furthermore, clinical development requires substantial capital investment, which we may not be able to support. We may incur unforeseen costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of OTX-2002 and our other product candidates.
- Our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.
- Our ability to manufacture our epigenomic controller candidates, or EC candidates, for preclinical or clinical supply could be limited, especially with the increased demand for the manufacture of mRNA- and LNP-based therapeutics, which could adversely affect our development plans.
- Our EC candidates are based on novel technology and may be complex and difficult to manufacture. We may encounter difficulties in manufacturing, product release, shelf life, testing, storage, supply chain management or shipping.
- We must adapt to rapid and significant technological change and respond to introductions of new products and technologies by competitors to remain competitive.
- We will rely on third parties for the foreseeable future for the manufacture and supply of materials for our research programs, preclinical studies and clinical trials and we do not have long-term contracts with many of these parties. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, including drug supplies for combination therapy, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

- Significant lawsuits, including intellectual property or stockholder litigation, including the derivative suit relating to the Research Collaboration Agreement with Novo Nordisk A/S, could be costly and time-consuming to defend and could result in additional liabilities.
- We continue to evaluate plans to acquire and establish our own manufacturing facility and infrastructure in addition to or in lieu of relying on contract development and manufacturing organizations for the manufacture of our product candidates. Any plan to establish our own manufacturing facility and infrastructure will be costly and time-consuming and we may not be successful.
- We have a limited number of suppliers for the lipid excipients used in our product candidates and certain of our suppliers are critical to our production. If we were to lose a critical supplier, it could have a material adverse effect on our ability to complete the development of our product candidates. If we obtain regulatory approval for any of our product candidates, we would need to expand the supply of lipid excipients in order to commercialize them.
- We are very early in our development efforts. Most of our product candidates are in preclinical development or discovery, and we recently received FDA clearance for our IND application for OTX-2002 and have initiated the associated clinical trial. It will be many years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- If we are unable to obtain, maintain, enforce and adequately protect our intellectual property rights with respect to our technology and product candidates, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.
- Third parties may obtain or control intellectual property rights that may prevent or limit the development of our technology or products. Third-party claims of intellectual property infringement, misappropriation or other violation may result in substantial costs or prevent or delay our development and commercialization efforts.

PART I—FINANCIAL INFORMATION

Item 1. Financial Statements.

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

	September 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 30,377	$ 68,443
Marketable securities	—	4,986
Accounts receivable, due from related party	486	1,006
Accounts receivable	—	5,125
Prepaid expenses and other current assets	8,090	10,324
Total current assets	38,953	89,884
Property and equipment, net	4,498	5,311
Operating lease right-of-use assets, net	109,245	108,736
Restricted cash	—	341
Other assets	31	94
Total assets	$ 152,727	$ 204,366
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,434	$ 1,620
Accrued expenses	4,650	7,914
Other current liabilities	2,170	1,972
Lease liabilities, current	11,919	11,300
Long-term debt, current portion	4,000	4,000
Total current liabilities	24,173	26,806
Lease liabilities, non-current	100,627	98,243
Long-term debt, net	11,587	14,885
Other liabilities	4,797	6,416
Total liabilities	141,184	146,350
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized as of September 30, 2024 and December 31, 2023; no shares issued and outstanding as of September 30, 2024 and December 31, 2023	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized as of September 30, 2024 and December 31, 2023; 55,159,219 and 55,144,982 issued and outstanding as of September 30, 2024 and December 31, 2023, respectively	55	55
Additional paid-in capital	399,000	392,609
Accumulated other comprehensive loss	—	(14)
Accumulated deficit	(387,512)	(334,634)
Total stockholders' equity	11,543	58,016
Total liabilities and stockholders' equity	$ 152,727	$ 204,366

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

Omega Therapeutics, Inc.
Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Collaboration revenue	$ 2,612	$ 831	$ 7,106	$ 2,105
Operating expenses:				
Research and development	12,807	16,506	41,162	61,638
General and administrative	6,225	7,228	19,395	20,029
Total operating expenses	19,032	23,734	60,557	81,667
Loss from operations	(16,420)	(22,903)	(53,451)	(79,562)
Other income (expense), net:				
Interest income, net	14	684	644	2,323
Other income (expense), net	(38)	(29)	(71)	25
Total other income (expense), net	(24)	655	573	2,348
Net loss	$ (16,444)	$ (22,248)	$ (52,878)	$ (77,214)
Net loss per common stock attributable to common stockholders, basic and diluted	$ (0.30)	$ (0.40)	$ (0.96)	$ (1.44)
Weighted-average common stock used in net loss per share attributable to common stockholders, basic and diluted	55,155,583	55,140,058	55,153,699	53,629,468
Comprehensive loss:				
Net loss	$ (16,444)	$ (22,248)	$ (52,878)	$ (77,214)
Other comprehensive income (loss):				
Unrealized gain on marketable securities	—	85	14	393
Comprehensive loss	$ (16,444)	$ (22,163)	$ (52,864)	$ (76,821)

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

Omega Therapeutics, Inc.
Condensed Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)
(Unaudited)

	COMMON STOCK					
	SHARES	PAR VALUE	ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE GAIN (LOSS)	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY
As of January 1, 2024	55,144,982	$ 55	$ 392,609	$ (14)	$ (334,634)	$ 58,016
Issuance of common stock for options exercised	10,003	—	22	—	—	22
Other comprehensive gain	—	—	—	14	—	14
Stock-based compensation	—	—	3,431	—	—	3,431
Net loss	—	—	—	—	(20,129)	(20,129)
As of March 31, 2024	55,154,985	$ 55	$ 396,062	$ —	$ (354,763)	$ 41,354
Stock-based compensation	—	—	1,213	—	—	1,213
Net loss	—	—	—	—	(16,305)	(16,305)
As of June 30, 2024	55,154,985	$ 55	$ 397,275	$ —	$ (371,068)	$ 26,262
Issuance of common stock for options exercised	4,234	—	2	—	—	2
Stock-based compensation	—	—	1,723	—	—	1,723
Net loss	—	—	—	—	(16,444)	(16,444)
As of September 30, 2024	55,159,219	$ 55	$ 399,000	$ —	$ (387,512)	$ 11,543

	COMMON STOCK					
	SHARES	PAR VALUE	ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE GAIN (LOSS)	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' EQUITY
As of January 1, 2023	48,072,517	$ 48	$ 343,608	$ (479)	$ (237,206)	$ 105,971
Issuance of common stock for registered direct offering, net of issuance costs	6,920,415	7	39,720	—	—	39,727
Issuance of common stock for options exercised	30,157	—	108	—	—	108
Other comprehensive gain	—	—	—	251	—	251
Stock-based compensation	—	—	2,222	—	—	2,222
Net loss	—	—	—	—	(25,279)	(25,279)
As of March 31, 2023	55,023,089	$ 55	$ 385,658	$ (228)	$ (262,485)	$ 123,000
Issuance of common stock for options exercised	113,819	—	371			371
Other comprehensive gain	—	—	—	57	—	57
Stock-based compensation	—	—	2,178	—	—	2,178
Net loss	—	—	—	—	(29,687)	(29,687)
As of June 30, 2023	55,136,908	$ 55	$ 388,207	$ (171)	$ (292,172)	$ 95,919
Issuance of common stock for options exercised	4,930	—	7	—	—	7
Other comprehensive gain	—	—	—	85	—	85
Stock-based compensation	—	—	2,280	—	—	2,280
Net loss	—	—	—	—	(22,248)	(22,248)
As of September 30, 2023	55,141,838	$ 55	$ 390,494	$ (86)	$ (314,420)	$ 76,043

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

Omega Therapeutics, Inc.
Condensed Consolidated Statements of Cash Flows
(in thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2024	2023
Operating activities		
Net loss	$ (52,878)	$ (77,214)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,320	1,146
Amortization of debt issuance costs and debt discount	35	33
Amortization of operating lease right-of-use assets	4,208	3,844
Accretion of discounts on marketable securities	—	(209)
Change in fair value of success fee obligation	—	92
Loss (gain) on disposal of fixed assets	2	(232)
Stock-based compensation expense	6,367	6,680
Changes in operating assets and liabilities:		
Accounts receivable, due from related party	520	221
Accounts receivable	5,125	—
Prepaid expenses and other current assets	2,575	(664)
Other assets	63	86
Accounts payable	(186)	(704)
Accrued expenses and other current liabilities	(3,906)	(5,688)
Other liabilities	(1,737)	(1,811)
Net cash used in operating activities	(38,492)	(74,420)
Investing activities		
Purchases of property and equipment	(947)	(1,758)
Purchases of marketable securities	—	(19,768)
Proceeds from maturities of marketable securities	5,000	66,901
Net cash provided by investing activities	4,053	45,375
Financing activities		
Proceeds from equity offering	—	40,000
Payments of equity offering costs	—	(273)
Payment of financing fees	—	(15)
Repayment of debt	(3,333)	—
Repayment of lease financing	(318)	—
Proceeds from issuance of common stock under equity incentive plans	24	486
Net cash (used in) provided by financing activities	(3,627)	40,198
Net change in cash, cash equivalents and restricted cash	(38,066)	11,153
Cash, cash equivalents and restricted cash—beginning of period	68,784	70,956
Cash, cash equivalents and restricted cash—end of period	$ 30,718	$ 82,109
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	$ 30,377	$ 81,768
Restricted cash	341	341
Cash, cash equivalents and restricted cash	$ 30,718	$ 82,109
Supplemental disclosures of cash flow information		
Cash paid for interest	$ 1,208	$ 1,279
Supplemental disclosure of noncash investing and financing activities		
Purchases of property and equipment included in accounts payable and accrued expenses	$ —	$ 318

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

1. Nature of the Business and Basis of Presentation

Organization

Omega Therapeutics, Inc. (the "Company" or "Omega") is a biotechnology company pioneering the development of a new class of programmable epigenomic mRNA medicines by leveraging its OMEGA platform. The OMEGA platform harnesses the power of epigenetics, the mechanism that controls gene expression and every aspect of an organism's life from cell genesis, growth and differentiation to cell death. The OMEGA platform enables control of fundamental epigenetic processes to correct the root cause of disease by restoring aberrant gene expression to a normal range without altering native nucleic acid sequences. The Company was incorporated in July 2016 ("inception") as a Delaware corporation and its offices are in Cambridge, Massachusetts.

Liquidity and Going Concern

Since its inception, the Company has devoted substantially all of its resources to building its platform and advancing development of its portfolio of programs, establishing and protecting its intellectual property, conducting research and development activities, organizing and staffing the Company, business planning, raising capital and providing general and administrative support for these operations. The Company is subject to risks and uncertainties common to early clinical-stage companies in the biotechnology industry including, but not limited to, technical risks associated with the successful research, development and manufacturing of product candidates, risks related to clinical development of product candidates, developments by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. Current and future programs will require significant research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

In February 2023, the Company completed a registered direct offering of common stock pursuant to which it issued and sold 6,920,415 shares of its common stock at a purchase price of $5.78 per share and secured approximately $39.7 million in net proceeds after deducting estimated offering expenses. In August 2023, the Company entered into an Open Market Sale Agreement (the "Sales Agreement"), with Jefferies LLC ("Jefferies"), as sales agent, pursuant to which the Company may, from time to time, issue and sell common stock with an aggregate value of up to $60.0 million in "at-the-market," or ATM, offerings under our Registration Statement on Form S-3 (File No. 333-268254) filed with the SEC on November 8, 2022, which was declared effective on November 18, 2022. During the nine months ended September 30, 2024, the Company did not sell any shares of common stock under the Sales Agreement.

The Company has had recurring losses since inception and incurred a loss of $52.9 million during the nine months ended September 30, 2024. Net cash used in operations for the nine months ended September 30, 2024 was $38.5 million. In order to ensure sufficient resources to advance its lead program and maximize near- and long-term value creation opportunities from its platform, the Company announced a strategic prioritization in March 2024. As part of this initiative, the Company streamlined the organization and optimized its research and development efforts and, as a result, the Company expects that its cash and cash equivalents of $30.4 million at September 30, 2024 will enable it to fund its operating expenses and capital expenditure requirements into the second quarter of 2025. The Company expects to continue to generate operating losses and use cash in operations for the foreseeable future. Additional funding will be necessary to fund future preclinical and clinical activities and to develop new product candidates. The Company expects to finance its future cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. Volatility in the capital markets and general economic conditions in the United States may be a significant obstacle to raising the required funds and, as a result, the Company may be unable to secure the necessary funding on acceptable terms. This raises substantial doubt about the Company's ability to continue as a going concern.

The accompanying unaudited condensed financial statements do not include any adjustments that might result from the outcome of these uncertainties. Accordingly, the unaudited condensed financial statements have been prepared on a basis that assumes the Company will continue as a going concern which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

Significant Risks and Uncertainties Related to Macroeconomic Conditions

The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including, for example, severely diminished liquidity and credit availability, rising interest and inflation rates, crises involving banking and financial institutions, declines in consumer confidence, declines in economic growth, and uncertainty about economic stability. In addition, unstable market and economic conditions and further disruption created by international political unrest, war and terrorism may have serious adverse consequences on our business, financial condition and results of operations.

Basis of Presentation

The accompanying condensed consolidated unaudited financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC"), and Accounting Standards Update ("ASU"), of the Financial Accounting Standards Board ("FASB"). All amounts herein are expressed in U.S. dollars ("USD") unless otherwise noted.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying condensed consolidated unaudited financial statements include the accounts of Omega Therapeutics, Inc. and its wholly owned subsidiary, Omega Therapeutics Security Corporation, which is a Massachusetts subsidiary***.*** All intercompany transactions and balances have been eliminated in consolidation.

Reclassification

The Company reclassified the related party expenses in the prior year to research and development and general and administrative expenses in the condensed consolidated statements of operations and comprehensive loss to conform to the current year's presentation.

Unaudited Interim Financial Information

The accompanying condensed consolidated unaudited financial statements included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission (the "SEC"). The unaudited financial statements have been prepared on the same basis as audited financial statements, except certain information and footnote disclosures normally included in financial statements prepared in accordance with GAAP have been consolidated or omitted from this report, as is permitted by such rules and regulations. In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair representation of the results for the reported periods. These condensed consolidated unaudited financial statements should be read in conjunction with the audited financial statements and notes thereto contained in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 filed with the SEC on March 28, 2024 (the "2023 10-K").

The results for the nine months ended September 30, 2024 are not necessarily indicative of results to be expected for the year ending December 31, 2024, any other interim periods, or any future year or period.

Use of Estimates

The preparation of the condensed consolidated unaudited financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses, and the disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases its estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances.

Significant estimates and assumptions reflected in these condensed consolidated unaudited financial statements include, but are not limited to, the selection of useful lives of property and equipment, the incremental borrowing rate used in the calculation of lease liabilities, research and development accruals, and certain judgments regarding revenue recognition and stock-based compensation. Actual results could differ from these estimates. Changes in estimates are reflected in reported results in the period in which they become known.

Summary of Significant Accounting Policies

The Company's significant accounting policies are described in Note 2, "Summary of significant accounting policies," to the Company's audited financial statements included in the 2023 10-K. There was no significant change of accounting policy during the nine months ended September 30, 2024.

Recent accounting pronouncements not yet adopted

In November 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280)*, *Improvements to Reportable Segment Disclosures*. The new standard requires enhanced disclosures about segment information and significant segment expenses. It does not change how a public entity identifies its operating segments. ASU 2023-07 is effective for fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. The new standard should be applied retrospectively to all prior periods presented in the financial statements. The Company is currently evaluating the impact on its consolidated financial statements.

In December 2023, the FASB issued 2023-09, *Income Taxes (Topic 740), Improvements to Income Tax Disclosures*. The new standard requires public business entities to disclose information about income taxes paid, specific categories in the rate reconciliation, and additional information for reconciling items that meet a quantitative threshold. The guidance should be applied on a prospective basis. For public business entities, ASU 2023-08 is effective for fiscal years beginning after December 15, 2024, with early adoption permitted. For all other entities, the standard is effective for annual periods beginning after December 15, 2025. The Company is currently evaluating the impact on its consolidated financial statements.

3. Marketable Securities

As of September 30, 2024, the Company did not hold any marketable securities. All of the Company's previous marketable securities matured during the nine months ended September 30, 2024.

The following table summarizes the Company's marketable securities at December 31, 2023 (in thousands):

	December 31, 2023		
	Amortized cost	Gross unrealized losses	Fair value
Corporate debt securities	$ 5,000	$ (14)	$ 4,986

4. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	September 30, 2024	December 31, 2023
Clinical development	$ 4,557	$ 5,168
Research and development	1,168	1,609
Insurance	922	716
Other receivables	477	855
Software	354	303
Restricted cash	341	—
Facilities	—	1,242
Other	271	431
Prepaid expenses and other current assets	$ 8,090	$ 10,324

5. Property and Equipment, Net

Property and equipment, net consists of the following (in thousands):

	September 30, 2024	December 31, 2023
Lab equipment	$ 7,472	$ 6,633
Furniture and fixtures	1,636	1,636
Leasehold improvements	1,431	1,290
Computer equipment	1,226	1,226
Construction in process	—	588
Total property and equipment	11,765	11,373
Less accumulated depreciation	(7,267)	(6,062)
Property and equipment, net	$ 4,498	$ 5,311

Depreciation expense for each of the three months ended September 30, 2024 and 2023 was $0.4 million. Depreciation expense for the nine months ended September 30, 2024 and 2023 was $1.3 million and $1.1 million, respectively.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	September 30, 2024	December 31, 2023
Employee related expenses	$ 2,664	$ 4,482
Professional and consulting fees	1,130	716
Manufacturing costs	483	547
Research costs	217	1,395
Interest	—	147
Other	156	627
Accrued expenses	$ 4,650	$ 7,914

In the first quarter of 2024, the Company accrued $0.8 million of severance and other costs associated with the Company's cost reduction activities, which was fully paid out in the second quarter of 2024.

In the second quarter of 2024, the Company accrued $0.7 million of severance and other costs associated with the separation of the Company's former Chief Financial Officer and Chief Medical Officer, which will be paid out in the form of salary continuation in regular installments over the 9-month period following their respective termination dates.

7. Term Loan

On March 9, 2018, the Company entered into the Loan Agreement with Banc of California (“BOC”, formerly known as Pacific Western Bank) to initially borrow $8.0 million, which was further amended on September 30, 2019 (the “First Amendment”), January 22, 2020 (the “Second Amendment”), December 30, 2020 (the “Third Amendment”), and December 20, 2021 (the “Fourth Amendment”).

On September 22, 2023, the Company entered into another amendment to the Loan Agreement (the “Fifth Amendment”), in which BOC extended the maturity date of the loan to September 30, 2027, subject to further extension to September 30, 2028 upon receipt by the Company on or before December 31, 2024 of at least $50.0 million of cash proceeds from the sale of its equity securities and/or non-refundable upfront strategic partnership proceeds. Repayment of the loan began on September 30, 2023, with monthly principal payments of $0.3 million plus interest, along with a closing payment of $4.0 million on September 30, 2027 if the maturity date is not extended to September 30, 2028. Interest will continue to be determined at a floating annual rate equal to the greater of (i) 0.50% above the prime rate then in effect and (ii) 5.50%. The Company incurred $15 thousand of debt issuance costs, which was recorded as a direct reduction against the additional term loan and will be amortized over the life of the associated term loan as a component of interest expense using the effective interest method. The Company is required to pay a success fee of $0.1 million pursuant to the Fifth Amendment, in addition to the $0.2 million success fee obligation pursuant to the Fourth Amendment. The success fees are contingent on achieving specified liquidity events. The Company determined that the success fee obligation represented a freestanding financial instrument, and it was classified as a liability on the Company’s condensed

consolidated balance sheet and initially recorded at fair value, with changes in fair value for each reporting period recognized in other expense, net in the condensed consolidated statements of operations and comprehensive loss. The fair value of such obligation is remeasured at the end of each reporting period until the liability is settled.

In addition, pursuant to the Fifth Amendment, the Company agreed to maintain with BOC, at all times, a balance of at least $5.0 million of unrestricted cash, subject to termination upon the Company's prepayment of outstanding loans in an aggregate amount of at least $5.0 million or if the principal balance of the loans is less than $10.0 million.

Borrowings under the Loan Agreement, as amended, are collateralized by substantially all of the Company's personal property, other than its intellectual property. There are no financial covenants associated with the Loan Agreement, as amended; however, the Company is subject to certain affirmative and negative covenants to which the Company will remain subject until maturity.

As of September 30, 2024, $4.0 million of the net carrying amount of the term loan was classified as short-term and $11.6 million was classified as long-term based on the repayment start date. The Company's outstanding term loan balance was comprised of the following (in thousands):

	September 30, 2024	December 31, 2023
Principal	$ 15,667	$ 19,000
Unamortized debt discount	(80)	(115)
Net carrying amount	$ 15,587	$ 18,885

The Company determined that the expected life of the debt was equal to the term on the term loan. The effective interest rate on the liability component ranged from 5.53% to 9.27% for the period from the date of issuance through September 30, 2024. The following table sets forth total interest expense recognized related to the term loan (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Contractual interest expense	$ 373	$ 469	$ 1,185	$ 1,336
Amortization of debt issuance costs and debt discount	11	13	35	33
Total interest expense	$ 384	$ 482	$ 1,220	$ 1,369

At September 30, 2024 and December 31, 2023, accrued interest on the term loan was zero and $147 thousand, respectively.

The Company is required to repay the following principal amounts in connection with its term loan (in thousands):

2024 (remaining 3 months)	$ 1,000
2025	4,000
2026	4,000
2027	6,667
Total	$ 15,667

8. Fair Value of Financial Instruments

The fair value of the Company's cash and cash equivalents and restricted cash are measured through quoted market prices; the fair value of the Company's marketable securities is determined based on the pricing inputs other than quoted prices in active markets, which are either directly or indirectly observable as of the reporting date. Other current assets, accounts payable and accrued liabilities approximate their fair values as of September 30, 2024 and December 31, 2023, due to their short-term nature. The carrying value of the Company's debt approximates its fair value due to its variable interest rate, which approximates a market interest rate. The success fee obligation associated with the Loan Agreement, as amended, contains unobservable inputs that reflect the Company's own assumptions in which there is little, if any, market activity at the measurement date, thus the success fee obligation is measured at its fair value on a recurring basis using unobservable inputs.

The fair value of the Company's financial instruments is summarized in the table below (in thousands):

	September 30, 2024			
	Level 1	Level 2	Level 3	Total
Financial Liabilities				
Success fee obligation	$ —	$ —	$ 300	$ 300

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
Financial Assets				
Money market funds	$ 10,402	$ —	$ —	$ 10,402
Corporate Debt Securities	—	4,986	—	4,986
Total	$ 10,402	$ 4,986	$ —	$ 15,388
Financial Liabilities				
Success fee obligation	$ —	$ —	$ 300	$ 300

In accordance with the Fourth and Fifth Amendments of the Loan Agreement with BOC, the Company will be required to pay success fees totaling $0.3 million upon the achievement of certain liquidity events; accordingly, the related obligation is recorded as other current liabilities on the condensed consolidated balance sheets as it is deemed more probable than not by the Company to be settled in less than one year. The fair value of the success fee obligation was determined using the probability-weighted expected return method. The key estimates and assumptions impacting the fair value included the probability of achieving a specified liquidity event, the expected timing of achieving a liquidity event and the discount rate. The fair value of the success fee obligation is remeasured at each reporting period, with changes in fair value recognized in the condensed consolidated statements of operations and comprehensive loss, until such liability was settled.

As of September 30, 2024, the Company determined it was 100% probable of achieving the specified liquidity events and therefore accrued the full amount of the success fee obligation. The following reflects the significant quantitative inputs used to determine the valuation of the success fee obligation as of September 30, 2024 and December 31, 2023:

	September 30, 2024	December 31, 2023
Discount rate	8.5 %	9.0 %
Expected timing of achieving liquidity events (years)	0.3	1.0
Probability of achieving liquidity events	100%	100%

The change in fair value of the Company's success fee obligation was immaterial in the nine months ended September 30, 2024.

9. Leases

The Company has the following operating leases for its corporate offices and lab space located in Cambridge, Massachusetts.

325 Vassar Street

In 2017, the Company entered a noncancelable operating lease agreement to lease its office space at 325 Vassar Street, Cambridge, Massachusetts. The Company is required to pay property taxes, insurance, and normal maintenance costs. The operating lease contains predetermined fixed escalations of minimum rentals during the lease term. In 2019 and 2020, the Company entered into sublease agreements with two related parties to sublease this office and laboratory space. The lease and subleases expired in September 2024. Refer to Note 17, *Related Party Transactions*, for further details.

20 Acorn Park Drive

On July 13, 2020, the Company entered into a Shared Space Arrangement (the "Arrangement") with Sail Biomedicines, Inc., (“Sail Bio”, also formerly known as Senda Biosciences, Inc. and Kintai Therapeutics, Inc. prior to its merger with LARONDE, Inc.) to share one-third of Sail Bio's 69,867 square feet of leased space at 20 Acorn Park Drive, Cambridge, Massachusetts. Sail Bio is a related party as it is an affiliate of Flagship Pioneering (“Flagship”). The Arrangement commenced on August 1, 2020, with an expiration date of July 31, 2022 and two options to extend the term

of the Arrangement for a period of 24 months each. The operating lease contains predetermined fixed escalations of minimum rentals during the lease term, and the Company is required to pay property taxes, insurance, and normal maintenance costs. In January 2022, the Company entered into an amendment to the Arrangement with Sail Bio to exercise the option to renew the lease through July 2023. The Company also modified certain provisions related to the extension term. The Company did not subsequently renew the lease, and the lease expired at the end of July 2023. Refer to Note 17, *Related Party Transactions*, for further details.

140 First Street (formerly known as One Charles Park)

On November 4, 2021, the Company entered into a lease with ARE-MA Region No. 94, LLC to lease an aggregate of approximately 89,246 rentable square feet of office and laboratory space located at 140 First Street, Cambridge, Massachusetts. The lease includes two phases. Phase 1 includes approximately 78,380 rentable square feet for the fifth floor. Phase 2 includes 10,866 rentable square feet in a separate suite on the first floor. In accordance with the lease agreement, the Company paid $0.8 million upon the execution of the lease, which has offset the first month's rent. Phase 1 of the lease commenced in May 2023, and Phase 2 commenced in August 2023.

On May 3, 2023, the Company entered into a first amendment to the lease to, among other things, delay the delivery date of part of the premises, increase the initial base rent by $1.00 per rentable square foot per year, and change the address. The operating lease commenced on May 1, 2023 for the fifth floor premises and August 1, 2023 for the first floor premises for accounting purposes. The lease term for each of the floor premises is fifteen years from the respective commencement date, subject to certain extension rights. The base rent for the leased space is $116.00 per square foot, subject to an annual upward adjustment of 3% of the then current rental rate, starting on the first anniversary of the first full payment of rent under the lease. The operating lease includes a tenant improvement allowance of $300 per rentable square foot that is incorporated into the base rent payments, as well as an additional improvement allowance that is required to be repaid to the landlord as additional monthly rent over the lease term at an interest rate of 8%. On June 24, 2024, the Company entered into a second amendment to the lease to no longer require landlord consent to enter into Shared Space Arrangements. On July 31, 2024, the Company entered into a third amendment to the lease for 140 First Street, Cambridge, Massachusetts, pursuant to which the Landlord made available $3.3 million from the Second Additional Improvement Allowance (as defined in the Lease), which was not previously used by the Company, for the design and construction of a portion of the Premises.

On July 11, 2023, the Company entered into a Shared Space Arrangement with Apriori Bio, Inc. (“Apriori”), and on July 12, 2023, the Company entered into two Shared Space Arrangements with Metaphore Biotechnologies, Inc. (“Metaphore”) and Flagship Labs 89, Inc., now known as Prologue Medicines, Inc., ("Prologue" and, together with Metaphore and Apriori, the “Subtenants”), pursuant to which the Company agreed to sublease an aggregate of approximately 22,500 rentable square feet of office and laboratory space located at 140 First Street, Cambridge, Massachusetts (the “Premises”). Metaphore, Apriori and Prologue are affiliates of Flagship. The term of the Shared Space Arrangement with Metaphore and Prologue commenced in August, 2023 and was scheduled to end in August, 2025, and the term of the Shared Space Arrangement with Apriori began in September, 2023 and was scheduled to end in September, 2025. The Shared Space Arrangements provide that the Subtenants will pay to the Company a monthly fee that is a proportionate share of the actual base rent, operating expenses and other costs for the use and occupancy of the subleased portion of the Premises charged by the Landlord under the Lease and paid by the Company. Such proportionate share was 12.0%, 8.4% and 8.4% for Metaphore, Apriori and Prologue, respectively. In June 2024, the Company entered into amendments to the Shared Space Arrangements with the Subtenants, which increased the proportionate share to 16.2%, 11.3% and 11.3% for Metaphore, Apriori and Prologue, respectively, effective July 1, 2024. On August 27, 2024, the Company entered into an Amended and Restated Shared Space Arrangement with each of the Subtenants, effective September 1, 2024 (the "Effective Date"), which further increased their proportionate share. Such proportionate share for each of Apriori and Prologue is 12.6% from the Effective Date until November 1, 2024 (the "November Effective Date"), 13.9% thereafter until April 1, 2025 (the "April Effective Date") and 14.3% thereafter until August 31, 2026 (the "Termination Date"). Such proportionate share for Metaphore is 17.5% from the Effective Date until the November Effective Date, 18.7% thereafter until the April Effective Date and 19.2% thereafter until the Termination Date.

On August 1, 2024, the Company entered into a Shared Space Arrangement with Flagship Labs 97, Inc. (“FL 97”), pursuant to which the Company agreed to sublease approximately 12.2% of its aggregate rentable square footage, for laboratory space located on the first floor at 140 First Street, Cambridge, Massachusetts commencing August 2024 and ending July 2027, with two options to extend for a period of 24 months each. On August 27, 2024, the Company also entered into Shared Space Arrangements with Flagship Labs 101, Inc. (“FL 101”) and Flagship Labs 104, Inc. ("FL 104"), and together with FL 101 and the other Subtenants, the "SSA Subtenants"), pursuant to which the Company agreed to sublease a portion of its rentable square footage located at 140 First Street, Cambridge, Massachusetts commencing on the Effective Date. Such proportionate share for FL 101 is 3.6% from January 1, 2025 until the April Effective Date and

6.4% thereafter until the Termination Date, and for FL101 is 1.0% from January 1, 2025 through the Termination Date for FL 104. Each of FL 97, FL 101, and FL 104 are affiliates of Flagship.

The total commitment for the SSA Subtenants' share of the base rent over the term of the six Shared Space Arrangements described above is $14.2 million. The Company may terminate each Shared Space Arrangement and require the applicable SSA Subtenant to immediately vacate the Premises if such SSA Subtenant causes a default under the Lease, is in default of any provision in the applicable Sublease or acts in a manner deemed by the Company, in its sole discretion, as dangerous or threatening. The Shared Space Arrangements contain customary covenants, obligations and indemnities in favor of either party. For the three and nine months ended September 30, 2024, the Company received rental income of $1.8 million and $3.9 million, respectively, under the Shared Space Arrangements, which was recorded as a reduction of research and development expense and general and administrative expense in the accompanying condensed consolidated statements of operations and comprehensive loss.

As of September 30, 2024, operating lease right-of-use assets, net were $109.2 million, which were recorded separately on the Company's condensed consolidated balance sheet. The corresponding operating lease liabilities were $112.5 million as of September 30, 2024, of which $11.9 million were recorded in current liabilities and $100.6 million were recorded in long-term liabilities on the Company's condensed consolidated balance sheet.

The right-of-use assets represent the Company's right to use an underlying asset during the lease term and the related lease liabilities represent the Company's obligation to make lease payments arising from the lease. Both the right-of-use assets and the corresponding liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. As the Company's leases do not provide an implicit rate, the Company estimated the incremental borrowing rate based on the interest rate from the amended Term Loan, which was fully collateralized, as well as a term matched secured market rate.

The following table summarizes the components of lease expense for the three and nine months ended September 30, 2024 and 2023 (in thousands).

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Operating lease expense	$ 3,871	$ 3,866	$ 11,496	$ 7,854
Variable lease expense	1,088	945	3,225	1,844
Total lease expense	$ 4,959	$ 4,811	$ 14,721	$ 9,698

Variable lease expense generally includes common area maintenance, utilities and property taxes. For the three and nine months ended September 30, 2024, $3.5 million and $10.6 million, respectively of lease expense was recorded within research and development expenses and $1.5 million and $4.1 million, respectively was recorded within general and administrative expenses in the condensed consolidated statement of operations and comprehensive loss. For the three and nine months ended September 30, 2023, $4.0 million and $7.8 million, respectively of lease expense was recorded within research and development expenses and $0.8 million and $1.9 million, respectively was recorded within general and administrative expenses in the condensed consolidated statement of operations and comprehensive loss.

The weighted average remaining lease term and discount rate related to the Company's leases were as follows:

	As of	
	September 30, 2024	December 31, 2023
Weighted average remaining lease term (years)	13.9	14.5
Weighted average discount rate	8.9%	8.9%

Supplemental cash flow information relating to the Company's leases for the nine months ended September 30, 2024 and 2023 were as follows (in thousands):

	Nine Months Ended September 30,	
	2024	2023
Cash paid for amounts included in the measurement of lease liabilities	$ 9,144	$ 4,473
Operating lease assets obtained in exchange for lease liabilities	$ —	$ 110,424

As of September 30, 2024, the estimated minimum lease payments for 140 First Street for each of the years ending December 31 were as follows (in thousands):

2024 (remaining 3 months)	$	3,070
2025		12,492
2026		12,819
2027		13,155
2028		13,501
Thereafter		144,664
Total minimum lease payments		199,701
Less: Imputed interest		(87,155)
Present value of operating lease liabilities	$	112,546

Thermo Furniture Sale-Leaseback

In December 2023, the Company entered into a sale-leaseback arrangement with Thermo Fisher Financial Services, Inc. to provide $2.6 million in cash proceeds for previously acquired furniture and equipment. The term of the leaseback is 5 years, with an option to purchase the assets for $1 at the end of the term. The Company concluded the leaseback would be classified as a financing lease. Therefore, the transaction was deemed a failed sale-leaseback and was accounted for as a financing arrangement. The Company will make monthly payments of $53 thousand over the term of the lease. As of September 30, 2024, $0.5 million of the financing obligation is included in current liabilities and $1.8 million is included in long-term liabilities on the Company's condensed consolidated balance sheet. The assets continue to be depreciated over their useful lives, and payments are allocated between interest expense and repayment of the financing liability.

10. Commitments and Contingencies

Legal Matters

From time to time, the Company may be a party to litigation, arbitration or other legal proceedings in the course of our business, including the matters described below. The claims and legal proceedings in which the Company could be involved include challenges to the scope, validity or enforceability of patents relating to its products or product candidates, and challenges by the Company to the scope, validity or enforceability of the patents held by others. These include claims by third parties that the Company infringes their patents or breaches its license or other agreements with such third parties. The outcome of any such legal proceedings, regardless of the merits, is inherently uncertain. In addition, litigation and related matters are costly and may divert the attention of the Company's management and other resources that would otherwise be engaged in other activities. If the Company was unable to prevail in any such legal proceedings, its business, results of operations, liquidity and financial condition could be adversely affected. At each reporting date, the Company evaluates whether or not a potential loss amount or a potential range of loss is probable and reasonably estimable under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company's accounting policy for accrual of legal costs is to recognize such expenses as incurred.

On June 11, 2024, a shareholder derivative suit captioned Joel Newman v. Flagship Pioneering, Inc., et al., was filed in the Court of Chancery of the State of Delaware (the "Complaint"), alleging breaches of fiduciary duty and unjust enrichment in connection with the Company's decision to enter into a Research Collaboration Agreement with Novo Nordisk A/S ("Novo Nordisk") and Pioneering Medicines 08, Inc. The Complaint names the Company as nominal defendant, and names certain of the Company's officers and directors, among others, as defendants. The Complaint seeks damages, rescissory relief, attorneys' fees and costs, and any other and further relief the court deems just and proper. The defendants filed a motion to dismiss on September 10, 2024. Thereafter, plaintiff gave notice that he intends to file an amended complaint, which is due by December 11, 2024. The Company is unable to reasonably estimate the potential loss or range of loss associated with this matter and intends to defend itself vigorously.

Refer also to contractual commitments as described in Note 7, *Term Loan*, Note 9, *Leases*, and Note 11, *License agreements*.

11. License Agreements

Flagship Pioneering Innovations V, Inc.

In March 2019, the Company entered into an exclusive license agreement with Flagship Pioneering Innovations V, Inc., an affiliate of Flagship, under which the Company was granted an exclusive, worldwide, royalty-bearing, sublicensable, transferable license under specified patent rights to develop, manufacture and commercialize licensed products (the "Flagship License"). Under the terms of the Flagship License, the Company is obligated to pay low single

digit percentage royalties on net sales of licensed products by the Company. Royalties shall be paid by the Company on a country-by-country basis until expiration or abandonment of the last valid patent claim covering such licensed product in such country. The Company is also obligated to reimburse Flagship for patent prosecution costs.

The royalty payment is contingent upon sales of licensed products under the Flagship License. As such, when such expense is considered probable and estimable at the commencement of sales, the Company will account for the royalty expense as cost of sales for the amount it is obligated.

Whitehead Institute for Biomedical Research

In May 2019, the Company entered into an exclusive license agreement with the Whitehead Institute for Biomedical Research ("WIBR"), an affiliate of one of the Company's board members, under which the Company was granted an exclusive, worldwide, royalty-bearing, sublicensable license under specified patent rights to research, make, have made, use, sell, offer to sell, lease and import products and to perform and have performed licensed processes (the "WIBR Exclusive License"). Under the terms of the WIBR Exclusive License, the Company paid a nonrefundable upfront fee of less than $0.1 million upon the commencement of the exclusive license agreement. The Company is obligated to pay WIBR annual license maintenance fees of less than $0.1 million and low single digit percentage royalties on net sales of licensed products by the Company and its affiliates and sublicensees. Additionally, the Company is required to make milestone payments of up to $1.7 million in the aggregate for each of the first three licensed products (excluding backup products) upon the achievement of specified clinical and regulatory milestones. In addition, the Company is required to pay to WIBR a percentage of the non-royalty payments that it receives from sublicensees of the WIBR Exclusive License. This percentage ranges from zero to low double-digits and will be based upon the stage of development of the licensed product at the time such sublicense is executed.

In May 2019, the Company also entered into a co-exclusive license agreement with WIBR under which the Company was granted a co-exclusive, worldwide, royalty-bearing, sublicensable license under specified patent rights to research, make, have made, use, sell, offer to sell, lease and import products and to perform and have performed licensed processes (the "WIBR Co-Exclusive License"). Under the terms of the WIBR Co-Exclusive License, the Company paid a nonrefundable upfront fee of less than $0.1 million upon the commencement of the co-exclusive license agreement. The Company is obligated to pay WIBR annual license maintenance fees of less than $0.1 million and low single digit percentage royalties on net sales of licensed products by the Company and its affiliates and sublicensees as well as low single digit percentage royalties on licensed service income received by the Company and its affiliates. Additionally, the Company is required to make milestone payments of up to $1.9 million in the aggregate for each of the first three licensed products (excluding backup products) upon the achievement of specified clinical and regulatory milestones. In addition, the Company is required to pay to WIBR annual fees of less than $0.1 million for each sublicense agreement.

For the three months ended September 30, 2024 and 2023, the Company recognized an immaterial amount and $0.1 million, respectively, of expenses for the license maintenance fees and milestone payments. For the nine months ended September 30, 2024 and 2023, the Company recognized expenses of $0.2 million and $0.3 million, respectively for the license maintenance fees and milestone payments. There were no outstanding payments due to WIBR as of September 30, 2024 and December 31, 2023.

The annual maintenance fees will be recorded as an expense on an annual basis based on the stated amount for the applicable year. Upon determination that a milestone payment is probable to occur, the amount due will be recorded as research and development expense. Lastly, the royalty payments and the sublicense non-royalty payments are contingent upon sales of licensed products or execution of a sublicense agreement under the WIBR Exclusive and Co-Exclusive Licenses. As such, when such expenses are considered probable and estimable at the commencement of sales or execution of a sublicense agreement, the Company will accrue royalty expense and sublicense non-royalty payments, as applicable, for the amount the Company is obligated.

Acuitas Therapeutics, Inc.

In October 2020, the Company entered into a development and option agreement (the "Development and Option Agreement") with Acuitas Therapeutics, Inc. ("Acuitas"). Under the terms of the Development and Option Agreement, the parties agreed to jointly develop certain products combining the Company's gene modulating therapeutics with Acuitas' lipid nanoparticles. Additionally, in accordance with the Development and Option Agreement, the Company has options to obtain non-exclusive, worldwide, sublicensable licenses under Acuitas' patents and know-how related to lipid nanoparticle technology ("Acuitas LNP Technology") with respect to two specified targets (e.g., EC constructs) ("Reserved Targets") to

develop and commercialize one or more therapeutic products relating to such targets. For each option and Reserved Target, the Company is obligated to pay an annual technology access fee and target reservation and maintenance fees collectively in the low-mid six figures until such Reserved Target is removed from the Reserved Target list or until the Company exercises an option with respect to such Reserved Target. In the event that the Company exercises the options, the Company will pay $1.5 million for the first non-exclusive license and $1.75 million for the second non-exclusive license. Under the terms of the Development and Option Agreement, the Company is also responsible for the full-time equivalent ("FTE") funding obligations, which is expected to be approximately $0.4 million per year, and reimbursements to Acuitas for certain development and material costs incurred by them.

In March 2021, the Company exercised the first option under the Development and Option Agreement and entered into a non-exclusive license agreement with Acuitas (the “Acuitas License Agreement”) under which the Company was granted a non-exclusive, worldwide, sublicensable license under the Acuitas LNP Technology to research, develop, manufacture, and commercially exploit products consisting of the Company’s gene modulating therapeutics and Acuitas’ lipid nanoparticles. In connection with the option exercise, the Company incurred an expense for the option exercise fee of $1.5 million. Under the Acuitas License Agreement, the Company is required to pay Acuitas an annual license maintenance fee in the high six figures until the Company achieves a certain development milestone. Acuitas is entitled to receive potential clinical and regulatory milestone payments of up to $18.0 million in the aggregate if the milestones are achieved. With respect to the sale of each licensed products, the Company is also obligated to pay Acuitas low single digit percentage royalties on net sales of the licensed products by the Company and its affiliates and sublicensees in a given country until the last to occur, in such country, of (i) the expiration or abandonment of all licensed patent rights covering the licensed product, (ii) expiration of any regulatory exclusivity for the licensed product, or (iii) ten years from the first commercial sale of the licensed product.

For each of the three months ended September 30, 2024 and 2023, the Company recorded less than $0.1 million of research and development expenses consisting of technology access fees, target reservation and maintenance fees, the costs of services performed by Acuitas, material costs and reimbursable costs. For each of the nine months ended September 30, 2024 and 2023, the Company recorded $0.1 million of research and development expenses consisting of technology access fees, target reservation and maintenance fees, the costs of services performed by Acuitas, material costs and reimbursable costs.

The option exercise fee under the Development and Option Agreement was recorded as research and development expense upon the Company’s exercise of the first option. Additionally, the technology access fees, target reservation and maintenance fees, expenses associated with the FTE funding obligations and reimbursements for development and material costs incurred by Acuitas are recorded as research and development expense when incurred. The annual maintenance fee will be recorded as an expense on an annual basis based on the stated amount for the applicable year. Upon determination that a milestone payment is probable to occur, the amount due will be recorded as research and development expense. There were no milestones triggered, and no milestone expense was recorded related to the Acuitas agreements for the nine months ended September 30, 2024 and 2023. Lastly, the royalty payment is contingent upon sales of licensed products under the Acuitas License Agreement. As such, when such expenses are considered probable and estimable at the commencement of sales, the Company will accrue royalty expense for the amount the Company is obligated.

Nitto Denko Corporation

On October 12, 2022, the Company entered into a Collaboration and License Agreement (the "Nitto Agreement”) with Nitto Denko Corporation (“Nitto”), pursuant to which, among other things, Nitto granted the Company an exclusive, worldwide, royalty-bearing, fully transferable and fully sublicensable license under all intellectual property owned or controlled by Nitto relating to its lipid nanoparticle delivery technology.

Under the terms of the Nitto Agreement, the Company made an upfront cash payment of $1.0 million, and developmental milestone payments of $1.0 million to Nitto in 2022. Both payments were recorded as research and development expenses. The Company may be required to make up to $83.0 million in future payments to Nitto based upon the achievement of specified development, regulatory and sales milestones. There were no milestones triggered, and no milestone expense was recorded related to the Nitto Agreement for the nine months ended September 30, 2024 and 2023. The Company is also obligated to pay to Nitto tiered, single-digit percentage royalties on a country-by-country basis based on net sales of the licensed product, subject to reduction in specified circumstances. As such, when these expenses are considered probable and estimable, the Company will accrue expense for the amount the Company is obligated. On May 2, 2024, the Company provided notice to terminate its Collaboration and License Agreement with Nitto

Denko Corporation pursuant to Section 10.3(b) of the agreement, with an effective date of June 1, 2024 or thirty (30) days from notification. There was no penalty or fee associated with the termination.

During the three and nine months ended September 30, 2024, the Company recorded no research and development expenses related to the Nitto Agreement. During the three and nine months ended September 30, 2023, the Company recorded $0.4 million and $0.9 million, respectively, of research and development expenses consisting of material costs, costs of services performed by Nitto, and reimbursable costs.

12. Collaboration Agreements

PMCo

In November 2021, the Company entered into a five-year collaboration agreement with PMCo, an affiliate of Flagship, under which PMCo was granted an exclusive license covering specified patent rights of the Company's lipid nanoparticle technology to develop one or more therapeutic products to treat diseases related to the cystic fibrosis transmembrane conductance regulator gene, like cystic fibrosis. Under the terms of the agreement, the Company will perform certain research activities in accordance with the research plan, and PMCo will be solely responsible for, at its sole cost and expense, and will have sole discretion with respect to, developing, manufacturing, seeking regulatory approval for and commercializing licensed products. The research plan funding may be adjusted upon mutual written agreement from both parties. Additionally, in the event PMCo is acquired or sold, the Company is entitled to receive a portion of the proceeds of such transaction, subject to various reductions and other amounts payable in accordance with the agreement.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, PMCo, is a customer. The Company determined that the research activities and the exclusive license granted under the collaboration agreement is considered as a single performance obligation, and therefore, the transaction price was allocated entirely to the single performance obligation. The Company recognizes revenue related to the single performance obligation over time as the underlying services are performed and/or external costs are incurred.

The total transaction price at September 30, 2024 was determined to be $7.0 million based on the current estimated required efforts to fulfill the performance obligation. This total includes an increase of $1.9 million in the fourth quarter of 2022, an increase of $2.4 million in the third quarter of 2023, an increase of $0.1 million in the fourth quarter of 2023, and a decrease of $0.9 million in the third quarter of 2024, all of which were agreed upon with PMCo, to the original transaction price as of the inception of the contract of $3.5 million. As of September 30, 2024, the transaction price had been fully recognized as revenue and no further research and development activities are expected to be performed.

The Company recognized funded research and collaboration revenue of $0.3 million and $1.9 million during the three and nine months ended September 30, 2024, respectively, and $0.8 million and $2.1 million during the three and nine months ended September 30, 2023, respectively in the condensed consolidated statement of operations and comprehensive loss. Costs incurred associated with this collaboration agreement were recorded as research and development expenses.

Pursuant to the agreement, the Company is entitled to receive a portion of the sales proceeds in the event PMCo is acquired or sold. At the end of each reporting period, the Company evaluates the probability of occurrence of such transaction. As of September 30, 2024, the Company determined that the proceeds from such transaction was not probable of recognition.

Novo Nordisk

On December 31, 2023, the Company entered into a Research Collaboration Agreement with Novo Nordisk A/S ("Novo Nordisk") and Pioneering Medicines 08, Inc., an affiliate of Flagship (and with respect to certain provisions set forth in the agreement, Pioneering Medicines (NN), LLC and PM (NN) Explorations, Inc.). Under the terms of the agreement, the Company granted to Novo Nordisk an exclusive, royalty-bearing, transferable license, with the right to grant sublicenses through multiple tiers, for certain of its intellectual property to conduct research and development activities under an agreed-upon research and development plan relating to a product candidate, or program target, for the prevention, treatment or control of a cardiometabolic disease, including diabetes.

In January 2024, the Company received an upfront nonrefundable payment of $5.1 million from Novo Nordisk and expects to receive approximately $21.6 million in cost reimbursement through 2027 to fund the related research and development activities. The research plan funding may be adjusted upon mutual written agreement from all the parties.

The Company is also eligible to receive development and commercial milestone payments, as well as tiered royalties on annual net sales of a licensed product. The term of the agreement expires at the end of the royalty term, which is the later of the 10th anniversary of the first commercial sale, the expiration of the last-to-expire payment claim, or expiration of regulatory exclusivity. Upon the expiration of the royalty term for a given licensed product in a given country in the territory, the licenses granted to Novo Nordisk pursuant to the agreement under the Omega licensed intellectual property survive and become perpetual, irrevocable, fully paid-up and royalty free with respect to such licensed product in such country.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Novo Nordisk, is a customer. The Company determined that the research activities and the exclusive license granted under the collaboration agreement is considered as a single combined performance obligation as they are incapable of being distinct. The Company recognizes revenue related to the single performance obligation over time using the input method. Under the input method, the extent of progress towards completion is measured based on the ratio of costs incurred to date to the total estimated costs at completion of the performance obligation, which the Company believes best measures its progress towards satisfying the combined performance obligation. A cost-based input method of revenue recognition requires management to make estimates of costs to complete performance obligation. In making such estimates, judgment is required to evaluate assumptions related to cost estimates.

As of September 30, 2024, the total transaction price was determined to be $26.7 million based on the upfront nonrefundable payment and estimated required research and development efforts. As of September 30, 2024, the remaining transaction price was estimated to be $21.5 million, which is expected to be recognized as revenue through 2027.

The Company recognized funded research and collaboration revenue of $2.3 million and $5.2 million in the condensed consolidated statement of operations and comprehensive loss during the three and nine months ended September 30, 2024, respectively. Additionally, the Company had $1.1 million of current deferred revenue and $3.0 million of noncurrent deferred revenue as of September 30, 2024 based on the period the services are expected to be performed and/or related costs to be incurred. Costs incurred associated with this collaboration agreement were recorded as research and development expenses.

The Company will assess the probability of achieving the milestones and include them in the transaction price when they are deemed probable. Royalties will be recognized when the subsequent sales occur based on the sales or usage-based royalty exception.

ASC 606 Disclosures

To-date, the Company has only generated revenues from its collaboration agreements with PMCo and Novo Nordisk. During the three and nine months ended September 30, 2024, the Company recognized total collaboration revenue of $2.6 million and $7.1 million, respectively. During the three and nine months ended September 30, 2023, the Company recognized total collaboration revenue of $0.8 million and $2.1 million, respectively.

The following table summarizes the Company's contract assets and liabilities (in thousands):

	September 30, 2024	December 31, 2023
Contract assets:		
Accounts receivable	$ 333	$ 6,131
Unbilled revenue	—	89
Contract liabilities:		
Deferred revenue- current	1,054	—
Deferred revenue- noncurrent	2,968	—

The timing of revenue recognition, billings and cash collections results in billed accounts receivable, unbilled revenue (contract assets) and deferred revenue (contract liabilities) on the condensed consolidated balance sheets. Deferred revenue is included in Other current liabilities and Other liabilities on the condensed consolidated balance sheets. During the nine months ended September 30, 2024 and 2023, the Company recognized $1.0 million and less than $0.1 million of revenue, respectively, which were included in the deferred revenue balances as of December 31, 2023 and 2022, respectively.

13. Preferred and Common Stock

In 2021, the Company's board of directors and stockholders approved the Company's Amended and Restated Certificate of Incorporation to, among other things, provide for 200,000,000 authorized shares of common stock with a par value of $0.001 per share and 10,000,000 authorized shares of preferred stock with a par value of $0.001 per share.

In February 2023, the Company completed a registered direct offering of common stock pursuant to which it issued and sold 6,920,415 shares of its common stock at a purchase price of $5.78 per share and secured approximately $39.7 million in net proceeds after deducting estimated offering expenses of $0.3 million.

The holders of common stock are entitled to one vote for each share of common stock. Subject to the payment in full of all preferential dividends to which the holders of the preferred stock are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available. In the event of any voluntary or involuntary liquidation, dissolution, or winding up of the Company, after the payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of preferred stock are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution.

As of September 30, 2024, the Company has reserved an aggregate of 9,666,626 shares of common stock for the potential exercise of outstanding stock options under its equity incentive plans. Upon the effectiveness of the 2021 Incentive Award Plan ("2021 Plan"), the Company ceased granting awards under the 2017 Equity Incentive Plan ("2017 Plan"), and the 3,709,118 shares of common stock subject to outstanding stock options issued under the 2017 Plan may become available for future issuance under the 2021 Plan to the extent such stock options are forfeited.

14. Equity Incentive Plans

2017 Equity Incentive Plan

In June 2017, the Company's board of directors adopted the 2017 Plan, which provided for the grant of qualified incentive stock options and nonqualified stock options, restricted stock or other awards to the Company's employees and non-employees for the issuance or purchase of shares of the Company's common stock. As of September 30, 2024, there were no shares available for future grants under the 2017 Plan and a total of 3,709,118 shares of the Company's common stock were subject to outstanding stock options issued under the 2017 Plan.

The 2017 Plan is administered by the Company's board of directors or a committee thereof to the extent the Company's board of directors has delegated its power or authority under the 2017 Plan. The exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, except that the exercise price per share of stock options may not be less than 100% of the fair market value of the common stock on the date of grant. Stock options awarded under the 2017 Plan expire 10 years after the grant date unless the board of directors sets a shorter term. Incentive stock options and nonqualified stock options granted to employees and non-employees typically vest over four years. Certain stock options provide for accelerated vesting if there is a change in control, as defined in the 2017 Plan.

2021 Incentive Award Plan

The Company's board of directors adopted, and the Company's stockholders approved, the 2021 Plan in July 2021. The 2021 Plan provides for the grant of incentive stock options, non-statutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards, and subsequent to the IPO, all equity-based awards are granted under the 2021 Plan. The Company initially reserved 2,960,000 shares of its common stock for future issuance under the 2021 Plan, and such number of shares of common stock is subject to an annual increase on the first day of each calendar year, beginning on January 1, 2022 and ending on and including January 1, 2031, equal to the lesser of (i) 4% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as is determined by the board of directors. As of September 30, 2024, there were 3,886,711 shares available for future grants under the 2021

Plan, and a total of 5,957,508 shares of the Company's common stock were subject to outstanding stock options issued under the 2021 Plan.

The Company recorded stock-based compensation expense as research and development and general and administrative expenses in the condensed consolidated statements of operations and comprehensive loss as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Research and development	$ 515	$ 1,093	$ 2,341	$ 3,358
General and administrative	1,208	1,187	4,026	3,322
Total stock-based compensation expense	$ 1,723	$ 2,280	$ 6,367	$ 6,680

Stock Options

A summary of option activity under the Company's equity incentive plans during the nine months ended September 30, 2024 was as follows:

	Number of options	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value [1] (in thousands)
Outstanding as of January 1, 2024	8,780,737	$ 5.69	7.52	$ 5,033
Granted	3,974,475	3.23		
Exercised	(14,237)	1.75		
Forfeited	(2,272,471)	5.60		
Expired	(801,878)	8.80		
Outstanding as of September 30, 2024	9,666,626	4.45	6.85	1,187
Vested and expected to vest as of September 30, 2024	9,666,626	4.45	6.85	1,187
Exercisable as of September 30, 2024	5,497,704	$ 4.66	5.22	$ 1,187

[1] The aggregate intrinsic value is calculated as the difference between the exercise price of the underlying options and the estimated fair value of the common stock for the options that were in the money as of September 30, 2024.

Included in the stock options granted during the nine months ended September 30, 2024, the Company granted the Chief Executive Officer an option to purchase 314,326 shares of the Company's common stock. The option vests as to 25% of the underlying shares on February 7, 2025 and as to the remainder in twelve equal quarterly installments thereafter, such that the option will be fully vested and exercisable on February 7, 2028. In the event the Board determines that the consummation of a transaction for business development purposes satisfies the corporate goals for business development collaborations, any outstanding, unvested portion of the option will fully vest on the first anniversary of the consummation of such transaction. The potential acceleration of vesting due to the transaction is a performance condition and as of September 30, 2024, the performance condition has not been achieved. Therefore, the Company recognizes the stock-based compensation expense for the stock option over the explicit service period.

The assumptions used in the Black-Scholes option-pricing model for all the stock options granted were as follows:

	Nine months ended September 30, 2024
Expected volatility	75.00% - 87.29%
Weighted-average risk-free interest rate	4.16%
Expected dividend yield	0.00%
Weighted-average expected term (in years)	5.89

The weighted-average grant date fair value per share of stock options granted during the nine months ended September 30, 2024 was $2.21. The aggregate intrinsic value of stock options exercised during the nine months ended September 30, 2024 was $0.03 million.

As of September 30, 2024, there was $10.4 million of unrecognized compensation cost related to unvested stock options, which is expected to be recognized over a weighted-average period of approximately 1.9 years.

2021 Employee Stock Purchase Plan

The Company's board of directors adopted, and the Company's stockholders approved, the Employee Stock Purchase Plan (the "2021 ESPP") in July 2021. The purpose of the 2021 ESPP is to provide eligible employees with an opportunity to purchase shares of the Company's common stock through accumulated contributions. The 2021 ESPP permits participants to purchase shares of common stock through contributions (generally in the form of payroll deductions) of up to an amount of their eligible compensation determined by the administrator. Subject to certain other limitations or unless otherwise determined by the administrator, a participant may purchase a maximum of 100,000 shares of common stock during an offering period. The offering periods under the 2021 ESPP will begin on such date as determined by the administrator and not exceed 27 months. Amounts deducted and accumulated by the participant are used to purchase shares of common stock on each exercise date. The purchase price of the shares will be determined by the administrator but in no event will be less than 85% of the lower of the fair market value of common stock on the enrollment date or on the exercise date. Participants may end their participation at any time during an offering period and will be paid their accrued contributions that have not yet been used to purchase shares of common stock, provided that they give notice of such withdrawal within the time period required by the administrator. Participation ends automatically upon termination of employment with the Company.

The 2021 ESPP provides for an annual increase to the number of shares available for issuance thereunder on the first day of each calendar year beginning on January 1, 2022 and ending on and including January 1, 2031, by an amount equal to the lesser of (i) 1% of the aggregate number of shares of common stock outstanding on the final day of the immediately preceding calendar year and (ii) such smaller number of shares of common stock as is determined by our board of directors, provided that no more than 6,450,000 shares of our common stock may be issued under the 2021 ESPP.

As of September 30, 2024, the Company had not consummated an offering period under the 2021 ESPP. As of September 30, 2024, the Company had 1,990,108 shares of common stock available for issuance under the 2021 ESPP.

15. Net Loss per Share Attributable to Common Stockholders

For periods in which the Company reports a net loss attributable to common stockholders, potentially dilutive securities have been excluded from the computation of diluted net loss per share as their effects would be anti-dilutive. Therefore, the weighted average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same.

The following table summarizes the computation of basic and diluted net loss per share attributable to common stockholders of the Company (in thousands except share and per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Numerator:				
Net loss attributable to common stockholders	$ (16,444)	$ (22,248)	$ (52,878)	$ (77,214)
Denominator:				
Weighted average number of common stock, basic and diluted	55,155,583	55,140,058	55,153,699	53,629,468
Net loss per common stock attributable to common stockholders, basic and diluted	$ (0.30)	$ (0.40)	$ (0.96)	$ (1.44)

The Company excluded the following potential common stock, presented based on amounts outstanding at period end, from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	As of September 30,	
	2024	2023
Outstanding options to purchase common stock	9,666,626	9,168,502

16. Income Taxes

During the three and nine months ended September 30, 2024 and 2023, the Company recorded a full valuation allowance on federal and state deferred tax assets since management does not forecast the Company to be in a taxable position in the near future.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the IRS and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect our stockholders or us. The Company assesses the impact of various tax reform proposals and modifications to existing tax treaties in all jurisdictions where it has operations to determine the potential effect on its business and any assumptions it has made about its future taxable income. The Company cannot predict whether any specific proposals will be enacted, the terms of any such proposals or what effect, if any, such proposals would have on its business if they were to be enacted.

17. Related Party Transactions

For the three and nine months ended September 30, 2024 and 2023, related party transactions consisted primarily of rent payments and reimbursable expenses, offset by sublease income received from related parties.

The majority ownership of the Company is held by Flagship, in which it holds shares representing approximately 53% of the Company's outstanding voting stock as of September 30, 2024. Flagship historically provided management services to the Company, and the Company reimburses Flagship for certain expenses, including insurance and benefits, and related fees, and software licenses incurred on the Company's behalf. For the three months ended September 30, 2024 and 2023, the Company incurred zero and $0.1 million, respectively, primarily for reimbursable expenses. For the nine months ended September 30, 2024 and 2023, the Company incurred an immaterial amount and $0.4 million, respectively, primarily for reimbursable expenses. These expenses are recorded as general and administrative expense in the accompanying condensed consolidated statements of operations and comprehensive loss. As of September 30, 2024 and December 31, 2023, there was zero and an immaterial amount of outstanding payments due to Flagship, respectively.

In July 2023 the Company entered into three Shared Space Agreements with related parties Metaphore, Apriori, and Prologue. These companies are affiliates of Flagship, a controlling stockholder of the Company. Pursuant to the agreements, the Company agreed to sublease an aggregate of approximately 22,500 rentable square feet of office and laboratory space at 140 First Street. In June 2024, the Company entered into amendments to the Shared Space Arrangements with the Subtenants, which increased the total sublease to 30,447 rentable square feet effective July 1, 2024. On August 27, 2024, the Company entered into an Amended and Restated Shared Space Arrangement with each of the Subtenants, which increased the total sublease to 33,447 rentable square feet effective September 1, 2024, with further increases in the future as defined in the arrangements.

On August 1, 2024, the Company entered into a Shared Space Arrangement with FL 97, pursuant to which the Company agreed to sublease approximately 10,866 rentable square feet, for laboratory space located on the first floor at 140 First Street, Cambridge, Massachusetts. On August 27, 2024, the Company entered into Shared Space Arrangements with FL 101 and FL 104, pursuant to which the Company agreed to sublease 3,550 rentable square feet, for laboratory space located at 140 First Street, effective September 1, 2024, with increases in the future as defined in the agreement. Under the Shared Space Arrangements, the Company has received aggregate rental income of $1.8 million and $3.9 million for the three and nine months ended September 30, 2024, respectively. Such rental income was reflected as a reduction of research and development expense and general and administrative expense in the accompanying condensed consolidated statements of operations and comprehensive loss. There were $0.2 million and zero of outstanding receivables due from the subtenants as of September 30, 2024 and December 31, 2023, respectively.

In September 2020, the Company sublet the entire space of its 325 Vassar Street facility, approximately 19,404 square feet, to Sail Bio (formerly known as LARONDE, Inc. and VL50, Inc.), which is an affiliate of Flagship. The rental rate for the sublease arrangement is equal to the Company's rental obligation per the agreement with BMR-325 Vassar

Street LLC, reduced by the sublease income received from Cygnal Therapeutics, Inc. (“Cygnal”). The sublessee is obligated to pay all real estate taxes and costs related to the subleased premises, including cost of operations, maintenance, repair, replacement and property management. The sublease expired at the end of the Company's lease agreement with the landlord in September 2024 with no extension. During each of the three months ended September 30, 2024 and 2023, the Company received rental income and reimbursement of related expenses of $0.6 million. During each of the nine months ended September 30, 2024 and 2023, the Company received rental income and reimbursement of related expenses of $1.8 million and $1.9 million, respectively, which was recorded within research and development expense and general and administrative expense in the condensed consolidated statements of operations and comprehensive loss. There were no outstanding receivables due from Sail Bio as of September 30, 2024 and December 31, 2023.

In July 2020, the Company entered into a Shared Space Arrangement (the Arrangement) with Sail Bio to share one-third of Sail Bio's 69,867 square feet of leased space at 20 Acorn Park Drive, Cambridge, Massachusetts. In January 2022, the Company entered into an amendment to the Arrangement with Sail Bio to exercise the option to renew the lease through July 2023. In connection with the amendment, the Company made an upfront payment of $2.9 million in January 2022, to cover the rent payments for the extended lease term. The Company did not subsequently renew the lease, and the lease expired at the end of July 2023. Additionally, upon the expiration of the extended lease term, the Company received $0.65 million from Sail Bio for all furniture, fixtures and equipment owned by the Company that will remain at the lease property. The net book value of these assets was determined to be $0.4 million, and the Company recognized a gain on this disposal of $0.2 million in June 2023.

Refer to other related party transactions as described in Note 9, *Leases*, Note 11, *License Agreements* and Note 12, *Collaboration Agreements*.

18. Employee Benefits

In 2018, the Company established a defined-contribution plan under Section 401(k) of the Internal Revenue Code, or the 401(k) Plan. The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. On May 1, 2022, the Company began matching 50% of employee contributions of up to 6% of eligible compensation contributed on a pre-tax and/or Roth after-tax basis to the 401(k) Plan. During the nine months ended September 30, 2024 and 2023, the Company made matching contributions totaling $0.4 million and $0.5 million, respectively.

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 unaudited financial statements and related notes appearing elsewhere in this Quarterly Report on Form 10-Q, or Quarterly Report, and our Annual Report on Form 10-K for the year ended December 31, 2023 filed with the United States Securities and Exchange Commission, or SEC, on March 28, 2024 (the "2023 10-K"). Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Quarterly Report, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also see the "Special Note Regarding Forward-Looking Statements" section of this Quarterly Report.

Overview

Omega Therapeutics is a biotechnology company pioneering a new class of programmable epigenomic mRNA medicines. Our OMEGA platform harnesses the power of epigenetics and our deep understanding of genomic architecture to precisely target and controllably modulate gene expression at the pre-transcriptional level to treat or cure diseases. We have deciphered the three-dimensional architecture of the human genome. Genes and their accompanying regulators are organized into distinct and evolutionarily conserved structures called Insulated Genomic Domains, or IGDs. IGDs are the fundamental structural and functional units of gene control and cell differentiation and act as nature's innate control system for gene expression. Most diseases are caused by aberrant gene expression rooted in alterations in IGDs. The OMEGA platform has enabled us to systematically identify and validate thousands of novel DNA-sequence-based epigenomic "zip codes" associated with individual regulatory elements within IGDs. We call these epigenomic targets EpiZips. We rationally design and engineer our mRNA therapeutics, called epigenomic controllers, or ECs, to target EpiZips for precision epigenomic control. This enables us to precisely tune genes to a desired level of expression and to control the duration of expression. Through this approach, we believe that the OMEGA platform has broad potential applicability across a range of diseases and conditions, including those with historically undruggable, intractable, and difficult-to-treat targets. Omega is advancing a pipeline of diverse programs derived from the OMEGA platform.

Since our inception, we have incurred significant operating losses. We have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our preclinical development activities and preparing for and initiating clinical trials of our product candidates. To date, we have funded our operations primarily with proceeds from sales of equity securities and borrowings under our loan and security agreement.

As of September 30, 2024, we had cash and cash equivalents of $30.4 million. In August 2021, we completed our initial public offering ("IPO") pursuant to which we issued and sold 8,300,976 shares of our common stock, including 900,976 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, for aggregate gross proceeds of $141.1 million. We received approximately $128.1 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us. In February 2023, we completed a registered direct offering of common stock pursuant to which we issued and sold 6,920,415 shares of our common stock at a purchase price of $5.78 per share and secured approximately $39.7 million in net proceeds after deducting estimated offering expenses. In August 2023, we entered into an Open Market Sale Agreement (the "Sales Agreement"), with Jefferies LLC ("Jefferies"), as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $60.0 million in "at-the-market," or ATM, offerings under our Registration Statement on Form S-3 (File No. 333-268254) filed with the SEC on November 8, 2022, which was declared effective on November 18, 2022. During the nine months ended September 30, 2024, we did not sell any shares of common stock under the Sales Agreement.

Our ability to generate product revenue will depend on the successful development, regulatory approval, and eventual commercialization of one or more of our product candidates. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. Additional sources of financing might not be available to us on favorable terms, if at all. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We expect to continue to incur significant additional operating losses for the foreseeable future as we seek to advance product candidates through clinical development, continue preclinical development, expand our research and development activities, develop new product candidates, complete preclinical studies and clinical trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products. Our expenses will also increase substantially if or as we:

- continue our research and development efforts and submit INDs for our product candidates;
- initiate and conduct clinical trials of our product candidates;
- continue to engineer and develop additional product candidates;
- continue to develop the OMEGA platform;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish manufacturing and supply chain capacity sufficient to provide clinical and, if applicable, commercial quantities of product candidates, including building our own manufacturing facility;
- establish a sales, marketing, internal systems and distribution infrastructure to commercialize any products for which we may obtain regulatory approval, if any, in geographies in which we plan to commercialize our products ourselves;
- maintain, expand, protect and enforce our intellectual property estate;
- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial, and support personnel, to execute our business plan and support our product development and potential future commercialization efforts;
- enter into collaborations or licenses for new technologies;
- make royalty, milestone, or other payments under our current and any future in-license agreements;
- incur additional legal, accounting, and other expenses in operating our business; and
- continue to operate as a public company.

Other Developments

On December 31, 2023, we entered into a Research Collaboration Agreement (the “Novo RCA”) with Novo Nordisk A/S (“Novo Nordisk”), Pioneering Medicines 08, Inc. (“PM SpinCo”), and, with respect to certain provisions set forth in the Novo RCA, Pioneering Medicines (NN), LLC (“Shareholder”) and PM (NN) Explorations, Inc. (“PMCo NN” and together with PM SpinCo and Shareholder, the “PM Entities”), affiliates of Flagship Pioneering ("Flagship"). Under the terms of the Novo RCA, we granted to Novo Nordisk an exclusive, royalty-bearing, transferable license, with the right to grant sublicenses through multiple tiers, for certain of our intellectual property to conduct research and development activities under an agreed-upon research and development plan, together with the PM Entities, relating to a product candidate, or program target, for the prevention, treatment or control of a cardiometabolic disease, including diabetes, in humans throughout the world. In connection with the execution of the Novo RCA, Novo Nordisk agreed to make an upfront cash payment of $10 million, up to $522 million in future development and sales milestone payments, and mid and high-single digit to low double-digit percentage royalties on net sales of the licensed product. These payments will be shared approximately equally between us and Shareholder. In January 2024, we received $5.1 million as our share of the upfront cash payment. Novo Nordisk’s obligations to pay royalties with respect to a licensed product and country will expire upon the latest of ten years following first commercial sale of a licensed product in such country, the expiration of the last-to-expire of certain valid patent claims applicable to such licensed product in such country, and the expiration of regulatory exclusivity for such licensed product in such country, subject to certain royalty reduction and step-down provisions set forth in the Novo RCA. For more information, see Note 12 - Collaboration Agreements in the notes to the unaudited financial statements appearing elsewhere in this Quarterly Report.

Development Programs

OTX-2002

In July 2022, we announced clearance of our investigational new drug (“IND”) application from the United States Food and Drug Administration ("FDA") to initiate a Phase 1/2, first-in-human, clinical trial of OTX-2002 for the treatment of hepatocellular carcinoma, or HCC.

In October 2022, we announced the first patient was dosed in the MYCHELANGELO™ I clinical trial. The Phase 1/2 MYCHELANGELO I trial is designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of OTX-2002 as a monotherapy (Part 1) and in combination with standard of care therapies (Part 2) in patients with relapsed or refractory HCC and other solid tumor types known for association with the MYC oncogene.

In November 2022, we announced that OTX-2002 was granted Orphan Drug Designation by the FDA for the treatment of HCC.

In March 2023, we entered into a Clinical Supply Agreement with Roche to evaluate OTX-2002 in combination with Roche’s anti-PD-L1 therapy, atezolizumab, in patients with advanced MYC-driven hepatocellular carcinoma as part of our Phase 1/2 MYCHELANGELO I clinical trial. Under the terms of this agreement, Roche will supply atezolizumab and Omega will evaluate the combination as part of the overall conduct of the trial.

In November 2024, we reported data from the completed Phase 1 portion of the trial. Twenty-four patients, including 19 with HCC, were enrolled across six dose cohorts (spanning 0.02 mg/kg to 0.3 mg/kg) and were treated with OTX-2002 intravenously once every two weeks.

Key Highlights

- Pharmacodynamics and pharmacokinetics:
  - Highly specific on-target engagement and intended epigenetic changes at the target genomic loci, as evidenced by a robust increase in cell-free DNA MYC methylation signal following administration of study drug. The increased methylation signal persisted throughout the two-week dosing interval and downregulation of MYC expression was observed.

- Safety and tolerability:
  - At the recommended dose for expansion (0.12 mg/kg), OTX-2002 showed a favorable safety profile, with infusion-related reactions being the most common adverse event.

- Preliminary anti-tumor activity:
  - The observed disease control rate (DCR) for response-evaluable HCC patients was 50%, with a best overall response of stable disease. This DCR is in-line with the historical benchmark range for completed Phase 1 trials for TKIs and PD-1 monotherapies in HCC (29-65%).

The Company plans to present these data at a future scientific conference.

Other EC programs

The Company is advancing other ECs from the OMEGA platform through preclinical studies.

Significant Risks and Uncertainties Related to Macroeconomic Conditions

The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including, for example, severely diminished liquidity and credit availability, rising interest and inflation rates, crises involving banking and financial institutions, declines in consumer confidence, declines in economic growth, and uncertainty about economic stability. Unstable market and economic conditions and further disruption created by pandemics or international political unrest, war and terrorism may have serious adverse consequences on our business, financial condition and results of operations.

Components of our results of operations

Revenue

To date, we have not generated any revenue from product sales, and do not expect to generate any revenue from the sale of products for the foreseeable future. Our revenue to date has been generated through our collaboration agreements with PM (CF) Explorations, Inc., or PMCo, an affiliate of Flagship Pioneering (“Flagship”), as well as with Novo Nordisk A/S ("Novo Nordisk") and Pioneering Medicines 08, Inc., an affiliate of Flagship. Under these collaboration agreements, we are entitled to receive reimbursement for the costs associated with our research activities performed. For the collaboration with Novo Nordisk, we also received an upfront nonrefundable payment.

Operating expenses

Research and development expenses

Research and development expenses consist primarily of costs incurred in performing research and development activities, which include:

- personnel-related expenses, including salaries, bonuses, benefits, and stock-based compensation for employees engaged in research and development functions;
- expenses incurred in connection with the discovery, preclinical development, and clinical development of our research programs, including under agreements with third parties, such as consultants, contractors, CROs and CDMOs that manufacture material for use in our discovery, preclinical development, and clinical development;
- laboratory supplies and research materials;
- costs of licensing technology; and
- facilities, depreciation, and other expenses which include direct and allocated expenses.

We expense research and development costs as incurred. Costs for research and development activities are recognized based on an evaluation of the progress to completion of specific tasks. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our unaudited financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and expensed as the related goods are delivered or the services are performed.

We do not allocate costs associated with our discovery efforts, laboratory supplies and facilities, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and the OMEGA platform. We use internal resources primarily to conduct our research and discovery activities as well as for managing our preclinical development, process development, manufacturing and clinical development activities. These employees work across multiple programs and our technology platform and, therefore, we do not track these costs by program.

We also include in research and development expenses certain related party expenses for general consulting, as well as facility costs and sublease income with Flagship affiliates.

We expect that our research and development expenses will remain consistent based on our strategic re-prioritization of our clinical and pre-clinical programs and platform efforts.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs such as bonuses and benefits, including stock-based compensation, for personnel in our executive, finance, legal, human resources, corporate business development, and administrative functions. General and administrative expenses also include professional fees for legal, patent, accounting, information technology, auditing, tax, consulting services, insurance and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We also include in general and administrative expenses certain related party expenses related to payments made to Flagship for general consulting, and software licenses incurred on our behalf. In addition, we include facility costs and sublease income with Flagship affiliates.

We expect that our general and administrative expenses will remain consistent as we continue to support our research and development and potential commercialization of our product candidates, and will continue to incur expenses required to operate as a public company.

Other income (expense), net

Interest income (expense), net

Interest expense primarily consists of interest payments, the amortization of the debt discount related to our loan and security agreement, and interest payments related to our lease financing. See Note 9 - *Leases* in the notes to the unaudited financial statements appearing elsewhere in this Quarterly Report for more detail on the lease financing arrangement. Interest income consists of interest earned from our marketable securities and money market accounts.

Other income (expense), net

Other income (expense), net primarily consists of foreign exchange gains and losses on invoices paid, as well as remeasurement gains and losses associated with changes in the fair value of the success fee obligation related to our loan and security agreement, as amended. Until settlement, fluctuations in the fair value of our success fee obligation are based on the remeasurement at each reporting period.

Results of operations

Comparison for the three months ended September 30, 2024 and 2023

The following table summarizes the results of our operations for the three months ended September 30, 2024 and 2023, together with the changes in those items in thousands of dollars and as a percentage.

	Three Months Ended September 30,		$ Increase / (Decrease)	% Change
	2024	2023		
Collaboration revenue	$ 2,612	$ 831	$ 1,781	214 %
Operating expenses:				
Research and development	12,807	16,506	(3,699)	(22)%
General and administrative	6,225	7,228	(1,003)	(14)%
Total operating expenses	19,032	23,734	(4,702)	(20)%
Loss from operations	(16,420)	(22,903)	(6,483)	(28)%
Other income (expense), net:				
Interest income, net	14	684	(670)	NM
Other expense, net	(38)	(29)	(9)	NM
Total other income (expense), net	(24)	655	(679)	NM
Net loss	$ (16,444)	$ (22,248)	(5,804)	

NM - Not meaningful

Revenue

Revenue for the three months ended September 30, 2024 of $2.6 million consisted of $2.3 million related to the collaboration agreement with Novo Nordisk, and $0.3 million related to the collaboration agreement with PMCo. Revenue for the three months ended September 30, 2023 of $0.8 million related to the reimbursement of research costs incurred in connection with the collaboration agreement with PMCo.

Research and development expenses

Research and development expenses decreased by $3.7 million to $12.8 million for the three months ended September 30, 2024, from $16.5 million for the three months ended September 30, 2023. The $3.7 million decrease was primarily driven by lower personnel-related expenses of $3.6 million, external research and manufacturing costs of $0.4 million, facilities expense of $0.4 million, and lab expenses of $0.3 million, partially offset by an increase in clinical development costs of $0.8 million and consulting and professional fees of $0.2 million.

General and administrative expenses

General and administrative expenses decreased by $1.0 million to $6.2 million for the three months ended September 30, 2024 from $7.2 million for the three months ended September 30, 2023. The $1.0 million decrease was primarily driven by lower personnel-related expenses of $0.7 million, and lower consulting and professional fees of $0.3 million.

Interest income, net

Interest income, net decreased by $0.7 million to an immaterial amount for the three months ended September 30, 2024, from $0.7 million for the three months ended September 30, 2023. The $0.7 million decrease in interest income, net was attributed to a decrease in interest income earned from marketable securities and money market accounts during the three months ended September 30, 2024 and an increase in interest expense due to the lease financing.

Other expense, net

Other expense, net was immaterial for each of the three months ended September 30, 2024 and 2023.

Comparison for the nine months ended September 30, 2024 and 2023

The following table summarizes the results of our operations for the nine months ended September 30, 2024 and 2023, together with the changes in those items in thousands of dollars and as a percentage.

	Nine Months Ended September 30,		$ Increase / (Decrease)	% Change
	2024	2023		
Collaboration revenue	$ 7,106	$ 2,105	$ 5,001	238 %
Operating expenses:				
Research and development	41,162	61,638	(20,476)	(33)%
General and administrative	19,395	20,029	(634)	(3)%
Total operating expenses	60,557	81,667	(21,110)	(26)%
Loss from operations	(53,451)	(79,562)	(26,111)	(33)%
Other income (expense), net:				
Interest income, net	644	2,323	(1,679)	NM
Other income (expense), net	(71)	25	(96)	NM
Total other income, net	573	2,348	(1,775)	NM
Net loss	$ (52,878)	$ (77,214)	(24,336)	

NM - Not meaningful

Revenue

Revenue for the nine months ended September 30, 2024 of $7.1 million consisted of $5.2 million related to the collaboration agreement with Novo Nordisk, and $1.9 million related to the collaboration agreement with PMCo. Revenue for the nine months ended September 30, 2023 of $2.1 million related to the reimbursement of research costs incurred in connection with the collaboration agreement with PMCo.

Research and development expenses

Research and development expenses decreased by $20.4 million to $41.2 million for the nine months ended September 30, 2024, from $61.6 million for the nine months ended September 30, 2023. The $20.4 million decrease was primarily driven by lower external research and manufacturing costs of $13.5 million, personnel-related expenses of $7.4 million, and lab expenses of $1.1 million, partially offset by an increase in facilities expense of $0.8 million, clinical development expense of $0.6 million, and consulting and professional fees of $0.2 million. The decrease in external research and manufacturing costs was primarily due to lower volume of activities associated with research and development programs compared to the prior year.

General and administrative expenses

General and administrative expenses decreased by $0.6 million to $19.4 million for the nine months ended September 30, 2024 from $20.0 million for the nine months ended September 30, 2023. The $0.6 million decrease was primarily driven by lower consulting and professional fees of $0.9 million, administrative expenses of $0.7 million, and personnel-related expenses of $0.6 million, partially offset by higher facilities expense of $1.6 million.

Interest income, net

Interest income, net decreased by $1.7 million to $0.6 million for the nine months ended September 30, 2024, from $2.3 million for the nine months ended September 30, 2023. The $1.7 million decrease in interest income, net was attributed to a decrease in interest income earned from marketable securities and money market accounts during the nine months ended September 30, 2024 and an increase in interest expense due to the lease financing.

Other income (expense), net

Other income (expense), net was an expense of $0.1 million for the nine months ended September 30, 2024 and income of less than $0.1 million for the nine months ended September 30, 2023. The prior year included a gain from the revaluation of the success fee obligation related to our loan and security agreement, as amended.

Liquidity and capital resources

Sources of liquidity

Since our inception, we have incurred significant operating losses. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we support our continued research activities and development of our programs and platform. We have not yet commercialized any products, and we do not expect to generate product revenue for several years, if at all. To date, we have funded our operations primarily with proceeds from sales of equity securities, including our IPO and registered direct offering, and borrowings under our loan and security agreement.

In August 2021, we completed our IPO pursuant to which we issued and sold 8,300,976 shares of our common stock, including 900,976 shares pursuant to the partial exercise of the underwriters' option to purchase additional shares, at a public offering price of $17.00 per share, for aggregate gross proceeds of $141.1 million. We received approximately $128.1 million in net proceeds after deducting underwriting discounts and commissions and other offering expenses payable by us. In February 2023, we completed a registered direct offering of common stock pursuant to which we issued and sold 6,920,415 shares of our common stock at a purchase price of $5.78 per share and secured approximately $39.7 million in net proceeds after deducting estimated offering expenses.

In August 2023, we entered into the Sales Agreement, with Jefferies as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $60.0 million in "at-the-market," or ATM, offerings under our Registration Statement on Form S-3 (File No. 333-268254) filed with the SEC on November 8, 2022, which was declared effective on November 18, 2022. Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a) of the Securities Act, including sales made directly through the Nasdaq Global Select Market or on any other existing trading market for our common stock or to or through a market maker. During the nine months ended September 30, 2024, we did not sell any shares of common stock under the Sales Agreement.

Cash flows

The following table summarizes our sources and uses of cash for each of the periods presented (in thousands):

	Nine Months Ended September 30,	
	2024	2023
Net cash used in operating activities	$ (38,492)	$ (74,420)
Net cash provided by investing activities	4,053	45,375
Net cash (used in) provided by financing activities	(3,627)	40,198
Net change in cash, cash equivalents, and restricted cash	$ (38,066)	$ 11,153

Operating activities

Net cash used in operating activities totaled $38.5 million for the nine months ended September 30, 2024 compared to $74.4 million for the nine months ended September 30, 2023. The $35.9 million decrease in operating cash outflows was primarily attributable to $24.3 million of lower net loss during the nine months ended September 30, 2024 and higher cash flows from changes in accounts receivable of $5.1 million, prepaid expenses and other current assets of $3.2 million, and accrued expenses and other current liabilities of $1.8 million.

Investing activities

Net cash provided by investing activities totaled $4.1 million for the nine months ended September 30, 2024 compared to $45.4 million for the nine months ended September 30, 2023. The decrease in cash provided by investing activities was primarily attributable to lower proceeds from maturities of marketable securities.

Financing activities

Net cash used in financing activities totaled $3.7 million for the nine months ended September 30, 2024 compared to net cash provided by financing activities of $40.2 million for the nine months ended September 30, 2023. Net cash used in financing activities for the nine months ended September 30, 2024 consisted primarily of cash used to repay debt and for lease financing. Net cash provided by financing activities for the nine months ended September 30, 2023 consisted primarily of the proceeds from our registered direct offering in February 2023, net of issuance costs.

Loan and security agreement

On March 9, 2018, we entered into a Loan Agreement with Banc of California (“BOC”, formerly known as Pacific Western Bank) to initially borrow $8.0 million, which was further amended on September 30, 2019 (the "First Amendment"), January 22, 2020 (the "Second Amendment"), December 30, 2020 (the “Third Amendment”), and December 20, 2021 (the "Fourth Amendment").

On September 22, 2023, we entered into another amendment to the Loan Agreement (the "Fifth Amendment"), in which BOC extended the maturity date of the loan to September 30, 2027, subject to further extension to September 30, 2028 upon receipt by us on or before December 31, 2024 of at least $50.0 million of cash proceeds from the sale of its equity securities and/or non-refundable upfront strategic partnership proceeds. Repayment of the loan began on September 30, 2023, with monthly principal payments of $0.3 million plus interest, along with a closing payment of $4.0 million on September 30, 2027 if the maturity date is not extended to September 30, 2028. Interest will continue to be determined at a floating annual rate equal to the greater of (i) 0.50% above the prime rate then in effect and (ii) 5.50%. We incurred $15 thousand of debt issuance costs, which was recorded as a direct reduction against the additional term loan and amortized over the life of the associated term loan as a component of interest expense using the effective interest method. We are required to pay a success fee of $0.1 million pursuant to the Fifth Amendment, in addition to the $0.2 million success fee obligation pursuant to the Fourth Amendment. The success fees are contingent on achieving specified liquidity events. We determined that the success fee obligation represented a freestanding financial instrument, and it was classified as a liability on our consolidated balance sheet and initially recorded at fair value, with changes in fair value for each reporting period recognized in other expense, net in the condensed consolidated statements of operations and comprehensive loss. The fair value of such obligation is remeasured at the end of each reporting period until the liability is settled.

In addition, pursuant to the Fifth Amendment, we agreed to maintain with BOC, at all times, a balance of at least $5.0 million of unrestricted cash, subject to termination upon our prepayment of outstanding loans in an aggregate amount of at least $5.0 million or if the principal balance of the loans is less than $10.0 million.

Borrowings under the Loan Agreement, as amended, are collateralized by substantially all of our personal property, other than our intellectual property. There are no financial covenants associated with the Loan Agreement, as amended; however, we are subject to certain affirmative and negative covenants to which we will remain subject until maturity.

Funding requirements

As of September 30, 2024, we had cash and cash equivalents of $30.4 million. We expect that our expenses will be consistent with our cost reductions through strategic re-prioritization of our clinical and pre-clinical programs and platform efforts. In addition, we will continue to incur additional costs associated with operating as a public company. The timing and amount of our operating and capital expenditures will depend largely on:

- the scope, progress, results, and costs of our preclinical studies, and clinical trials of OTX-2002 and any future clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for our current and future product candidates in regions where we choose to commercialize any products;
- the number of future product candidates and potential additional indications that we may pursue and their development requirements;
- the stability, scale, yield, and cost of our manufacturing process as we scale-up production and formulation of our product candidates for clinical trials, in preparation for regulatory approval and in preparation for commercialization, including our ability to build our own manufacturing facility;
- the costs of pre- and post-commercialization activities for any approved product, including the costs and timing of establishing product sales, marketing, distribution, and manufacturing capabilities;
- revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- the costs and timing of changes in pharmaceutical pricing and reimbursement infrastructure;
- the costs and timing of changes in the regulatory environment and enforcement rules;
- our ability to compete with other therapeutics in the indications we target;
- the effect of competing technological and market developments;
- the extent to which we enter into collaborations or licenses for products, product candidates, or technologies;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs of preparing, filing, and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims; and
- the costs of operating as a public company.

In order to ensure sufficient resources to advance our lead program and maximize near- and long-term value creation opportunities from our platform, we announced a strategic prioritization in March 2024. As part of this initiative, we streamlined the organization and optimized our research and development efforts and, as a result, we believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2025. However, we have based this estimate on assumptions that may prove to be incorrect, and we could utilize our available capital resources sooner than we expect. We have had recurring losses since inception and we expect to continue to generate operating losses and use cash in operations for the foreseeable future. We expect to finance our future cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. Volatility in capital markets and general economic conditions in the United States may be a significant obstacle to raising the required funds and, as a result, we may be unable to secure the necessary funding on acceptable terms. This raises substantial doubt about our ability to continue as a going concern.

Contractual obligations

There have been no material changes to our contractual obligations as of September 30, 2024 from those disclosed in our 2023 10-K.

Critical accounting policies and estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our unaudited financial statements, which have been prepared in accordance with accounting principles generally accepted in the U.S., or GAAP. The preparation of these unaudited financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses. On an ongoing basis, we evaluate these estimates and judgments, including those described below. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results and experiences may differ materially from these estimates.

Our critical accounting policies are described under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies and Estimates" in our 2023 10-K and the notes to the unaudited financial statements appearing elsewhere in this Quarterly Report. During the nine months ended September 30, 2024, there were no material changes to our critical accounting policies from those discussed in our 2023 10-K.

Recently Issued Accounting Pronouncements

We have reviewed all recently issued accounting pronouncements and have determined that, other than as disclosed in Note 2 - *Summary of Significant Accounting Policies* in the notes to the audited financial statements included in our 2023 10-K and the notes to the unaudited financial statements appearing elsewhere in this Quarterly Report, such standards do not otherwise apply to our current operations.

Emerging growth company and smaller reporting company status

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As a result, we may take advantage of specified reduced disclosure and other reporting requirements that are otherwise applicable generally to public companies. In particular, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we may adopt the new or revised standard at the time private companies adopt the new or revised standard and may do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company.

We are also a "smaller reporting company" as defined under the Securities Act and Exchange Act. We may continue to be a smaller reporting company so long as either (i) the market value of shares of our common stock held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of shares of our common stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and have reduced disclosure obligations regarding executive compensation, and, similar to emerging growth companies, if we are a smaller reporting company under the requirements of (ii) above, we would not be required to obtain an attestation report on internal control over financial reporting issued by our independent registered public accounting firm.

Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company as defined in Rule 12b-2 of the Exchange Act and are not required to provide the information otherwise required under this Item 3.

Item 4. Controls and Procedures.

Limitations on effectiveness of controls and procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of disclosure controls and procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on the evaluation, our principal executive officer and principal financial officer concluded that, as of September 30, 2024, our disclosure controls and procedures as of such date were effective at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended September 30, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II—OTHER INFORMATION

Item 1. Legal Proceedings.

On June 11, 2024, a shareholder derivative suit captioned Joel Newman v. Flagship Pioneering, Inc., et al., was filed in the Court of Chancery of the State of Delaware (the "Complaint"), alleging breaches of fiduciary duty and unjust enrichment in connection with the Company's decision to enter into a Research Collaboration Agreement with Novo Nordisk A/S ("Novo Nordisk") and Pioneering Medicines 08, Inc. The Complaint names the Company as nominal defendant, and names certain of the Company's officers and directors, among others, as defendants. The Complaint seeks damages, rescissory relief, attorneys' fees and costs, and any other and further relief the court deems just and proper. The defendants filed a motion to dismiss on September 10, 2024. Thereafter, plaintiff gave notice that he intends to file an amended complaint, which is due by December 11, 2024.

Item 1A. Risk Factors.

You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Quarterly Report, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in evaluating our company. If any of the events or developments described below were to occur, our business, prospects, operating results and financial condition could suffer materially, and the trading price of our common stock could decline. The risks and uncertainties described below are not the only ones we face.

Risks Related to Our Financial Condition and Capital Requirements

We have a limited operating history and no history of successfully developing or commercializing any approved product candidates, which may make it difficult to evaluate the success of our business to date and to assess the prospects for our future viability.

We are a clinical-stage biopharmaceutical company. Our operations to date have been limited to financing and staffing our company, developing our technology and identifying and developing our product candidates. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by biopharmaceutical companies in their early stages of operations. We have not yet demonstrated an ability to conduct or complete any clinical trials, obtain marketing approval, manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions 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, obtaining marketing approval for, and commercializing product candidates. In addition, we may encounter unforeseen expenses, difficulties, complications, delays, and other obstacles.

As we continue to build our business, we expect our financial condition and operating results 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 particular quarterly or annual period as indications of future operating performance.

We have incurred significant losses since inception and expect to incur significant additional losses for the foreseeable future.

We have incurred significant net losses since our inception, including net losses of $97.4 million and $102.7 million for the years ended December 31, 2023 and 2022, respectively. As of September 30, 2024, we had an accumulated deficit of $387.5 million. In addition, we have not commercialized any products and have never generated any revenue from product sales. We have devoted almost all of our financial resources to research and development, including our preclinical development activities and preparing for and conducting clinical trials of our product candidates.

We expect to continue to incur significant additional net losses for the foreseeable future as we seek to advance product candidates through clinical development, continue preclinical development, expand our research and development activities, develop new product candidates, complete preclinical studies and clinical trials, seek regulatory approval and, if we receive regulatory approval, commercialize our products. In order to obtain FDA approval to market any product candidate in the United States, we must submit to the FDA a Biologics License Application, or BLA, demonstrating to the FDA's satisfaction that the product candidate is safe and effective for its intended use(s). Foreign regulatory authorities impose similar requirements. This demonstration requires significant research and extensive data from animal tests, which are referred to as nonclinical or preclinical studies, as well as human tests, which are referred to as clinical trials. Furthermore, the costs of advancing product candidates into each succeeding clinical phase tend to

increase substantially over time. The total costs to advance any of our product candidates to marketing approval in even a single jurisdiction would be substantial and difficult to accurately predict. Because of the numerous risks and uncertainties associated with the development of drug products, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to begin generating revenue from the commercialization of products or achieve or maintain profitability. Our expenses will also increase substantially if or as we:

- continue our research and development efforts and submit INDs, or similar foreign applications, for our product candidates;
- initiate and conduct clinical trials of our product candidates;
- continue to engineer and develop additional product candidates;
- continue to develop the OMEGA platform;
- seek regulatory and marketing approvals for product candidates that successfully complete clinical trials, if any;
- establish manufacturing and supply chain capacity sufficient to provide clinical and, if applicable, commercial quantities of product candidates, including potentially building our own manufacturing facility;
- establish a sales, marketing, internal systems and distribution infrastructure to commercialize any products for which we may obtain regulatory approval, if any, in geographies in which we plan to commercialize our products ourselves;
- maintain, expand, protect and enforce our intellectual property estate;
- hire additional staff, including clinical, scientific, technical, regulatory, operational, financial, commercial, and support personnel, to execute our business plan and support our product development and potential future commercialization efforts;
- enter into collaborations or licenses for new technologies;
- make royalty, milestone, or other payments under our current and any future in-license agreements;
- incur additional legal, accounting, and other expenses in operating our business; and
- continue to operate as a public company.

The amount of future losses and when, if ever, we will achieve profitability are uncertain. We have no commercial-stage products, will not generate revenues from the commercial sale of products until we have successfully developed one or more product candidates, and might never generate revenues from the sale of products. We expect to continue to incur operating losses and negative cash flows for the foreseeable future. These operating losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital.

We require substantial additional financing, which may not be available on acceptable terms, or at all. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce, or terminate our product development.

Our operations have incurred substantial expenses since inception. We expect to continue to incur substantial expenses to continue the preclinical development and to initiate and conduct the clinical development of our product candidates, and to continue to identify new product candidates.

We continue to need additional capital beyond the proceeds of our IPO and February 2023 registered direct offering to fund our planned preclinical development and clinical trials, and to develop new product candidates, which we may raise through equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. Additional sources of financing might not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we might be unable to initiate or complete clinical trials, or seek regulatory approvals, of any of our product candidates from the FDA, or any foreign regulatory authorities, and could be forced to discontinue product development. In addition, attempting to secure additional financing may divert the time and attention of our management from day-to-day activities and harm our development efforts.

Our existing cash and cash equivalents as of September 30, 2024 will not be sufficient to fund all of our efforts that we plan to undertake. In order to ensure sufficient resources to advance our lead program and maximize near- and long-term value creation opportunities from our platform, we announced a strategic prioritization in March 2024. As part of this initiative, we streamlined the organization and optimized our research and development efforts and, as a result, we believe that our cash and cash equivalents as of September 30, 2024 will be sufficient to fund our operating expenses and

capital expenditure requirements into the second quarter of 2025. This estimate is based on assumptions that may prove to be incorrect, and we could use our available capital resources sooner than we currently expect. In addition, as noted below, we have identified conditions and events about our ability to continue as a going concern. We will require significant additional funds in order to launch and commercialize our current and any future product candidates. In addition, other unanticipated costs may arise in the course of our development efforts. Because most of our product candidates are in preclinical development and we have not conducted any clinical trials, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. In addition, we maintain the majority of our cash and cash equivalents in accounts with major financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position.

Our future capital requirements depend on many factors, including:

- the scope, progress, results, and costs of our preclinical studies and clinical trials of OTX-2002 and any future clinical trials;
- the timing of, and the costs involved in, obtaining marketing approvals for our current and future product candidates in regions where we choose to commercialize any products;
- the number of future product candidates and potential additional indications that we may pursue and their development requirements;
- the stability, scale, yield, and cost of our manufacturing process as we scale-up production and formulation of our product candidates for clinical trials, in preparation for regulatory approval and in preparation for commercialization, including if we pursue plans to build our own manufacturing facility;
- the costs of pre- and post-commercialization activities for any approved product, including the costs and timing of establishing product sales, marketing, distribution, and manufacturing capabilities;
- revenue, if any, received from commercial sales of our products, should any of our product candidates receive marketing approval;
- the costs and timing of changes in pharmaceutical pricing and reimbursement infrastructure;
- the costs and timing of changes in the regulatory environment and enforcement rules;
- our ability to compete with other therapeutics in the indications we target;
- the effect of competing technological and market developments;
- the extent to which we enter into collaborations or licenses for products, product candidates, or technologies;
- our headcount growth and associated costs as we expand our research and development capabilities and establish a commercial infrastructure;
- the costs of preparing, filing, and prosecuting patent applications and maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property-related claims; and
- the costs of operating as a public company.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts, on terms acceptable to us, or on a timely basis, we may have to significantly delay, scale back, or discontinue the development or commercialization of our product candidates or other research and development initiatives.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidate, or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common stock to decline.

Our recurring losses from operations raise substantial doubt regarding our ability to continue as a going concern.

We have incurred significant losses since our inception and have never generated revenue or profit from product sales, and it is possible we will never generate revenue or profit from product sales. As of September 30, 2024, we had cash and cash equivalents of $30.4 million. In order to ensure sufficient resources to advance our lead program and maximize near- and long-term value creation opportunities from our platform, we announced a strategic prioritization in March 2024. As part of this initiative, we streamlined the organization and optimized our research and development efforts and, as a result, based on our current operating plans, we believe we will have sufficient funds to meet our obligations into the second quarter of 2025. However, we will need to raise additional capital to fund our future operations and remain as a going concern. There can be no assurance that we will be able to obtain additional funding, including through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources on acceptable terms, if at all. To the extent that we raise additional capital through future equity offerings, the ownership interest of common stockholders will be diluted, which dilution may be significant. We cannot guarantee that we will be able to obtain any or sufficient additional funding or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that we are unable to obtain any or sufficient additional funding, there can be no assurance that we will be able to continue as a going concern, and we will be forced to delay, reduce or discontinue our product development programs or consider other various strategic alternatives.

Moreover, these factors raise substantial doubt about our ability to continue as a going concern. Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock, and it may be more difficult for us to obtain financing. If existing or potential collaborators decline to do business with us or potential investors decline to participate in any future financings due to such concerns, our ability to increase our cash position may be limited. The perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

We have prepared our condensed consolidated financial statements on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. Our condensed consolidated financial statements included in this Quarterly Report do not include any adjustments to reflect the possible inability of the Company to continue as a going concern within one year after the issuance of such financial statements. If we are unable to continue as a going concern, you could lose all or part of your investment in our Company.

Raising additional capital may cause additional dilution to our stockholders, restrict our operations, require us to relinquish rights to our technologies or product candidates, and could cause our share price to fall.

Until such time, if ever, as we can generate substantial revenue from product sales, we may finance our cash needs through a combination of equity offerings, debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or other sources. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our operations, our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends, redeeming our stock, making certain investments, and engaging in certain merger, consolidation, or asset sale transactions, among other restrictions. If we raise additional funds through collaborations, strategic alliances, or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams, or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce, or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our existing and any future indebtedness could adversely affect our ability to operate our business.

As of September 30, 2024, we had $15.7 million of outstanding borrowings under an amended loan and security agreement, the Loan Agreement, with Banc of California (formerly known as Pacific Western Bank), or BOC. The maturity date of the Loan Agreement is September 30, 2027, subject to further extension to September 30, 2028. Repayment of the loan began on September 30, 2023, with monthly principal payments of $0.3 million plus interest, along with a closing payment of $4.0 million on September 30, 2027 if the maturity date is not extended to September 30, 2028. The outstanding balance under the Loan Agreement bears interest at a floating annual rate equal to the greater of (i) 0.50% above the prime rate then in effect and (ii) 5.50%, due monthly starting the first month after December 20, 2021. Our outstanding indebtedness, including any additional indebtedness beyond our borrowings from BOC, combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a portion of our cash resources to the payment of interest and principal, reducing money available to fund working capital, capital expenditures, product candidate development and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- subjecting us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

We intend to satisfy our current and future debt service obligations with our then existing cash and cash equivalents. However, we may not have sufficient funds, and may be unable to arrange for additional financing, to pay the amounts due under the Loan Agreement or any other debt instruments. Failure to make payments or comply with other covenants under the Loan Agreement or such other debt instruments could result in an event of default and acceleration of amounts due. For example, the affirmative covenants under our Loan Agreement include, among others, covenants requiring us (and us to cause our subsidiaries) to maintain our legal existence and governmental approvals, deliver certain financial reports and notifications, maintain proper books of record and account, timely file and pay tax returns, maintain inventory and insurance coverage, and maintain cash with BOC (subject to exceptions) and in accounts subject to control agreements (subject to exceptions). Under the Loan Agreement, the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, assets or condition is an event of default. If an event of default occurs and BOC accelerates the amounts due, we may not be able to make accelerated payments and the lender could seek to enforce security interests in the collateral securing such indebtedness. In addition, the covenants under the Loan Agreement, the pledge of our assets as collateral and the negative pledge with respect to our intellectual property could limit our ability to obtain additional debt financing.

We have not generated any product revenue and may never be profitable.

Our ability to become profitable depends upon our ability to generate product revenue. To date, we have not generated any product revenue and do not expect to generate significant product revenue unless or until we successfully complete clinical development and obtain regulatory approval of, and then successfully commercialize, our product candidates. Most of our product candidates are in the preclinical stages of development and will require additional preclinical studies and clinical development, regulatory review and approval, a secure manufacturing supply, established sales capabilities for commercialization, substantial investment and sufficient funds, and significant marketing efforts before we can generate any revenue from product sales. Our ability to generate product revenue depends on a number of factors, including:

- our ability to complete IND-enabling or other clinical trial-enabling studies and successfully submit INDs or comparable applications to allow us to initiate clinical trials of our product candidates;
- timely initiation and completion of any clinical trials of our product candidates, which may be significantly slower or more costly than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- whether we are required by the FDA or similar foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates;
- our ability to demonstrate to the satisfaction of the FDA or similar foreign regulatory authorities the safety and efficacy of our product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates, if any;
- the timely receipt of necessary marketing approvals from the FDA or similar foreign regulatory authorities;
- the willingness of physicians, operators of clinics, and patients to utilize or adopt epigenetic therapeutics;
- our ability and the ability of third parties with whom we contract to manufacture adequate clinical and commercial supplies of our product candidates or any future product candidates, remain in good standing with regulatory authorities, and develop, validate and maintain commercially viable manufacturing processes that

are compliant with current good manufacturing practices, or cGMP, or similar regulatory requirements outside the United States;

- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates, whether alone or in collaboration with others; and
- our ability to establish, maintain, protect, and enforce intellectual property rights in and to our product candidates.

Many of the factors listed above are beyond our control, and could cause us to experience significant delays or prevent us from obtaining regulatory approvals or commercialize our product candidates. Even if we are able to commercialize our product candidates, we may not achieve profitability soon after generating product sales, if ever. If we are unable to generate sufficient revenue through the sale of our product candidates, we may be unable to continue operations without continued funding.

Risks Related to the Discovery, Development, Preclinical and Clinical Testing, and Regulatory Approval of Our Product Candidates

Our product candidates are based on a novel technology, which makes it difficult to predict the time and cost of preclinical and clinical development and of subsequently obtaining regulatory approval, if at all.

Our success depends on the OMEGA platform technology which is a novel technology. As such, it is difficult to accurately predict the preclinical and clinical developmental challenges we may incur for our programs and product candidates as they proceed through product discovery or identification, preclinical studies, and clinical trials. In addition, because we have only recently commenced clinical trials of our pipeline product candidates, we have not yet been able to assess the safety or efficacy of our technology in humans and there may be short-term or long-term effects from treatment with any product candidates that we develop that we cannot predict at this time. Also, animal models may not exist for some of the diseases we choose to pursue in our programs. Given the novelty of our technology platform, there can be no assurance as to the length of preclinical work, clinical development, the number of patients that FDA or comparable foreign regulatory authority may require to be enrolled in clinical trials to establish the safety and efficacy, purity and potency of our product candidates, or that the data generated in these clinical trials will be acceptable to the FDA or comparable foreign regulatory authorities to support marketing approvals. The FDA and comparable regulatory authorities may take longer than usual to come to a decision on any biologics license application, or BLA, or foreign marketing application, that we submit and may ultimately determine that there is not adequate data, information, or experience with our product candidate to support approval. The FDA or comparable foreign regulatory authorities may also require that we conduct additional post-marketing studies or implement risk management programs, such as a risk evaluation and mitigation strategy, or REMS, or similar risk management measures, until more experience with our product candidates are obtained. Each of these factors could increase our expected development costs, and delay, prevent, or limit the scope of any commercialization of our product candidates. The validation process takes time and resources, may require independent third-party analyses, and may not be accepted or approved by the FDA and comparable foreign regulatory authorities. We cannot be certain that our approach will lead to the development of approvable or marketable products, alone, or in combination with other therapies.

Moreover, even if we obtain data from our planned clinical trials, because the OMEGA platform technology applied in our programs is novel and has not been externally verified, our data may be difficult to replicate and/or subject to misinterpretation by us or others. Epigenomic controllers present a new class of medicines and have not been evaluated in clinical trials or received regulatory approval. As a result, we may need to develop new evaluation methods or metrics for clinical data, which may make it more difficult to analyze data, or it may take more time or be more costly for us to develop our ECs than other therapeutics for the same indications. As a result of these factors, it is difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of the OMEGA platform technology, or any similar or competitive epigenetic technologies, will result in the identification, development, and regulatory approval of any products. There can be no assurance that any development challenges we experience in the future related to the OMEGA platform technology or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty, and intended use as well as market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities and approaches. Further, as we are developing novel treatments, there is heightened risk

that the FDA or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. To date, few gene therapy products have been approved by the FDA and comparable foreign regulatory authorities, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union, or EU, or other jurisdictions. Further, approvals by one regulatory authority may not be indicative of what other regulatory authorities may require for approval.

Regulatory requirements governing programmable epigenetic medicines have evolved and may continue to change in the future. For example, the FDA established the Office of Tissues and Advanced Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In addition to FDA oversight and oversight by IRBs, under guidelines promulgated by the National Institutes of Health, or NIH, gene therapy clinical trials are also subject to review and oversight by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. Before a clinical study can begin at any institution, that institution's IRB, and its IBC assesses the safety of the research and identifies any potential risk to public health or the environment. While the NIH guidelines are not mandatory unless the research in question is being conducted at or sponsored by institutions receiving NIH funding of recombinant or synthetic nucleic acid molecule research, many companies and other institutions not otherwise subject to the NIH Guidelines voluntarily follow them. Moreover, serious adverse events or developments in clinical trials of gene therapy product candidates conducted by others may cause the FDA or other regulatory bodies to initiate a clinical hold on our clinical trials or otherwise change the requirements for approval of any of our product candidates. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. These and other regulatory review agencies, committees, and advisory groups and the requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates, or lead to significant post-approval limitations or restrictions. Similar requirements apply in the EU. The European Medicines Agency, or the EMA, has a Committee for Advanced Therapies, or CAT, which is responsible for assessing the quality, safety and efficacy of advanced therapy medicinal products, or ATMP(s). ATMPs include gene therapy medicines, somatic-cell therapy medicines and tissue-engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for ATMP candidate that is submitted to the EMA. In the EU, the development and evaluation of an ATMP must be considered in the context of the relevant EU guidelines. The EMA may issue new guidelines concerning the development and marketing authorization for gene therapy medicinal products and require that we comply with these new guidelines. Similarly complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape.

Changes in applicable regulatory guidelines may lengthen the regulatory review process, require us to perform additional studies or trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates, or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with regulatory authorities and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of such product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delays as a result of an increased or lengthier regulatory approval process or further restrictions on the development of our product candidates can be costly and could negatively impact our ability to complete clinical trials and commercialize our current and future product candidates in a timely manner, if at all.

No epigenomic controller medicines have been approved in this potentially new class of medicines, and may never be approved as a result of efforts by others or us. mRNA drug development has substantial development and regulatory risks due to the novel and unprecedented nature of this new category of medicines.

As a potential new category of medicines, no epigenomic controller medicines have been approved to date by the FDA or other regulatory authority. Successful discovery and development of epigenomic controller medicines by either us or our strategic collaborators is highly uncertain and depends on numerous factors, many of which are beyond our or their control. We have made and will continue to make a series of business decisions and take calculated risks to advance our development efforts and pipeline, including those related to mRNA technology, delivery technology, and manufacturing processes which may be shown to be incorrect based on further work by us, our strategic collaborators, or others.

Our medicines that appear promising in the early phases of development may fail to advance, experience delays in preclinical stages or the clinic, experience clinical holds, or fail to reach the market for many reasons, including:

- discovery efforts at identifying potential epigenomic controller medicines may not be successful;

- nonclinical or preclinical study results may show potential epigenomic controller medicines to be less effective than desired or to have harmful or problematic side effects;
- clinical trial results may show the epigenomic controller medicines to be less effective than expected (e.g., a clinical trial could fail to meet one or more endpoints) or to have unacceptable side effects or toxicities;
- adverse effects in any one of our preclinical studies or clinical trials or adverse effects relating to our mRNA, or lipid nanoparticles, or LNPs, may lead to delays in or termination of one or more of our programs; and
- the insufficient ability of our translational models to reduce risk or predict outcomes in humans, particularly given that each component of our investigational medicines and development candidates, may have a dependent or independent effect on safety, tolerability, and efficacy, which may, among other things, be species-dependent.

Our investigational medicines are currently formulated and administered in an LNP. These LNPs may cause systemic side effects related to the components of the LNP and some may have not yet been tested in humans. A recognized limitation of LNPs is the potential for inflammatory reactions upon single and repeat administration that can impact tolerability and therapeutic index. Our licensed and internally developed, proprietary LNP systems are therefore designed to be highly tolerated and minimize LNP vehicle-related toxicities with repeat administration in vivo. While we continue to optimize our LNPs, there can be no assurance that our LNPs will not have undesired effects. Certain aspects of our investigational medicines may induce immune reactions from either the mRNA or the lipid as well as adverse reactions within biological pathways or due to degradation of the mRNA or the LNP, any of which could lead to significant adverse events in one or more of our preclinical or clinical studies. Our LNPs could contribute, in whole or in part, to one or more of the following: immune reactions, infusion reactions, complement reactions, opsonation reactions, antibody reactions including IgA, IgM, IgE or IgG or some combination thereof, or reactions to the polyethylene glycol, or PEG, from some lipids or PEG otherwise associated with the LNP. Many of these types of side effects have broadly been observed for LNPs. There may be resulting uncertainty as to the underlying cause of any such adverse event, which would make it difficult to accurately predict side effects in future clinical trials and would result in significant delays in our programs.

Preclinical development is uncertain, especially for a new class of medicines such as epigenomic controllers, and therefore our preclinical programs or development candidates may be delayed, terminated, or may never advance into the clinic, any of which may a have a material adverse impact on our platform or our business.

Most of our programs are in preclinical development. Before we can initiate clinical trials for a development candidate, we must complete extensive preclinical studies, including IND-enabling good laboratory practices, or GLP, and equivalent requirements outside the United States, toxicology testing. Preclinical development is uncertain, including due to variability in the disease models used. We may not identify development candidates with the treatment activity or safety characteristics required to advance them into further preclinical studies or results from preclinical studies of initially promising development candidates may not support further testing. We must also complete extensive work on Chemistry, Manufacturing, and Controls, or CMC, activities (including yield, purity and stability data) to be included in any IND or similar foreign filing. CMC activities for a new class of medicines such as epigenomic controllers require extensive manufacturing processes and analytical development, which is uncertain and lengthy. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept the results of our preclinical testing or our proposed clinical programs or if the outcome of our preclinical testing, studies, and CMC activities will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Clinical development of OTX-2002 may be delayed or terminated, and we may never obtain regulatory approval of OTX-2002, which may have a material adverse impact on our platform or our business. Furthermore, clinical development requires substantial capital investment, which we may not be able to support. We may incur unforeseen costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of OTX-2002 and our other product candidates.

Before obtaining marketing approval from the FDA or other comparable foreign regulatory authorities for the sale of our product candidates, we must complete preclinical development and extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, time-consuming, and subject to uncertainty. A failure of one or more clinical trials can occur at any stage of the process, and the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates

performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

In July 2022, we announced clearance of our IND application from the FDA to initiate a Phase 1/2, first-in-human, clinical trial of OTX-2002 for the treatment of HCC, which has launched under the MYCHELANGELO clinical program. We have not initiated or completed any other clinical trials for any of our product candidates. We cannot guarantee that any of our clinical trials will be initiated or conducted as planned or completed on schedule, if at all. We also cannot be sure that submission of any future IND or similar application will result in the FDA or other regulatory authority, as applicable, allowing future clinical trials to begin in a timely manner, if at all. Moreover, even if these trials begin, issues may arise that could cause regulatory authorities to suspend or terminate such clinical trials. A failure of one or more clinical trials can occur at any stage of testing, and our clinical trials may not be successful. Events that may prevent successful or timely initiation or completion of clinical trials include:

- inability to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to support the initiation or continuation of clinical trials;
- delays in reaching a consensus with regulatory authorities on trial design or implementation of the clinical trials;
- delays or failure in obtaining regulatory authorization to commence a trial;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among CROs and clinical trial sites;
- delays in identifying, recruiting, and training suitable clinical investigators;
- delays in obtaining required institutional review board, or IRB, or ethics committee approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our clinical trials;
- delays in manufacturing, testing, releasing, or importing/exporting sufficient stable quantities of our product candidates for use in clinical trials or the inability to do any of the foregoing;
- insufficient or inadequate supply or quality of product candidates or other materials necessary for use in clinical trials, or delays in sufficiently developing, characterizing, or controlling a manufacturing process suitable for clinical trials;
- imposition of a temporary or permanent clinical hold by regulatory authorities for a number of reasons, including after review of an IND or amendment or equivalent foreign application or amendment; as a result of a new safety finding that presents unreasonable risk to clinical trial participants; or a negative finding from an inspection of our clinical trial operations or study sites;
- delays in recruiting, screening, and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- difficulty collaborating with patient groups and investigators;
- failure by our CROs, clinical sites, other third parties or us to adhere to clinical trial protocols, to perform in accordance with the FDA's or any other regulatory authority's good clinical practice requirements, or GCPs, or similar applicable regulatory guidelines in other countries;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits, or occurrence of adverse events in trial of the same class of agents conducted by other companies;
- changes to the clinical trial protocols;
- clinical sites dropping out of a trial;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- the cost of clinical trials of our product candidates being greater than we anticipate;

- clinical trials of our product candidates producing negative or inconclusive results, which may result in our deciding, or regulators requiring us, to conduct additional clinical trials or abandon development of such product candidates;
- transfer of manufacturing processes to larger-scale facilities operated by a contract development and manufacturing organization, or CDMO, and delays or failure by our CDMOs or us to make any necessary changes to such manufacturing process; and
- third parties being unwilling or unable to satisfy their contractual obligations to us.

Clinical trials must be conducted in accordance with the legal requirements, regulations, or guidelines of the FDA and other applicable regulatory authorities and are subject to oversight by these governmental agencies and ethics committees or IRBs at the medical institutions where the clinical trials are conducted. We could also encounter delays if a clinical trial is suspended or terminated by us, by the data safety monitoring board, or DSMB, for such trial or by the FDA or any other regulatory authority, or if the IRBs of the institutions in which such trials are being conducted suspend or terminate the participation of their clinical investigators and sites subject to their review. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Delays in the completion of any clinical trial of our product candidates will increase our costs, slow down our product candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate product revenue. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Any delays to our clinical trials that occur as a result could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, which could significantly reduce the commercial viability of our product candidates. Any of these occurrences may harm our business, financial condition, results of operations, and prospects significantly.

In addition, the FDA's and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The EU Clinical Trials Regulation, or CTR, which was adopted in April 2014 and repeals the EU 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 in which the clinical trial takes place, 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 for multi-center trials. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state's decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical trial development may proceed. The CTR foresees a three-year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. Clinical trials for which an application was submitted (i) prior to January 31, 2022 under the Clinical Trials Directive, or (ii) between January 31, 2022 and January 31, 2023 and for which the sponsor has opted for the application of the Clinical Trials Directive remain governed by said Directive until January 31, 2025. After this date, all clinical trials (including those which are ongoing) will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans.

It is currently unclear to what extent the United Kingdom, or UK, will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law,

through secondary legislation). On January 17, 2022, the UK Medicines and Healthcare products Regulatory Agency, or MHRA launched an eight-week consultation on reframing the UK legislation for clinical trials with specific aims to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, and promote patient and public involvement in clinical trials. The MHRA published its consultation outcome on March 21, 2023 in which it confirmed that it would update the existing legislation. The resulting legislative changes, which are yet to be published, will ultimately determine the extent to which the UK regulations align with the (EU) CTR. A decision by the UK not to closely align its regulations with the new approach that has been adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries.

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 also be impacted.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, expensive, time-consuming, and inherently unpredictable. If we are ultimately unable to obtain regulatory approval for our product candidates, we will be unable to generate product revenue and our business will be seriously harmed.

We are not permitted to commercialize, market, promote, or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities impose similar requirements. The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate in the United States or any other jurisdiction, and it is possible that any product candidates we may seek to develop in the future will never obtain regulatory approval.

Prior to obtaining approval to commercialize a product candidate in the United States or elsewhere, we must demonstrate with substantial evidence from well-controlled trials, and to the satisfaction of the FDA, or other regulatory authorities, that such product candidates are safe and effective, pure, and potent for their intended uses. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA or other regulatory authorities. The FDA or other regulatory authorities may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program.

The FDA or any foreign regulatory authorities can delay, limit, or deny approval of our product candidates, or require us to conduct additional nonclinical or clinical testing or abandon a program for many reasons, including, but not limited to, the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design, implementation, or interpretation of results of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective, pure, and potent for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required for approval by the FDA or comparable foreign regulatory authorities;
- serious and unexpected product candidate-related side effects experienced by participants in our clinical trials or by individuals using products similar to our product candidates;
- we may be unable to demonstrate to the FDA or comparable foreign regulatory authorities that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be acceptable or sufficient to support the submission of a BLA or other submission, or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may disagree regarding the formulation, labeling, and/or the specifications of our product candidates;

- our clinical sites, investigators or other participants in our clinical trials may deviate from a trial protocol, fail to conduct the trial in accordance with regulatory requirements, or drop out of a trial;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes, test procedures and specifications, or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our or our collaborators' clinical data insufficient for approval.

Furthermore, FDA and foreign regulatory authorities may change their approval policies and new regulations may be enacted. For instance, the EU 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 European Commission's proposal for a revision of several legislative instruments related to medicinal products (potentially reducing the duration of regulatory exclusivity, 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. The proposals may be substantially revised before adoption, which is not anticipated before early 2025. The revisions may however have a significant impact on the pharmaceutical industry and our business in the long term.

This lengthy approval process, as well as the unpredictability of the results of clinical trials, may result in our failing to obtain regulatory approval to market any of our product candidates, which would seriously harm our business.

Even if we eventually complete clinical trials and obtain approval of a BLA or foreign marketing application for our product candidates, the FDA, or comparable foreign regulatory authorities may grant approval contingent on the performance of costly additional trials, including Phase 4 clinical trials, and/or the implementation of a REMS or similar risk management measures, which may be required to ensure the benefits of the drug outweigh its risks after approval. The FDA or comparable foreign regulatory authorities may also approve a product candidate for a more limited indication or patient population than we originally requested. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate, and would materially adversely impact our business and prospects.

Our product candidates may be associated with serious adverse events, undesirable side effects or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Adverse events or other undesirable side effects caused by our product candidates could cause us, any DSMB for a trial, or regulatory authorities to interrupt, delay, or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, results of operations, and prospects significantly.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. It is possible that as we test our product candidates in larger, longer, and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts, and other adverse events that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval.

If any serious adverse events occur during clinical development, clinical trials of any product candidates or products we develop could be suspended or terminated, and our business could be seriously harmed. Treatment-related side effects could also affect patient recruitment and the ability of enrolled patients to complete the trial or result in potential liability claims. Regulatory authorities could order us to cease further development of, or deny approval of any product candidates for any or all targeted indications. If we are required to delay, suspend, or terminate any clinical trial, the commercial prospects of such product candidates may be harmed, and our ability to generate product revenues from them or other product candidates that we develop may be delayed or eliminated.

Additionally, if one or more of our product candidates receives marketing approval and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may suspend, limit, or withdraw approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including “boxed” warnings, or issue safety alerts, Dear Healthcare Provider letters, press releases, or other communications containing warnings or other safety information about the product;
- we may be required to change the way the product is administered or conduct additional clinical trials or post-approval studies;
- we may be required to create a REMS or similar risk management measures which could include a medication guide outlining the risks of such side effects for distribution to patients;
- we may be subject to fines, injunctions, or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could seriously harm our business.

Our company has never commercialized a product candidate and may experience delays or unexpected difficulties in obtaining regulatory approval for our current and future product candidates.

We have never obtained regulatory approval for, or commercialized any product candidate. It is possible that the FDA may refuse to accept any or all of our planned BLAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any product candidates. If the FDA does not approve any of our planned BLAs, it may require that we conduct additional costly clinical trials, preclinical studies or CMC studies before it will reconsider our applications. Depending on the extent of these or any other FDA required studies, approval of any BLA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any failure or delay in obtaining regulatory approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any BLA or other application that we submit. Similar risks may exist in foreign jurisdictions. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in foreign jurisdictions.

If we encounter difficulties enrolling patients in any clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the trial until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the target disease population;
- the size of the patient population required for analysis of the trial’s primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians’ and patients’ perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;

- competing clinical trials for similar therapies or other new therapeutics not involving our product candidates and or related technologies;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the trials before trial completion; and
- other factors outside of our control, such as the COVID-19 pandemic.

In addition, our planned clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates or similar areas, and this competition will reduce the number and types of patients available to us because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of our ongoing and planned clinical trials, which could prevent completion or commencement of these trials and adversely affect our ability to advance the development of our product candidates.

Interim, "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations, and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line and preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the top-line or preliminary data we previously published. As a result, top-line and preliminary data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions, or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects, or financial condition.

We may not be successful in our efforts to identify and successfully develop additional product candidates.

Part of our strategy involves identifying novel product candidates. The OMEGA platform may fail to yield product candidates for clinical development for a number of reasons, including those discussed in these risk factors and also:

- we may not be able to assemble sufficient resources to acquire or discover additional product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete or less attractive;
- potential product candidates we develop may nevertheless be covered by third-parties' patent or other intellectual property or exclusive rights;

- potential product candidates may, on further study, be shown to have harmful side effects, toxicities, or other characteristics that indicate that they are unlikely to be products that will receive marketing approval or achieve market acceptance, if approved;
- potential product candidates may not be effective in treating their targeted diseases or symptoms;
- the market for a potential product candidate may change so that the continued development of that product candidate is no longer reasonable;
- a potential product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- the regulatory pathway for a potential product candidate is highly complex and difficult to navigate successfully or economically.

If we are unable to identify and successfully commercialize additional suitable product candidates, this would adversely impact our business strategy and our financial position.

We have received orphan drug designation from the FDA for OTX-2002 for the treatment of HCC, and we may seek orphan drug designation for additional product candidates in the future, but we may be unable to obtain such designations or maintain the benefits associated with orphan drug designation, including market exclusivity, which may cause our product revenue, if any, to be reduced.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs or biologics intended to treat relatively small patient populations as orphan drug products. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States.

In the United States, orphan drug designation entitles a party to financial incentives such as tax advantages and user fee waivers. Opportunities for grant funding toward clinical trial costs may also be available for clinical trials of drugs or biologics for rare diseases, regardless of whether the drugs or biologics are designated for the orphan use. In addition, if a drug or biologic with an orphan drug designation subsequently receives the first marketing approval for the disease or condition for which it has such designation, the product is entitled to a seven year period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same disease or condition for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the “same drug” and treat the same diseases or conditions as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

We have obtained orphan drug designation from the FDA for OTX-2002 for the treatment of HCC. We may seek orphan designation for certain of our future product candidates. However, we may be unsuccessful in obtaining orphan drug designation for these and may be unable to maintain the benefits associated with orphan drug designation. Even if we obtain orphan drug exclusivity for any of our product candidates, that exclusivity may not effectively protect those product candidates from competition because different drugs can be approved for the same condition, and orphan drug exclusivity does not prevent the FDA from approving the same or a different drug for another disease or condition. Even after an orphan drug is granted orphan exclusivity and approved, the FDA can subsequently approve a later application for the same drug for the same condition before the expiration of the seven-year exclusivity period if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan-drug-exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We have invested, and expect to continue to invest, in research and development efforts that further enhance the OMEGA platform. Such investments may affect our operating results, and, if the return on these investments is lower or develops more slowly than we expect, our revenue and operating results may suffer.

We use our technological capabilities for the discovery of new product candidates and, since our inception, we have invested, and expect to continue to invest, in research and development efforts that further enhance the OMEGA platform. These investments may involve significant time, risks, and uncertainties, including the risk that the expenses associated with these investments may affect our margins and operating results and that such investments may not

generate sufficient technological advantages relative to alternatives in the market, which would in turn, impact revenues to offset liabilities assumed and expenses associated with these new investments. The biotechnology industry changes rapidly as a result of technological and product developments, which may render our platform's ability to identify and develop product candidates less efficient than other technologies and platforms. We believe that we must continue to invest a significant amount of time and resources in the OMEGA platform to maintain and improve our competitive position. If we do not achieve the benefits anticipated from these investments, if the achievement of these benefits is delayed, or if our technology is not able to accelerate the process of drug discovery as quickly as we anticipate, our revenue and operating results may be adversely affected.

We must adapt to rapid and significant technological change and respond to introductions of new products and technologies by competitors to remain competitive.

In addition to using our platform for the discovery and development of our own product candidates, we collaborate with other biopharmaceutical and pharmaceutical companies in the discovery and development of our ECs. The technological landscape around artificial intelligence and precision drug design is characterized by significant enhancements and evolving industry standards. As a result, our and our collaborators' needs are rapidly evolving. If we do not appropriately innovate and invest in new technologies, our platform may become less competitive, and our collaborators could move to new technologies offered by our competitors, or engage in drug discovery themselves. We believe that because of the initial time investment required by many of our collaborators to reach a decision about whether to collaborate with us, it may be difficult to regain a commercial relationship with such collaborator should they enter into a partnership or collaboration agreement with a competitor. Without the timely introduction of new solutions and technological enhancements, our offerings will likely become less competitive over time, in which case our competitive position and operating results could suffer. Accordingly, we focus significant efforts and resources on the development and identification of new technologies and markets to further broaden and deepen our capabilities and expertise in drug discovery and development. For example, to the extent we fail to timely introduce new and innovative technologies or solutions, adequately predict our collaborators' needs or fail to obtain desired levels of market acceptance, our business may suffer and our operating results could be adversely affected.

The potential market opportunities for our product candidates may be smaller than we anticipated or may be limited to those patients who are ineligible for or have failed prior treatments, and our estimates of the prevalence of our target patient populations may be inaccurate.

Our current and future target patient populations are based on our beliefs and estimates regarding the incidence or prevalence of certain types of cancers that may be addressable by our product candidates, which is derived from a variety of sources, including scientific literature and surveys of clinics. Our projections may prove to be incorrect and the number of potential patients may turn out to be lower than expected. Even if we obtain significant market share for our product candidates, because the potential target populations could be small, we may never achieve profitability without obtaining regulatory approval for additional indications, including use of our product candidates for front-line and second-line therapy.

Cancer therapies are sometimes characterized by line of therapy (first-line, second-line, third-line, etc.), and the FDA often approves new therapies initially only for a particular line or lines of use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first-line therapy, usually chemotherapy, antibody drugs, tumor-targeted small molecules, hormone therapy, radiation therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second-line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third-line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect to initially seek approval of some of our product candidates as second- or third-line therapies for patients who have failed other approved treatments. Subsequently, for those product candidates that prove to be sufficiently beneficial, if any, we would expect to seek approval as a second-line therapy and potentially as a first-line therapy, but there is no guarantee that our drug candidates, even if approved for third-line therapy, would be approved for second-line or first-line therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for second-line or first-line therapy.

We may focus on potential product candidates that may prove to be unsuccessful and we may have to forego opportunities to develop other product candidates that may prove to be more successful.

We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful, or to license or purchase a marketed product that does not meet our financial expectations. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases that may later prove to have greater commercial potential, or relinquish valuable rights to such product candidates through collaboration, licensing, or other royalty

arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. If we are unable to identify and successfully commercialize additional suitable product candidates, this would adversely impact our business strategy and our financial position.

Furthermore, we have limited financial and personnel resources and are placing significant focus on the development of our lead product candidates, and as such, we may forgo or delay pursuit of opportunities with other future product candidates that later prove to have greater commercial potential. 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 research and development programs and other future product candidates for specific indications may not yield any commercially viable future product candidates. If we do not accurately evaluate the commercial potential or target market for a particular future product candidate, we may relinquish valuable rights to those future product candidates through collaboration, licensing, or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such future product candidates.

We may pursue Fast Track, breakthrough, and regenerative medicine advanced therapy designation by FDA. These designations may not actually lead to a faster development or regulatory review or approval process, and they do not assure FDA approval of any product candidates we may develop.

FDA's Fast Track, breakthrough, and regenerative medicine advanced therapy, or RMAT, programs are intended to expedite the development of certain qualifying products intended for the treatment of serious diseases and conditions. If a product candidate is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the product's potential to address an unmet medical need for this condition, the sponsor may be eligible for FDA Fast Track designation. A product candidate may be designated as a breakthrough therapy if it is intended to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A product candidate may receive RMAT designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening condition, and preliminary clinical evidence indicates that the product candidate has the potential to address an unmet medical need for such condition. While we may seek Fast Track, breakthrough, and/or RMAT designation, there is no guarantee that we will be successful in obtaining any such designation. Even if we do obtain such designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. A Fast Track, breakthrough, or RMAT designation does not ensure that the product candidate will receive marketing approval or that approval will be granted within any particular timeframe. In addition, the FDA may withdraw Fast Track, breakthrough, or RMAT designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track, breakthrough, and/or RMAT designation alone do not guarantee qualification for the FDA's priority review procedures.

Even if we obtain FDA approval of any of our product candidates, we may never obtain approval or commercialize such products outside of the United States, which would limit our ability to realize their full market potential.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties, and costs for us and may require additional preclinical studies or clinical trials which would be costly and time-consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. Satisfying these and other regulatory requirements is costly, time-consuming, uncertain, and subject to unanticipated delays. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. We do not have any product candidates approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, our ability to realize the full market potential of our products will be harmed.

Even if a current or 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.

If any current or future product candidate we develop receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors, and others in the medical community. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product

revenues and we may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our products, if approved, for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the ability to obtain sufficient third-party coverage and adequate reimbursement, including with respect to the use of the approved product as a combination therapy;
- adoption of a companion diagnostic and/or complementary diagnostic; and
- the prevalence and severity of any side effects.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain, or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and foreign regulatory authorities to review or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA's or foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's or foreign regulatory authorities' ability to perform routine functions. Average review times at the FDA and foreign regulatory authorities have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies, such as the EMA, following its relocation to Amsterdam and related reorganization (including staff changes), may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Separately, in response to the COVID-19 pandemic, the FDA postponed most inspections of domestic and foreign manufacturing facilities at various points. Even though the FDA has since resumed standard inspection operations of domestic facilities where feasible, the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates as it adapts to developments with COVID-19, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays. Regulatory authorities outside the U.S. have adopted similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities, which could have a material adverse effect on our business. If a prolonged government shutdown occurs, or if global health concerns continue to hinder or prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Our insurance policies are expensive and protect us only from some business risks, which leaves us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, property, auto, employment practices, workers' compensation, environmental liability, and directors' and officers' insurance.

Any additional product liability insurance coverage we acquire in the future may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If we obtain marketing approval for any of our product candidates, we intend to acquire insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business, including preventing or limiting the development and

commercialization of any product candidates we develop. Although our environment liability insurance provides certain coverage for claims attributable to the release of biological or hazardous materials, our property, casualty, and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Operating as a public company has and will make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our board of directors, our board committees or as executive officers. We do not know, however, if we will be able to maintain existing insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our cash and cash equivalents position and results of operations.

Risks Related to Healthcare Laws and Other Legal Compliance Matters

We will be subject to extensive and costly government regulation.

Our product candidates will be subject to extensive and rigorous domestic government regulation, including regulation by the FDA, the Centers for Medicare & Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice, state and local governments, and their respective equivalents outside of the United States. The FDA regulates the research, development, preclinical and clinical testing, manufacture, safety, effectiveness, record-keeping, reporting, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import, and export of pharmaceutical products. If our products are marketed abroad, they will also be subject to extensive regulation by foreign governments, whether or not they have obtained FDA approval for a given product and its uses. Such foreign regulation may be equally or more demanding than corresponding United States regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing, and selling our products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive, and uncertain. We must obtain and maintain regulatory authorization to conduct preclinical studies and clinical trials. We must obtain regulatory approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires the submission of extensive preclinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product's safety and efficacy, potency, and purity, for each intended use. The development and approval process takes many years, requires substantial resources, and may never lead to the approval of a product.

Even if we are able to obtain regulatory approval for a particular product, the approval may limit the indicated medical uses for the product, may otherwise limit our ability to promote, sell, and distribute the product, may require that we conduct costly post-marketing surveillance, and/or may require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, may require further regulatory review and approval. Once obtained, any approvals may be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue.

If we, our consultants, CDMOs, CROs, or other vendors, fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things, delays in the approval of applications or supplements to approved applications; refusal of a regulatory authority, including the FDA or other regulatory authorities, to review pending market approval applications or supplements to approved applications; warning letters; fines; import and/or export restrictions; product recalls or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawals of previously approved marketing applications or licenses; recommendations by the FDA or other regulatory authorities against governmental contracts; and/or criminal prosecutions.

Enacted and future healthcare legislation and policies may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and could adversely affect our business.

In the United States, the EU and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could prevent or delay marketing approval of our products in development, restrict or regulate post-approval activities involving any product candidates for which we obtain marketing approval, impact pricing and reimbursement and impact our ability to sell any such products profitably. In particular, there have been and continue to be a number of initiatives at the U.S. federal and

state levels that seek to reduce healthcare costs and improve the quality of healthcare. In addition, new regulations and interpretations of existing healthcare statutes and regulations are frequently adopted.

In March 2010, the Patient Protection and Affordable Care Act, or ACA, was enacted, which substantially changed the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA, those of greatest importance to the pharmaceutical and biotechnology industries include the following:

- an annual, non-deductible fee payable by any entity that manufactures or imports certain branded prescription drugs and biologic agents (other than those designated as orphan drugs), which is apportioned among these entities according to their market share in certain government healthcare programs;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of the Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Since its enactment, there have been judicial, Congressional and executive challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures will impact our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011 resulted in aggregate reductions of Medicare payments to providers, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect as of the date of this report through 2031, unless additional Congressional action is taken. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers, and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Additionally, the orphan drug tax credit was reduced as part of a broader tax reform. These new laws or any other similar laws introduced in the future may result in additional reductions in Medicare and other healthcare funding, which could negatively affect our customers and accordingly, our financial operations.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as outcomes-based reimbursement. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. 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 Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. On August 29, 2023, HHS announced the list of the first ten drugs that will be subject to price negotiations, although the Medicare drug price negotiation program is currently subject to legal challenges. For that and other reasons, it is currently unclear how the IRA will be effectuated. In addition, in response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Centers for Medicare and Medicaid Services (CMS) Innovation Center which will be evaluation on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates or put pressure on our product pricing.

In the EU, similar political, economic, and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU or member state level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of healthcare and the pricing and reimbursement of products in that context. EU member states are free to restrict the range of pharmaceutical products for which their national health insurance systems provide reimbursement, and to control the prices and reimbursement levels of pharmaceutical products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. EU member states may approve a specific price or level of reimbursement for the pharmaceutical product, or alternatively adopt a system of direct or indirect controls on the profitability of the company responsible for placing the pharmaceutical product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval in some EU member states, we may be required to conduct studies that compare the cost-effectiveness of our product candidates to other therapies that are considered the local standard of care. Other EU member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. Generally, the healthcare budgetary constraints in most EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict, or regulate post-approval activities, and affect our ability to commercialize our product candidates, if approved.

On December 13, 2021, Regulation No 2021/2282 on Health Technology Assessment, or HTA, amending Directive 2011/24/EU, was adopted. While the regulation entered into force in January 2022, it will only begin to apply from January 2025 onwards, with preparatory and implementation-related steps to take place in the interim. Once the regulation becomes applicable, it will have a phased implementation depending on the concerned products. This regulation intends to boost cooperation among EU member states in assessing health technologies, including new medicinal products, and providing the basis for cooperation at the EU level for joint clinical assessments in these areas. The regulation will permit EU member states to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU member states will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technology, and making decisions on pricing and reimbursement.

In markets outside of the United States and the EU, reimbursement and healthcare payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies.

In addition, in the United States, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA's regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative action in the United States, the EU, or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

If our product candidates obtain regulatory approval, we and they will be subject to ongoing regulatory review and significant post-market regulatory requirements and oversight.

If the FDA or other regulatory authorities approve any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, and record-keeping of our product candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submission of safety and other post-marketing information and reports, registration, as well as ongoing compliance with cGMPs and similar foreign requirements and GCPs for any clinical trials that we conduct post-approval. In addition, manufacturers of biological products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities to ensure compliance with cGMP regulations and similar foreign requirements. If we or a regulatory authority discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. In addition, any regulatory approvals that we may receive for our product candidates may contain significant limitations related to use restrictions for specified age groups, warnings, precautions, or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician training, and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries, and other risk minimization tools.

Failure to comply with applicable regulatory requirements, may subject us to administrative or judicially imposed sanctions, including:

- delays in reviewing or the rejection of product applications or supplements to approved applications;
- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- warning or untitled letters;
- civil or criminal penalties;
- injunctions;
- suspension or withdrawal of regulatory approvals;
- product seizures, detentions, or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- total or partial suspension of production; and
- imposition of restrictions on our operations, including costly new manufacturing requirements.

The occurrence of any such event may inhibit our ability to commercialize our product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

Moreover, the policies of the FDA and of other regulatory authorities may change, and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature, or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. Further, three decisions from the U.S. Supreme Court in July 2024 may lead to an increase in litigation against regulatory agencies that could create uncertainty and thus negatively impact our business. The first decision overturned established precedent that required courts to defer to regulatory agencies' interpretations of ambiguous statutory language. The second decision overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. The third decision extended the statute of limitations within which entities may challenge agency actions. These cases may result in increased litigation by industry against regulatory agencies and impact how such agencies choose to pursue enforcement and compliance actions. However, the specific, lasting effects of these decisions, which may vary within different judicial districts and circuits, is unknown. We also cannot predict the extent to which FDA and SEC regulations, policies, and decisions may become subject to increasing legal challenges, delays, and changes.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

The Hatch-Waxman Act in the United States provides for the opportunity to seek a patent term extension on one selected patent for each of our products, and the length of that patent term extension, if at all, is subject to review and approval by the U.S. Patent and Trademark Office, or the USPTO, and the FDA.

In the United States, the Hatch-Waxman Act permits one patent term extension of up to five years beyond the normal expiration of one patent per product, which if a method of treatment patent, is limited to the approved indication (or any additional indications approved during the period of extension). The length of the patent term extension is typically calculated as one half of the clinical trial period plus the entire period of time during the review of the BLA by the FDA, minus any time of delay by us during these periods. There is also a limit on the patent term extension to a term that is no greater than fourteen years from drug approval. Therefore, if we select and are granted a patent term extension on a recently filed and issued patent, we may not receive the full benefit of a possible patent term extension, if at all. We might also not be granted a patent term extension at all, because of, for example, failure to apply within the applicable period, failure to apply prior to the expiration of relevant patents or otherwise failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authorities in other countries, may not agree with our assessment of whether such extensions are available, may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate product revenue.

In 1997, as part of the Food & Drug Administration Modernization Act, or FDAMA, Congress enacted a law that provides incentives to drug manufacturers who conduct studies of drugs in children. The law, which provides six months of exclusivity in return for conducting pediatric studies, is referred to as the pediatric exclusivity provision. If clinical studies are carried out by us that comply with the FDAMA, we may receive an additional six-month term added to any regulatory data exclusivity period and our patent term extension period, if received, on our product. However, if we choose not to carry out pediatric studies that comply with the FDAMA, or are not accepted by the FDA for this purpose, we would not receive this additional six-month exclusivity extension to our data exclusivity or our patent term extension.

In the EU, supplementary protection certificates, or SPCs, are available to extend a patent term up to five years to compensate for patent term lost during regulatory review, and can be extended (if any is in effect at the time of approval) for an additional six months if data from clinical trials is obtained in accordance with an agreed-upon pediatric investigation plan. Although all EU member states must provide SPCs, SPCs must be applied for and granted on a country-by-country basis. This can lead to a substantial cost to apply for and receive these certificates, which may vary among countries or not be granted at all**.**

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations, and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell, and distribute our product candidates, if approved. Such laws include:

- the U.S. federal Anti-Kickback Statute, which makes it illegal for any person to knowingly and willfully solicit, offer, receive, pay, or provide any remuneration (including any kickback, bribe, or certain rebate), directly or

indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under U.S. federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- the U.S. federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the U.S. federal government, claims for payment or approval that are false, fictitious, or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease, or conceal an obligation to pay money to the U.S. federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;
- the federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program, unless an exception applies;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing, or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items, or services relating to healthcare matters. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the Federal Food, Drug and Cosmetic Act, or FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics, and medical devices;
- the U.S. Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics, and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous U.S. state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the U.S. federal government, or otherwise restrict payments that may be made to healthcare providers and other

potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws that require the registration of pharmaceutical sales representatives; and

- similar healthcare laws and regulations in the EU and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom are compensated in the form of stock or stock options for services provided to us and may be in the position to influence the ordering of or use of our product candidates, if approved, may not comply with current or future statutes, regulations, agency guidance, 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal, and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight, and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil, or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant 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.

We are subject to governmental regulation and other legal obligations, particularly related to privacy, data protection and information security. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, and financial condition.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and regulations promulgated thereunder, or collectively, HIPAA, imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. We do not believe that we are currently classified as a covered entity or business associate under HIPAA and thus are not directly subject to its requirements or penalties. However, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered healthcare provider or research institution that has not satisfied HIPAA's requirements for disclosure of individually identifiable health information.

Certain states have also adopted comparable privacy and security laws and regulations, which govern the privacy, processing and protection of health-related and other personal information. For example, on June 28, 2018, California enacted the California Consumer Privacy Act, or CCPA, which took effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers, increases the privacy and security obligations of entities handling certain personal information, requires certain disclosures to California individuals, affords such individuals new abilities to opt out of certain sales of personal information, and provides for civil penalties for violations as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with data breach litigation. Further, the California Privacy Rights Act, or CPRA, went into effect on January 1, 2023 and significantly amends the CCPA. It imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also created a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. Additional compliance investment and potential business process changes may be required. Complying with these numerous, complex, and often changing regulations is expensive and difficult, and failure to comply with any privacy laws or data security laws or any security incident or breach involving the misappropriation, loss or other unauthorized processing, use or disclosure of sensitive or confidential patient, consumer or other personal information, whether by us, one of our CROs or another third party, could adversely affect our business, financial condition, and results of operations, including but not limited to: investigation costs; material fines and penalties; compensatory, special, punitive, and statutory damages; litigation; consent orders regarding our privacy and security

practices; requirements that we provide notices, credit monitoring services, and/or credit restoration services or other relevant services to impacted individuals; adverse actions against our licenses to do business; reputational damage; and injunctive relief. Similar laws have passed in other states and are continuing to be proposed at the state and federal level, reflecting a trend toward more stringent privacy legislation in the United States. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

Our activities outside the United States may be subject to additional compliance requirements and generate additional risks of enforcement for noncompliance. For example, on May 25, 2018, the General Data Protection Regulation, or GDPR, went into effect and imposes strict requirements for processing the personal data of individuals within the EEA. For example, the GDPR applies extraterritorially, and requires us to make detailed disclosures to data subjects, disclose the legal basis on which we can process personal data, to obtain valid consent for collecting and processing personal data (including data from clinical trials), appoint data protection officers when sensitive personal data, such as health data, is processed on a large scale, provides robust rights for data subjects, and adopt appropriate privacy governance, including policies, procedures, training, and data audit. It also imposes mandatory data breach notification and certain obligations on us when contracting with service providers. The GDPR provides that EEA countries may establish their own laws and regulations limiting the processing of personal data, including genetic, biometric, or health data, which could limit our ability to use and share personal data or could cause our costs to increase. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition to fines, a breach of the GDPR may result in regulatory investigations, reputational damage, orders to cease/ change our data processing activities, enforcement notices, assessment notices (for a compulsory audit) and/ or civil claims (including class actions). Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the United States, and the efficacy and longevity of current transfer mechanisms between the EEA and the United States remains uncertain. Case law from the Court of Justice of the European Union, or CJEU, states that reliance on the standard contractual clauses - a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism - alone may not necessarily be sufficient in all circumstances and that transfers must be assessed on a case-by-case basis. On October 7, 2022, President Biden signed an Executive Order on ‘Enhancing Safeguards for United States Intelligence Activities’ which introduced new redress mechanisms and binding safeguards to address the concerns raised by the CJEU in relation to data transfers from the EEA to the United States and which formed the basis of the new EU-US Data Privacy Framework, or DPF, as released on December 13, 2022. The European Commission adopted its Adequacy Decision in relation to the DPF on July 10, 2023, rendering the DPF effective as a GDPR transfer mechanism to U.S. entities self-certified under the DPF. The DPF also introduced a new redress mechanism for EU citizens which addresses a key concern in the previous CJEU judgments and may mean transfers under standard contractual clauses are less likely to be challenged in future. We currently rely on the EU standard contractual clauses and the UK Addendum to the EU standard contractual clauses and the UK International Data Transfer Agreement and the DPF relevant to transfer personal data outside the EEA and the UK, including to the United States, with respect to both intragroup and third party transfers. We expect the existing legal complexity and uncertainty regarding international personal data transfers to continue. In particular, we expect the DPF Adequacy Decision to be challenged and international transfers to the United States and to other jurisdictions more generally to continue to be subject to enhanced scrutiny by regulators. As a result, we may have to make certain operational changes and we will have to implement revised standard contractual clauses and other relevant documentation for existing data transfers within required time frames.

Additionally, since January 2021, we have had to comply with the GDPR and the United Kingdom GDPR, with each regime having the ability to fine up to the greater of €20 million (£17.5 million) or 4% of global turnover for violations. On October 12, 2023, the UK Extension to the DPF came into effect (as approved by the UK Government), as a UK GDPR data transfer mechanism to U.S. entities self-certified under the UK Extension to the DPF.

We cannot assure you that our CDMOs, CROs or other third-party service providers with access to our or our customers’, suppliers’, trial patients’ and employees’ personally identifiable and other sensitive or confidential information in relation to which we are responsible will not breach contractual obligations imposed by us, or that they will not experience data security breaches or attempts thereof, which could have a corresponding effect on our business, including putting us in breach of our obligations under privacy laws and regulations and/or which could in turn adversely affect our business, results of operations, and financial condition. We cannot assure you that our contractual measures and our own privacy and security-related safeguards will protect us from the risks associated with the third-party processing, use, storage, and transmission of such information. Moreover, patients about whom we or our collaborators obtain health information, as well as the providers who share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other

resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business. If we or third-party CDMOs, CROs, or other contractors or consultants fail to comply with applicable federal, state, or local regulatory privacy requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our product candidates and could harm or prevent sales of any affected products that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing, and marketing our products. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security, or reputational damage. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We are subject to environmental, health and safety laws and regulations, and we may become exposed to liability and substantial expenses in connection with environmental compliance or remediation activities.

Our operations, including our development, testing and manufacturing activities, are subject to numerous environmental, health and safety laws, and regulations. These laws and regulations govern, among other things, the controlled use, handling, release, and disposal of and the maintenance of a registry for, hazardous materials and biological materials, such as chemical solvents, human cells, carcinogenic compounds, mutagenic compounds, and compounds that have a toxic effect on reproduction, laboratory procedures, and exposure to blood-borne pathogens. If we fail to comply with such laws and regulations, we could be subject to fines or other sanctions.

As with other companies engaged in activities similar to ours, we face a risk of environmental liability inherent in our current and historical activities, including liability relating to releases of or exposure to hazardous or biological materials. Environmental, health and safety laws and regulations are becoming more stringent. We may be required to incur substantial expenses in connection with future environmental compliance or remediation activities, in which case, the production efforts of our third-party manufacturers or our development efforts may be interrupted or delayed.

We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally.

Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our product candidates or business may cause us to be found in violation of applicable requirements. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with applicable laws and regulations, our policies, and other legal or contractual requirements, which may give rise to regulatory enforcement action, liability, lead to the loss of trade secrets or other intellectual property or result in public exposure of personal information of our employees, clinical trial patients, customers, and others. Furthermore, negative posts or comments about us or our product candidates in social media could seriously damage our reputation, brand image, and goodwill. Any of these events could have a material adverse effect on our business, prospects, financial condition, and results of operations, and could adversely affect the price of our common stock.

Risks Related to Commercialization

We are very early in our development efforts. Most of our product candidates are in preclinical development or discovery and we received FDA clearance for our IND application for OTX-2002 and have initiated the associated clinical trial. It will be many years before we commercialize a product candidate, if ever. If we are unable to advance our product candidates to clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are very early in our development efforts and have focused our research and development efforts to date on developing the OMEGA platform, identifying our initial targeted disease indications and engineering our initial ECs. We have only conducted in vivo preclinical studies for some of our programs and there is no guarantee that we will conduct preclinical in vivo studies for other programs. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful clinical development and eventual commercialization of our product candidates, which may never occur.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND or by foreign regulatory authorities of a similar application and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA or foreign regulatory authorities require us to complete additional preclinical studies or we are required to satisfy other FDA or foreign regulatory authorities requests, the start of our clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other

regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or change their position on the acceptability of our trial designs or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect.

Commercialization of our product candidates will require additional preclinical and clinical development and regulatory and marketing approval. Our ability to conduct development or attain marketing approval will depend on the sufficiency of our financial and other resources to complete the necessary preclinical studies, IND-enabling studies or similar studies, and clinical trials and the successful enrollment in, and completion of, clinical trials.

If we do not successfully achieve one or more of these activities in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize any product candidates we may develop, which would materially harm our business. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Developments by competitors may render our products or technologies obsolete or non-competitive or may reduce the size of our markets.

Our industry has been characterized by extensive research and development efforts, rapid developments in technologies, intense competition, and a strong emphasis on proprietary products. We expect our product candidates to face intense and increasing competition as new products enter the relevant markets and advanced technologies become available. We face potential competition from many different sources, including pharmaceutical, biotechnology, and specialty pharmaceutical companies. Academic research institutions, governmental agencies, and public and private institutions are also potential sources of competitive products and technologies. Our competitors may have or may develop superior technologies or approaches, which may provide them with competitive advantages. Many of these competitors may also have compounds already approved or in development in the therapeutic categories that we are targeting with our product candidates. In addition, many of these competitors, either alone or together with their collaborators, may operate larger research and development programs or have substantially greater financial resources than we do, as well as greater experience in:

- developing product candidates;
- undertaking preclinical testing and clinical trials;
- obtaining BLA approval by the FDA or comparable foreign regulatory approvals of product candidates;
- formulating and manufacturing products; and
- launching, marketing, and selling products.

If these competitors access the marketplace before we do with safer, more effective, or less expensive therapeutics, our product candidates, if approved for commercialization, may not be profitable to sell or worthwhile to continue to develop. Technology in the pharmaceutical industry has undergone rapid and significant change, and we expect that it will continue to do so. Any compounds, products, or processes that we develop may become obsolete or uneconomical before we recover any expenses incurred in connection with their development. The success of our product candidates will depend upon factors such as product efficacy, safety, reliability, availability, timing, scope of regulatory approval, acceptance and price, among other things. Other important factors to our success include speed in developing product candidates, completing clinical development and laboratory testing, obtaining regulatory approvals and manufacturing, and selling commercial quantities of potential products.

We may face competition from new entrants to the epigenetic medicine space. We also compete with many companies that are using other technologies targeting the same indications we are currently pursuing. We expect our product candidates to compete with companies developing technologies that focus on gene-expression control using various technologies, such as CRISPR gene editing, gene therapies, non-coding RNA therapeutics, and small-molecule epigenetics, including Alnylam Pharmaceuticals Inc., Beam Therapeutics, Inc., Biogen Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Intellia Therapeutics, Inc., Ionis Pharmaceuticals, Inc., Janssen Pharmaceuticals, Inc., Pfizer Inc., and Sangamo Therapeutics, Inc. Even if approved and commercialized, our product candidates may fail to achieve market acceptance with hospitals, physicians, or patients. Hospitals, physicians, or patients may conclude that our products are less safe or effective or otherwise less attractive than existing drugs. If our product candidates do not receive market acceptance for any reason, our revenue potential would be diminished, which would materially adversely affect our ability to become profitable.

Many of our competitors have substantially greater capital resources, robust product candidate pipelines, established presence in the market, and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement, and marketing approved products than we do. As a result, our competitors may achieve product commercialization or patent or other intellectual property protection earlier than we can.

Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified clinical, regulatory, scientific, sales, marketing, and management personnel, and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any products that we may develop or that would render any products that we may develop obsolete or noncompetitive.

Our product candidates may face competition sooner than anticipated.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until twelve years from the date on which the reference product was first licensed. During this twelve-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of its product.

We believe that any of our future product candidates approved as a biological product under a BLA should qualify for the twelve-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to Congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation. Jurisdictions in addition to the United States have established abbreviated pathways for regulatory approval of biological products that are biosimilar to earlier approved reference products. For example, the EU has had an established regulatory pathway for biosimilars since 2006. Moreover, the extent to which a biosimilar, once approved, could be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing.

The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels, and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate product revenue.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers, and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford treatments.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs and biologics when an equivalent generic drug, biosimilar, or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates and may not be able to obtain a satisfactory financial return on our product candidates.

In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered and reimbursed. The Medicare program is increasingly used as a model for how private and other governmental payors

develop their coverage and reimbursement policies for new drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, 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 our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Some third-party payors may require pre-approval of coverage for new or innovative drug therapies before they will reimburse healthcare providers who use such therapies. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in the EU and other jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the United States and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

If we are unable to establish sales, marketing, and distribution capabilities either on our own or in collaboration with third parties, we may not be successful in commercializing any of our product candidates, if approved, and we may not be able to generate any product revenue.

We have limited personnel or infrastructure for the sales, marketing, or distribution of products, and no experience as a company in commercializing a product candidate. The cost of building and maintaining such an organization may exceed the cost-effectiveness of doing so.

We may build our own focused sales, distribution and marketing infrastructure to market our product candidates, if approved, in the United States and other markets around the world. There are significant expenses and risks involved with building our own sales, marketing, and distribution capabilities, including our ability to hire, retain, and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing, and distribution capabilities could delay any product launch, which would adversely impact the commercialization of our product candidate, if approved. Additionally, if the commercial launch of our product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our product candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe our future products;
- our inability to equip medical and sales personnel with effective materials, including medical and sales literature to help them educate physicians and other healthcare providers regarding applicable diseases and our future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- our inability to develop or obtain sufficient operational functions to support our commercial activities; and

- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable or decide not to establish internal sales, marketing, and distribution capabilities, or decide not to do so for a particular country, we may pursue collaborative arrangements. If we pursue a collaborative arrangement, our sales will largely depend on the collaborator's strategic interest in the product and such collaborator's ability to successfully market and sell the product.

If we are unable to build our own sales force or access a collaborative relationship for the commercialization of any of our product candidates, we may be forced to delay the potential commercialization of our product candidates or reduce the scope of our sales or marketing activities for such product candidates. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. We could enter into arrangements with collaborators at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to any of our product candidates or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business, operating results, and prospects.

If we are unable to establish adequate sales, marketing, and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing our other product candidates and may not become profitable and may incur significant additional losses. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

In addition, even if we do establish adequate sales, marketing, and distribution capabilities, the progress of general industry trends with respect to pricing models, supply chains, and delivery mechanisms, among other things, could deviate from our expectations. If these or other industry trends change in a manner which we do not anticipate or for which we are not prepared, we may not be successful in commercializing our product candidates or become profitable.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates, if approved, in foreign markets, including the EU, for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approvals in other countries, we may be required to comply with numerous and varying regulatory requirements of such countries regarding the safety and efficacy of our product candidates and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

- our customers' ability to obtain reimbursement for our product candidates in foreign markets;
- our inability to directly control commercial activities if we are relying on third parties;
- the burden of complying with complex and changing foreign regulatory, tax, accounting, and legal requirements;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- import or export licensing requirements;
- longer accounts receivable collection times;
- our ability to supply our product candidates on a timely and large-scale basis in local markets;
- longer lead times for shipping which may necessitate local manufacture of our product candidates;
- language barriers for technical training and the need for language translations;
- reduced protection of patent and other intellectual property rights in some foreign countries;
- the existence of additional potentially relevant third-party intellectual property rights;
- foreign currency exchange rate fluctuations; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions, and changes in tariffs.

If any of our product candidates is approved for commercialization, we may selectively partner with third parties to market it in certain jurisdictions outside the United States. We expect that we will be subject to additional risks related to international pharmaceutical operations, including:

- different regulatory requirements for drug approvals and rules governing drug commercialization in foreign countries, including requirements specific to biologics or gene therapy products;
- reduced protection for patent and other intellectual property rights;
- foreign reimbursement, pricing, and insurance regimes;
- potential noncompliance with the U.S. Foreign Corrupt Practices Act, the U.K. Bribery Act 2010 and similar anti-bribery and anticorruption laws in other jurisdictions;
- international terrorism, political unrest and wars, which could delay or disrupt business activity, and if any conflict escalates or spills over to or otherwise impacts additional regions, it could heighten many of the other risk factors described in this Item 1A; and
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor, and other legal requirements imposed by both the EU and many of the individual EU member states with which we will need to comply. Many U.S.-based biotechnology companies have found the process of marketing their own products in the EU to be very challenging.

Certain legal and political risks are also inherent in foreign operations. There is a risk that foreign governments may nationalize private enterprises in certain countries where we may operate. In certain countries or regions, terrorist activities, political unrest and wars, and the response to such activities may threaten our operations more than in the United States. Social and cultural norms in certain countries may not support compliance with our corporate policies, including those that require compliance with substantive laws and regulations. Also, changes in general economic and political conditions in countries where we may operate are a risk to our financial performance and future growth. Additionally, the need to identify financially and commercially strong partners for commercialization outside the United States who will comply with the high manufacturing and legal and regulatory compliance standards we require is a risk to our financial performance. As we operate our business globally, our success will depend, in part, on our ability to anticipate and effectively manage these and other related risks. There can be no assurance that the consequences of these and other factors relating to our international operations will not have an adverse effect on our business, financial condition, or results of operations.

In some countries, particularly in the EU, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we may be required to conduct clinical trials that compare the cost-effectiveness of our product candidates 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 harmed, possibly materially.

Potential product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs, which may not be covered by insurance. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical trials;
- injury to our reputation;

- initiation of investigations by regulators;
- significant costs to defend the related litigation and related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize a product candidate;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- exhaustion of any available insurance and our capital resources, and the inability to commercialize any product candidate;
- decreased demand for a product candidate, if approved for commercial sale; and
- loss of revenue.

Failure to obtain or retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop, alone or with corporate collaborators. Although we plan to obtain clinical trial insurance, our insurance policies may have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

Risks Related to our Dependence on Third Parties and Manufacturing

Our ability to manufacture our EC candidates for preclinical or clinical supply could be limited, especially with the increased demand for the manufacture of mRNA- and LNP-based therapeutics, which could adversely affect our development plans.

We rely on third-party CDMOs of mRNA therapeutics and lipid excipients, a lipid that serves as the vehicle or medium for a drug or other active substance, to manufacture our preclinical and clinical supply of our EC candidates. Vaccines to treat COVID-19 include mRNA vaccines and vaccines that utilize lipid excipients. Several vaccines for COVID-19 have been approved by the FDA. As a result, there is unprecedented demand on these CDMOs to manufacture COVID-19 vaccines and capacity for mRNA- and LNP-based therapeutics is limited and may be further limited by the potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, which may make it more difficult to obtain materials or manufacturing slots for the products needed for our planned clinical trials. While we are working to obtain sufficient supply of our ECs for our anticipated preclinical and clinical development, we may experience supply constraints and disruptions as manufacturers prioritize supply for COVID-19 vaccines over our ECs. If we are unable to obtain the supplies we need at a reasonable price or on a timely basis or in the amounts we desire, our ability to complete the development of our EC candidates or, if we obtain regulatory approval for our EC candidates, to commercialize them, could be materially adversely affected.

Our EC candidates are based on novel technology and may be complex and difficult to manufacture. We may encounter difficulties in manufacturing, product release, shelf life, testing, storage, supply chain management or shipping.

Due to the novel nature of our technology and limited experience at larger scale production, we may encounter difficulties in manufacturing, product release, shelf life, testing, storage and supply chain management, or shipping. These difficulties could be due to any number of reasons including, but not limited to, complexities of producing batches at larger scale, equipment failure, choice and quality of raw materials and excipients, analytical testing technology, and product instability. As a result, the preclinical or clinical development of our EC candidates could be materially delayed or we could be required to begin a new study or trial with a newly formulated drug product.

The process to generate mRNA-encoded EC candidates encapsulated in LNPs is complex and, if not developed and manufactured under well-controlled conditions, can adversely impact pharmacological activity. Furthermore, we have not manufactured our ECs at commercial scale. We may encounter difficulties in scaling up our manufacturing process, thereby potentially impacting clinical and commercial supply.

As we continue developing manufacturing processes for our drug substance and drug product, the changes we implement to manufacturing process may in turn impact specification and stability of the drug product. Changes in our manufacturing processes may lead to failure of lots and this could lead to a substantial delay in our preclinical studies or

any clinical trials. Our EC candidates may prove to have a stability profile that leads to a lower than desired shelf life of the final approved EC, if any. This poses risk in supply requirements, wasted stock, and higher cost of goods.

Our product and product intermediates are extremely temperature sensitive, and we may learn that any or all of our products are less stable than desired. We may also find that transportation conditions negatively impact product quality. This may require changes to the formulation or manufacturing process for one or more of our EC candidates and result in delays or interruptions to clinical or commercial supply. In addition, the cost associated with such transportation services and the limited pool of vendors may also add additional risks of supply disruptions.

Our rate of innovation is high, which has resulted in and will continue to cause a high degree of technology change that can negatively impact product comparability during and after clinical development. Furthermore, technology changes may drive the need for changes in, modification to, or the sourcing of new manufacturing infrastructure.

We will rely on third parties for the foreseeable future for the manufacture and supply of materials for our research programs, preclinical studies and clinical trials and we do not have long-term contracts with many of these parties. This reliance on third parties increases the risk that we will not have sufficient quantities of such materials, including drug supplies for combination therapy, product candidates, or any therapies that we may develop and commercialize, or that such supply will not be available to us at an acceptable cost, which could delay, prevent, or impair our development or commercialization efforts.

Although we continue to evaluate plans to develop our own manufacturing facility, we expect to rely on third parties at least for the next several years for the manufacture of materials for our planned clinical trials and preclinical and clinical development. We expect to rely in part on third parties for commercial manufacture if any of our product candidates receive marketing approval. We do not have a long-term agreement with any of the third-party manufacturers we currently use to provide preclinical and clinical materials, and we purchase any required materials on a purchase order basis. Certain of these manufacturers are critical to our production and the loss of these manufacturers to one of our competitors or otherwise, or an inability to obtain quantities at an acceptable cost or quality, could delay, prevent, or impair our ability to timely conduct preclinical studies or clinical trials, and would materially and adversely affect our development and commercialization efforts.

We expect to continue to rely in part on third-party manufacturers for the foreseeable future for the commercial supply of any of our product candidates for which we obtain marketing approval, if any. We may be unable to maintain or establish required agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the failure of the third party to manufacture our product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the termination or nonrenewal of arrangements or agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third party to manufacture our product candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- 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 misappropriation or unauthorized disclosure of our intellectual property or other proprietary information, including our trade secrets and know-how.

We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP or similar foreign regulations for manufacturing our product candidates. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that

conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain authorization for their manufacturing facilities. In addition, we do not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance, and qualified personnel. If the FDA or a comparable foreign regulatory authority does not authorize these facilities for the manufacture of our product candidates or if it withdraws any such authorization in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension, or withdrawal of approvals, license revocation, seizures, or recalls of product candidates or drugs, operating restrictions, and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates or drugs and harm our business and results of operations.

We continue to evaluate plans to acquire and establish our own manufacturing facility and infrastructure in addition to or in lieu of relying on CDMOs for the manufacture of our product candidates. Any plan to establish our own manufacturing facility and infrastructure will be costly and time-consuming and we may not be successful.

We may decide to lease a facility to buildout a manufacturing facility as an alternative or in addition to our reliance on CDMOs for the manufacture of drug substance for preclinical and clinical needs. If a lease is entered into, we plan to renovate and customize the manufacturing facility for our use. We expect that construction of our own manufacturing facility would provide us with enhanced control of material supply for preclinical studies and clinical trials, enable the more rapid implementation of process changes, and allow for better long-term margins. However, we have no experience as a company in construction of a manufacturing facility and may never be successful in building our own manufacturing facility or capability. As a result, we would also need to hire additional personnel to manage our operations and facilities and develop the necessary infrastructure to continue the research and development, manufacture and eventual commercialization, if approved, of our product candidates. We, as a company, have no experience in setting up, building, or eventually managing a manufacturing facility. If we fail to select the correct location, or if we fail to enter into the lease agreement, or fail to complete the planned renovation and customization in an efficient manner, or fail to recruit the required personnel and generally manage our growth effectively, the development and production of our product candidates could be curtailed or delayed. Even if we are successful, our manufacturing capabilities could be affected by cost-overruns, unexpected delays, equipment failures, labor shortages, natural disasters, power failures and numerous other factors that could prevent us from realizing the intended benefits of our manufacturing strategy and have a material adverse effect on our business.

In addition, the FDA and other foreign regulatory authorities may require us to submit samples of any lot of any approved product together with the protocols showing the results of applicable tests at any time. Under some circumstances, the FDA or other foreign regulatory authorities may require that we not distribute a lot until the relevant agency authorizes its release. Slight deviations in the manufacturing process, including those affecting quality attributes and stability, may result in unacceptable changes in the product that could result in lot failures or product recalls. Lot failures or product recalls could cause us to delay clinical trials or product launches, which could be costly to us and otherwise harm our business, financial condition, results of operations, and prospects. Problems in our manufacturing process could restrict our ability to meet clinical and market demand for our products.

We also may encounter problems hiring and retaining the experienced scientific, quality-control, and manufacturing personnel needed to operate our manufacturing processes, which could result in delays in production or difficulties in maintaining compliance with applicable regulatory requirements.

Any problems in our manufacturing process or facilities could make us a less attractive collaborator for potential partners, including larger pharmaceutical companies and academic research institutions, which could limit our access to additional attractive development programs.

We do not have experience as a company managing a manufacturing facility.

Operating our own manufacturing facility would require significant resources, and we do not have experience as a company in managing a manufacturing facility. In part because of this lack of experience, we cannot be certain that our manufacturing plans would be completed on time, if at all, or if manufacturing of product candidates from our own manufacturing facility for our planned clinical trials will begin or be completed on time, if at all. In part because of our inexperience, we may have unacceptable or inconsistent product quality success rates and yields, and we may be unable to maintain adequate quality control, quality assurance, and qualified personnel. In addition, if we switch from our current CDMOs to our own manufacturing facility for one or more of our product candidates in the future, we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions. Failure to successfully obtain and operate our planned manufacturing facility could adversely affect the commercial viability of our product candidates.

We or our third-party manufacturers may be unable to successfully scale up manufacturing of our product candidates in sufficient quality and quantity, which may impair the clinical advancement and commercialization of our product candidates.

In order to conduct clinical trials of our product candidates and commercialize any approved product candidates, we and our manufacturing partners need to manufacture them in large quantities. However, we or they may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities, as discussed above. If we, or any manufacturing partners, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of these product candidates may be delayed or infeasible, and regulatory approval or commercial launch of any resulting products may be delayed or not obtained, which could significantly harm our business. Supply sources could be interrupted from time to time and, if interrupted, it is not certain that supplies could be resumed (whether in part or in whole) within a reasonable timeframe and at an acceptable cost, or at all. If we are unable to obtain or maintain third-party manufacturing for commercial supply of our product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully.

We have a limited number of suppliers for the lipid excipients used in our product candidates and certain of our suppliers are critical to our production. If we were to lose a critical supplier, it could have a material adverse effect on our ability to complete the development of our product candidates. If we obtain regulatory approval for any of our product candidates, we would need to expand the supply of lipid excipients in order to commercialize them.

We have a limited number of suppliers for the lipid excipient component of our product candidates. We also do not have long-term supply agreements with all of our lipid suppliers. We may not be able to establish additional sources of supply for the lipid excipient component of our product candidates or may be unable to do so on acceptable terms.

The number of suppliers of the lipid excipients for our product candidates is limited. In the event it is necessary or desirable to acquire lipid excipients from alternative suppliers, we might not be able to obtain them on commercially reasonable terms, if at all. It could also require significant time and expense to redesign our manufacturing processes to work with another company, and redesign of processes can trigger the need for conducting additional studies such as comparability or bridging studies. Additionally, certain of our suppliers are critical to our production, and the loss of these suppliers to one of our competitors or otherwise would materially and adversely affect our development and commercialization efforts.

We rely, and expect to continue to rely, on third parties to conduct certain aspects of our preclinical studies and will rely on third parties to conduct our planned clinical trials. Any failure by a third party to conduct the planned clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We have relied upon and plan to continue to rely upon third parties to conduct certain aspects of our preclinical studies and will depend on third parties to conduct our planned clinical trials and to monitor and manage data for our ongoing preclinical and planned clinical programs. We rely on these parties for execution of our preclinical studies and will rely on these parties for execution of our planned clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol and legal, regulatory, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs will be required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations or similar foreign regulations outside of the United States. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Any third parties conducting our planned clinical trials or preclinical studies are not and will not be our employees and, except for remedies available to us under our agreements with such third parties, we cannot guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our planned clinical trials may be extended, delayed, or terminated. In addition, many of the third parties with whom we contract may also have relationships with

other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities that could harm our competitive position. In addition, principal investigators for our planned clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash and cash equivalents or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or comparable foreign regulatory authorities conclude that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned, and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit to the FDA, or any comparable foreign regulatory applications we submit to foreign regulatory authorities. Any such delay or rejection could prevent us from commercializing our product candidates.

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

We collaborate with third parties for the development and potential commercialization of our product candidates. We may not succeed in maintaining existing collaborative relationships and establishing and maintaining future collaborative relationships, which may significantly limit our ability to develop and commercialize our product candidates successfully, if at all.

We have entered into collaboration agreements and may in the future seek other collaborative relationships for the development and commercialization of our product candidates. For example, in November 2021, we entered into a five-year collaboration with PM (CF) Explorations, Inc., and, in December 2023, we entered into a Research and Collaboration Agreement with Novo Nordisk A/S, Pioneering Medicines 08, Inc. and other parties. Under these and any similar future arrangements with any third parties, we have or will likely have shared or limited control over the amount and timing of resources that our collaborators dedicate to the development or potential commercialization of any product candidates we may seek to develop with them. Our ability to generate product revenue from these arrangements with commercial entities will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements. We cannot predict the success of any collaboration that we enter into. Collaborations involving our product candidates pose the following risks to us:

- collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not properly obtain, maintain, enforce, or defend intellectual property or proprietary rights relating to our product candidates or may use our proprietary information inappropriately or in such a way as to expose us to potential litigation or other intellectual property-related proceedings, including proceedings challenging the scope, ownership, validity, and enforceability of our intellectual property;
- collaborators may own or co-own intellectual property rights covering our product candidates that result from our collaboration with them, and in such cases, we may not have the exclusive right to commercialize such intellectual property or such product candidates;
- disputes may arise with respect to the ownership of intellectual property developed pursuant to collaborations;
- we may need the cooperation of our collaborators to enforce or defend any intellectual property we contribute to or that arises out of our collaborations, which may not be provided to us;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and resources;
- collaborators may decide not to pursue development and commercialization of any product candidates we develop 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 that diverts resources or creates competing priorities;

- collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more product candidates may not commit sufficient resources to the marketing and distribution of such product candidates;
- we may lose certain valuable rights under circumstances identified in our collaborations, including if we undergo a change of control;
- collaborators may become party to a business combination transaction and the continued pursuit and emphasis on our development or commercialization program by the resulting entity under our existing collaboration could be delayed, diminished, or terminated;
- collaborators may become bankrupt, which may significantly delay our research or development programs, or may cause us to lose access to valuable technology, devices, materials, know-how, or intellectual property of the collaborator relating to our product candidates;
- key personnel at our collaborators may leave, which could negatively impact our ability to productively work with our collaborators;
- collaborations may require us to incur short- and long-term expenditures, issue securities that dilute our stockholders, or disrupt our management and business;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

We may face significant competition in seeking appropriate collaborations from other companies with substantially greater financial, marketing, sales, technology, or other business resources. Business combinations among biotechnology and pharmaceutical companies have also resulted in a reduced number of potential collaborators. In addition, the negotiation process is time-consuming and complex, and 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 or delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to 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 product candidates or bring them to market and generate product revenue.

We may not be able to realize the benefit of our existing or future collaborations if we or our collaborator elect not to exercise the rights granted under the agreement or if we or our collaborator are unable to successfully integrate a product candidate into existing operations. In addition, if our agreement with any of our collaborators terminates, our access to technology and intellectual property licensed to us by that collaborator may be restricted or terminate entirely, which may delay our continued development of our product candidates utilizing the collaborator's technology or intellectual property or require us to stop development of those product candidates completely. We may also find it more difficult to find a suitable replacement collaborator or attract new collaborators, and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. Any collaborator may also be subject to many of the risks relating to product development, regulatory approval, and commercialization described in this "Risk Factors" section, and any negative impact on our collaborators may adversely affect us.

Our employees and independent contractors, including principal investigators, CDMOs, CROs, consultants, vendors and any third parties we may engage in connection with research, development, regulatory, manufacturing, quality assurance and other pharmaceutical functions and commercialization may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

Misconduct by our employees and independent contractors, including principal investigators, CDMOs, CROs, consultants, vendors, and any third parties we may engage in connection with research, development, regulatory,

manufacturing, quality assurance, and other pharmaceutical functions and commercialization, could include intentional, reckless, or negligent conduct or unauthorized activities that violate: (i) the laws and regulations of the FDA, and other similar regulatory authorities as well as similar healthcare laws and regulations in foreign jurisdictions, including those laws that require the reporting of true, complete, and accurate information to such authorities; (ii) manufacturing standards; (iii) data privacy, security, fraud, and abuse and other healthcare laws and regulations; or (iv) laws that require the reporting of true, complete, and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing, and promotion, sales commission, customer incentive programs, and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of preclinical studies or clinical trials, creation of fraudulent data in preclinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 comply with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 civil, criminal, and administrative penalties, damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid, other U.S. federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight, and reporting obligations to resolve allegations of non-compliance, individual imprisonment, other sanctions, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations.

If our CDMOs use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research and development activities involve the controlled use of potentially hazardous substances, including chemical and biological materials, by our manufacturers. Our manufacturers are subject to federal, state, and local laws and regulations in the United States and in the countries in which they operate governing the use, manufacture, storage, handling and disposal of medical and hazardous materials. Although we believe that our manufacturers' procedures for using, handling, storing, and disposing of these materials comply with legally prescribed standards, we cannot completely eliminate the risk of contamination or injury resulting from medical or hazardous materials. As a result of any such contamination or injury, we may incur liability or local, city, state, or federal authorities may curtail the use of these materials and interrupt our business operations. In the event of an accident, we could be held liable for damages or penalized with fines, and the liability could exceed our resources. Generally, we do not have any insurance for liabilities arising from medical or hazardous materials. Compliance with applicable environmental laws and regulations is expensive, and current or future environmental regulations may impair our research, development, and production efforts, which could harm our business, prospects, financial condition or results of operations.

Risks Related to Intellectual Property

If we are unable to obtain, maintain, enforce and adequately protect our intellectual property rights with respect to our technology and product candidates, or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect our intellectual property and prevent others from duplicating our pipeline product candidates, or their use or manufacture, or any of and any future product candidates, and our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to such product candidates.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. Although we enter into confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, such as our employees, CROs, consultants, scientific advisors, and other contractors, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, and some remain so until issued. 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 any patent application related to an invention or product candidate. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal, factual, and scientific questions and can be uncertain. It is possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent applications that we own may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may challenge the inventorship, ownership, validity, enforceability, or scope of such patents, which may result in such patents being narrowed or invalidated, or being held unenforceable. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Additionally, any U.S. provisional patent application that we file is not eligible to become an issued patent until, among other things, we file a non-provisional patent application within 12 months of filing the related provisional patent application. If we do not timely file any non-provisional patent application, we may lose our priority date with respect to the provisional patent application and any patent protection on the inventions disclosed in the provisional patent application.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. In addition, no assurances can be given that third parties will not create similar or alternative products or methods that achieve similar results without infringing upon our patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we hold with respect to our programs or product candidates fail to issue, if the breadth or strength of protection of our current or future issued patents is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, or threaten our ability to commercialize our current or future product candidates. Several patent applications covering our product candidates have been filed recently by us. We cannot offer any assurances about which, if any, will result in issued patents, the breadth of any such patents or whether any issued patents will be found invalid or unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop.

The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity, or enforceability, and our patents may be challenged in courts or patent offices in the United States and abroad. In addition, the issuance of a patent does not give us the right to practice the patented invention, as third parties may have blocking patents that could prevent us from marketing our product candidate, if approved, or practicing our own patented technology.

Wide-ranging patent reform legislation in the United States, including the Leahy-Smith America Invents Act of 2011, or the Leahy-Smith Act, may increase the uncertainty of the strength or enforceability of our intellectual property and the cost to defend it. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted and also affect patent litigation. Under the Leahy-Smith Act, the United States transitioned from a “first-to-invent” to a “first-to-file” system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. This will require us to be prompt going forward during the time from invention to filing of a patent application and to be diligent in filing patent applications, but circumstances could prevent us from promptly filing or prosecuting patent applications on our inventions. The Leahy-Smith Act also enlarged the scope of disclosures that qualify as prior art. Furthermore, if a third party filed a patent application before effectiveness of applicable provisions of the Leahy-Smith Act, on March 16, 2013, an interference proceeding in the United States can be initiated by a third party to determine if it was the first to invent any of the subject matter covered by the claims of our patent applications. We may also be subject to a third party preissuance submission of prior art to the USPTO.

The Leahy-Smith Act created for the first time new procedures to challenge issued patents in the United States, including post-grant review, inter partes review and derivation proceedings, which are adversarial proceedings conducted at the USPTO, 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 a priority date of March 16, 2013 or later, which all of our patent filings have, 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 was filed 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 a priority date of March 16, 2013 or later. Post-grant review proceedings can be brought on any

ground of challenge, whereas inter partes review proceedings can only be brought to raise a challenge based on published prior art. These adversarial actions at the USPTO include review of patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts. The USPTO issued a final rule effective November 13, 2018 announcing that it will now use the same claim construction standard currently used in the U.S. federal courts to interpret patent claims in USPTO proceedings, which is the plain and ordinary meaning of words used. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we will be successful in defending the patent, which would result in a loss of the challenged patent right to us, including loss of exclusivity, or in patent claims being narrowed, invalidated, or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

As a result of all of the foregoing, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Third parties may obtain or control intellectual property rights that may prevent or limit the development of our technology or products. Third-party claims of intellectual property infringement, misappropriation or other violation may result in substantial costs or prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding actual and allegations of infringement, misappropriation or other violation of the patents and other proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, re-examination, and post-grant and inter partes review proceedings before the USPTO and similar proceedings in foreign jurisdictions, such as oppositions before the European Patent Office, or EPO. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. Many companies in intellectual property-dependent industries, including the pharmaceutical industry, have employed intellectual property litigation as a means to gain an advantage over their competitors. As biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to composition of matter, drug delivery, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. We cannot guarantee that our technologies, products, compositions, and their uses do not or will not infringe, misappropriate or otherwise violate third-party patent or other intellectual property rights. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. In order to successfully challenge the validity of a U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If any third-party patents were held by a court of competent jurisdiction to cover the composition of matter of any of our product candidates, the manufacturing process of any of our product candidates or the method of use for any of our product candidates, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, which may not be available at all or on commercially reasonable terms, or until such patents expire.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation

and proceedings may increase if and as our product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of the merit of such claims. We may not be aware of all intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third-party intellectual property is invalid or that our activities and product candidates do not infringe, misappropriate, or otherwise violate such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate, or otherwise violate any third party's intellectual property.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates and/or harm our reputation and financial results. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could be a substantial diversion of management and employee resources from our business. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, in the case of claims concerning registered trademarks, rename our product candidates, or obtain one or more licenses from third parties, which may require substantial time and monetary expenditure, and which might be impossible or technically infeasible. Furthermore, 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 and other third parties access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. 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. For patents that are eligible for extension of patent term, we expect to seek extensions of patent terms in the United States and, if available, in other countries, however there can be no assurance that we will be granted any patent term extension we seek, or that any such patent term extension will provide us with any competitive advantage.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be harmed.

In the United States, a patent that covers an FDA-approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration, and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In the EU, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial.

We depend on proprietary technology licensed from others. If we lose our existing licenses, we may not be able to continue developing our product candidates.

We are dependent on patents, know-how and proprietary technology, both our own and licensed from others.

We depend substantially on our agreements with Flagship Pioneering Innovations V, Inc., or Flagship, the Whitehead Institute for Biomedical Research, or WIBR, Acuitas Therapeutics, Inc., or Acuitas. On May 2, 2024, we terminated our Collaboration and License Agreement with Nitto Denko Corporation. Our remaining licenses may be terminated upon certain conditions. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates.

We may also enter into additional agreements, including license agreements, with other parties in the future that impose diligence, development and commercialization timelines, milestone payments, royalties, insurance, and other obligations on us. We are also obligated to achieve certain development milestones with respect to licensed products in our fields of use within specified time periods. If we fail to comply with our obligations to Flagship, WIBR, Acuitas, or any of our other current or future licensors or collaborators, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture, or market any product candidate that is covered by these agreements, which could adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in us having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We rely on Flagship, WIBR, and Acuitas to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over their activities or their use or licensing of any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights.

If we are unable to obtain licenses from third parties on commercially reasonable terms or at all, or fail to comply with our obligations under such agreements, our business could be harmed.

It is necessary for us to use the patented or other proprietary technology of third parties to commercialize our products. 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 in the future, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning or otherwise controlling 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. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them, or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations, and prospects significantly.

Additionally, if we fail to comply with our obligations under any future license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing, or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology, or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

Although we are not currently involved in any relevant litigation, we may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate, or otherwise violate our or our future licensors' patents, trademarks, copyrights, or other intellectual property. As a result, we may need to file infringement, misappropriation, or other intellectual property-related claims against third parties. To counter infringement or other unauthorized use, we may be required to file claims on a country-by-country basis, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. There can be no assurance that we will have sufficient financial or other resources to file and pursue such claims, which often last for years before they are concluded.

Our license agreements have certain limitation on our ability to enforce the licensed patents against third party infringers. For example, with regard to our license agreements with WIBR, we cannot enforce the licensed patents against a certain third party, who previously entered into a sponsored research agreement with WIBR, with respect to inventions arising out of such sponsored research agreement. In addition, with respect to the WIBR Co-Exclusive Agreement, the WIBR patent rights are co-exclusively licensed to both us and one other third party. As such, we are not permitted to assert the co-exclusively licensed patent rights against the co-exclusive licensee.

Any claims we assert against third parties could also provoke these parties to assert counterclaims against us alleging that we infringe, misappropriate, or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we have asserted are invalid or unenforceable, or both. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

In any such proceeding, a court may decide that a patent of ours, or a patent that we in-license, is not valid, is unenforceable and/or is not infringed, or may construe such patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, interpreted narrowly or held unenforceable in whole or in part, could put our patent applications at risk of not issuing, and could limit our ability to assert those patents against those parties or other competitors and 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, which could materially harm our business and negatively affect our position in the marketplace.

Even if we establish infringement, misappropriation, or other violation of our intellectual property, the court may decide not to grant an injunction against further such 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 this type of 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 have a material adverse effect on the price of our common stock. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Weakening patent laws and enforcement by courts and other authorities in the United States and other jurisdictions may impact our ability to protect our patents.

The U.S. Supreme Court has issued opinions in patent cases in the last few years that many consider may weaken patent protection in the United States, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making and other 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 and defend our existing patents and patents that we might obtain in the future.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed. For example, we could become a party to foreign opposition proceedings, such as at the EPO, or patent litigation and other proceedings in a foreign court. If so, uncertainties resulting from the initiation and continuation of such proceedings could have a material adverse effect on our ability to compete in the marketplace. The cost of foreign adversarial proceedings can also be substantial, and in many foreign jurisdictions, the losing party must pay the attorney fees of the winning party.

Obtaining and maintaining our 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.

The USPTO, EPO and other patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay such fees due to non-U.S. patent agencies. While, in many cases, an inadvertent lapse can 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. In such an event, our competitors or other third parties might be able to enter the market with similar or identical products or technology, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and even in countries where we have sought protection for our intellectual property, such protection can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly developing countries, and the breadth of patent claims allowed can be inconsistent. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in-licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but where enforcement is not as strong as that in the United States or the EU. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened requirement for patentability and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic drug manufacturers or other competitors may challenge the scope, validity, or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy, and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the EU, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, or other forms of intellectual property, particularly those relating to biotechnology products, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put at risk our or our licensors' patents of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or

other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions including EU countries, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

We rely on our ability to stop others from competing by enforcing our patents, however some jurisdictions may require us to grant licenses to third parties. Such compulsory licenses could be extended to include some of our product candidates, which may limit our potential revenue opportunities.

Many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties, in certain circumstances. For example, compulsory licensing, or the threat of compulsory licensing, of life-saving products and expensive products is becoming increasingly popular in developing countries, either through direct legislation or international initiatives. Compulsory licenses could be extended to include some of our product candidates, if they receive marketing approval, which may limit our potential revenue opportunities. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may also use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. 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. Furthermore, while we intend to protect our intellectual property rights in major markets for our products where such patent rights exist, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief and may be unable to enjoin infringement if a government is the infringer, which could materially diminish the value of the patent.

Some of our intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies, and compliance with such regulations may limit our exclusive rights and our ability to contract with non-U.S. manufacturers.

The United States federal government retains certain rights in inventions produced with its financial assistance under the Bayh-Dole Act. The federal government retains a "nonexclusive, nontransferable, irrevocable, paid-up license" for its own benefit. The Bayh-Dole Act also provides federal agencies with "march-in rights". March-in rights allow the government, in specified circumstances, to require the contractor or successors in title to the patent to grant a "nonexclusive, partially exclusive, or exclusive license" to a "responsible applicant or applicants" if it determines that (1) adequate steps have not been taken to commercialize the invention and achieve practical application of the government-funded technology, (2) government action is necessary to meet public health or safety needs, (3) government action is necessary to meet requirements for public use under federal regulations or (4) we fail to meet requirements of federal regulations. If the patent owner refuses to do so, the government may grant the license itself. Some of our licensed patents are subject to the provisions of the Bayh-Dole Act. If our licensors fail to comply with the regulations of the Bayh-Dole Act, they could lose title to any patents subject to such regulations, which could affect our license rights under the patents and our ability to stop others from using or commercializing similar or identical technology and products, or limit patent protection for our technology and products.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is either not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with parties who have access to them, such as our employees, CROs, consultants, scientific advisors, and other contractors. We cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary technology and processes. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements, or security measures may be breached and our trade secrets could be disclosed, and we may not have adequate remedies for any such breach. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Misappropriation or unauthorized disclosure of our trade secrets or other confidential proprietary information could cause us to lose trade secret protection, impair our competitive position and have a material adverse effect on our business. We may need to share our proprietary information, including trade secrets, with future business partners, collaborators, contractors, and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. Additionally, if the steps taken to maintain our trade secrets or other confidential proprietary information are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret or other confidential proprietary information.

Further, we cannot provide any assurances that competitors or other third parties will not otherwise gain access to our trade secrets and other confidential proprietary information or independently discover or develop substantially equivalent technology and processes. If we are unable to prevent disclosure of the trade secrets and other non-patented intellectual property related to our product candidates and technologies to third parties, there is no guarantee that we will have any such enforceable trade secret protection and we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations, and financial condition.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties, that our employees have wrongfully used or disclosed alleged trade secrets of their former employers, or asserting ownership of what we regard as our own intellectual property.

We have employed, and may in the future employ, individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and independent contractors 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 our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of such individuals' former employers or other third parties. Litigation may be necessary to defend against these 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 our ability to hire personnel, which, in any case of the foregoing, could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Although it is our policy to require all of our employees and consultants to assign their inventions to us, to the extent that employees or consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. We may also be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Our proprietary rights may not adequately protect our technologies and product candidates, and intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are the same as or similar to our product candidates but that are not covered by the claims of our patents;
- others, including inventors or developers of our patented technologies who may become involved with competitors, may independently develop similar technologies that function as alternatives or replacements for any of our technologies without infringing, misappropriating, or otherwise violating our intellectual property rights;
- we might not have been the first to conceive and reduce to practice the inventions covered by our patents or patent applications;
- we might not have been the first to file patent applications covering certain of our inventions;
- we may choose not to file a patent in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property;
- our pending patent applications might not result in issued patents;
- there might be prior public disclosures that could invalidate our patents;
- our issued patents may not provide us with any commercially viable products or competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors or other third parties;
- the Supreme Court of the United States, other U.S. federal courts, Congress, the USPTO or similar foreign authorities may change the standards of patentability and any such changes could narrow or invalidate, or change the scope of, our patents;
- patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership, validity, or enforceability of our patents or patent applications may be challenged by third parties; and
- the patents or pending or future applications of third parties, if issued, may have an adverse effect on our business.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects.

Risks Related to Employee Matters, Managing Growth, and Other Risks Related to Our Business

We will need to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

We expect to experience significant growth over time in the number of our employees and the scope of our operations, particularly in the areas of product candidate development, regulatory and clinical affairs, medical affairs, legal, finance, sales, marketing, and distribution. To manage our growth activities, we must continue to implement and improve our managerial, operational, and financial systems and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. As we expand our organization, we may have difficulty identifying, hiring, and integrating new personnel. Future growth would impose significant additional responsibilities on our management, including:

- the need to identify, recruit, maintain, motivate, and integrate additional employees, consultants, and contractors;

- managing our internal development efforts effectively, including clinical development and regulatory review for our product candidates, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems, and procedures.

Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which 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. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow product revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to develop and commercialize our product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors, and consultants to provide certain services, including preclinical and clinical development activities and manufacturing. There can be no assurance that the services of independent organizations, advisors, and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our planned clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval of our product candidates or otherwise advance our business. There can be no assurance that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all. If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, or we are not able to effectively build out new facilities to accommodate this expansion, we may not be able to successfully implement the tasks necessary to further develop and commercialize our product candidates and, accordingly, may not achieve our research, development, and commercialization goals.

Many of the biotechnology and pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. If we are unable to continue to attract and retain high-quality personnel and consultants, the rate and success at which we can discover and develop product candidates and operate our business will be limited.

If we lose our executive officers, are unable to recruit qualified officers or other key personnel, our business may materially suffer.

We are highly dependent on our management, including our Chief Executive Officer, Mahesh Karande. Due to the specialized knowledge each of our executive officers possesses with respect to our product candidates and our operations, the loss of service of any of our executive officers could delay development of our product candidates or adversely impact our business operations. We do not carry key person life insurance on any of our executive officers. In general, the employment arrangements that we have with our executive officers do not prevent them from terminating their employment with us at any time.

In addition, our future success and growth will depend in part on the continued service of our employees and management personnel and our ability to identify, hire, and retain additional personnel. Replacing key employees and management personnel may be difficult or costly and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize product candidates successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain, or effectively incentivize key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for scientific and clinical personnel from universities and research institutions. In addition, 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 engaged by entities other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to develop and commercialize product candidates will be limited.

Many of our employees have become or will soon become vested in a substantial amount of our common stock or a number of common stock options. Our employees may be more likely to leave us if the shares they own have

significantly appreciated in value relative to the original purchase prices of the shares, or if the exercise prices of the options that they hold are significantly below the market price of our common stock.

We may engage in acquisitions or strategic collaborations that could disrupt our business, cause dilution to our stockholders, reduce our financial resources, cause us to incur debt or assume contingent liabilities, and subject us to other risks.

In the future, we may enter into transactions to acquire other businesses, products, or technologies or enter into strategic collaborations, including licensing. If we do identify suitable acquisition or collaboration, we may not be able to complete such acquisitions or collaboration on favorable terms, or at all. Any acquisitions or collaboration we enter into may not strengthen our competitive position, and we may never realize the anticipated benefits of such acquisitions or collaborations. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business or collaboration that are not covered by the indemnification we may obtain from the seller or our collaborator. In addition, we may not be able to successfully integrate any acquired personnel, technologies, and operations into our existing business in an effective, timely, and non-disruptive manner. Acquisitions or collaborations may also divert management attention from day-to-day responsibilities, lead to a loss of key personnel, increase our expenses and reduce our cash and cash equivalents available for operations and other uses. We cannot predict the number, timing, or size of future acquisitions or collaborations or the effect that any such transactions might have on our operating results.

Litigation against us could be costly and time-consuming to defend and could result in additional liabilities.

We may from time to time be subject to legal proceedings and claims that arise in the ordinary course of business or otherwise, such as claims brought by third parties in connection with commercial disputes and employment claims made by our current or former employees. Claims may also be asserted by or on behalf of a variety of other parties, including government agencies, patients, or stockholders. For example, on June 11, 2024, a shareholder derivative suit captioned Joel Newman v. Flagship Pioneering, Inc., et al., was filed in the Court of Chancery of the State of Delaware, alleging breaches of fiduciary duty and unjust enrichment in connection with the Company's decision to enter into a Research Collaboration Agreement with Novo Nordisk A/S and Pioneering Medicines 08, Inc. The complaint names the Company as nominal defendant, and names certain of the Company's officers and directors, among others, as defendants. The Complaint seeks damages, rescissory relief, attorneys' fees and costs, and any other and further relief the court deems just and proper. The defendants filed a motion to dismiss on September 10, 2024. Thereafter, plaintiff gave notice that he intends to file an amended complaint, which is due by December 11, 2024.

Any litigation involving us may result in substantial costs, operationally restrict our business, and may divert management's attention and resources, which may seriously harm our business, overall financial condition, and results of operations. Insurance may not cover existing or future claims, be sufficient to fully compensate us for one or more of such claims, or continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs, thereby adversely impacting our results of operations.

Risks Related to Our Common Stock

The market price of our common stock may be volatile and fluctuate substantially.

Our stock price is likely to be volatile. As a result of this volatility, you may not be able to sell your common stock at a profit. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- actual or expected changes in our growth rate relative to our competitors;
- results of our ongoing, planned, or any future preclinical studies, clinical trials, or clinical development of our product candidates or those of our competitors;
- unanticipated serious safety concerns related to the use of our product candidates;
- developments related to any future collaborations;
- developments concerning our manufacturers or our manufacturing plans;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;

- regulatory or legal developments in the United States and other countries;
- development of third-party product candidates that may address our markets and make our product candidates less attractive;
- changes in physician, hospital or healthcare provider practices that may make our product candidates less attractive;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate a clinical trial;
- our failure to commercialize our product candidates;
- announcements by us, our collaborators or our competitors of significant acquisitions, joint ventures, collaborations or capital commitments;
- developments or disputes concerning patent applications, issued patents, or other intellectual property or proprietary rights;
- the recruitment or departure of key scientific or management personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- changes in accounting practices;
- the trading volume of our common stock;
- our cash and cash equivalents position;
- our ability to effectively manage our growth;
- sales of our common stock by us or our stockholders in the future;
- expiration of market stand-off or lock-up agreements;
- publication of research reports about us or our industry, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- ineffectiveness of our internal controls;
- significant lawsuits, including intellectual property or stockholder litigation;
- the results of our efforts to engineer, develop, acquire, or in-license additional product candidates or products;
- actual or expected changes in estimates as to financial results, development timelines, or recommendations by securities analysts;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

In addition, the stock market in general, and the Nasdaq Global Select Market, or Nasdaq, and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company’s securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management’s attention and resources, which would harm our business, financial condition, and results of operations.

Our executive officers, directors, and principal stockholders, if they choose to act together, will continue to have the ability to control all matters submitted to stockholders for approval.

Based on the number of shares of common stock outstanding as of December 31, 2023, our executive officers, directors, and stockholders who owned more than 5% of our outstanding common stock and their respective affiliates, in the aggregate, hold shares representing approximately 71% of our outstanding voting stock. As a result, if these stockholders choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders would control the election of directors, the composition of our management and approval of any merger, consolidation, or sale of all or substantially all of our assets. This may prevent a change in our management or discourage unsolicited acquisition proposals or offers for our shares of common stock that you may feel are in your best interest as one of our stockholders.

A significant portion of our total outstanding shares are eligible to be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Moreover, holders of an aggregate of 24,284,625 shares of our common stock have rights, subject to specified 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, until such shares can otherwise be sold without restriction under Rule 144 or until the rights terminate pursuant to the terms of the stockholders' agreement between us and such holders. We also have registered all shares of common stock that we may issue under our equity compensation plans and these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

We are an "emerging growth company," and the reduced disclosure requirements applicable to emerging growth companies 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 until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the date of the closing of our IPO, (b) in which we have total annual gross revenue of at least $1.235 billion, subject to adjustment for inflation or (c) in which we are deemed to be a large accelerated filer, which requires the market value of our common shares that are held by non-affiliates to exceed $700 million as of the last business day of our most recently completed second fiscal quarter, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. For so long as we remain an emerging growth company, we are permitted and intend 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 in the assessment of our internal control over financial reporting;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We have taken advantage of reduced reporting burdens in this Quarterly Report and intend to continue to do so in the future. In particular, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. Further, 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 reduced obligations regarding executive compensation in our periodic reports and proxy statements. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile.

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

We are considered a "smaller reporting company." We are therefore entitled to rely on certain reduced disclosure requirements for as long as we remain a smaller reporting company, such as an exemption from providing three years of audited financial statements and executive compensation information. If we qualify as a smaller reporting company because we meet the revenue limits under the definition of a smaller reporting company, we will be a "low-revenue smaller reporting company." Low-revenue smaller reporting companies are not required to obtain an external audit on the effectiveness of their internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404. These exemptions and reduced disclosures may make it harder for investors to analyze our results of

operations and financial prospects. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock prices may be more volatile.

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

As a public company, and particularly after we are no longer an emerging growth company, we continue to incur significant legal, accounting and other expenses that we did not incur before we became a public company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select 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. Our management and other personnel are devoting a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn 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 predict or estimate the amount of additional costs we may incur or the timing of such costs. These 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.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company or a low-revenue smaller reporting company, 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 Section 404 within the prescribed period, are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we need to continue to dedicate internal resources, engage outside consultants, 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 whether such 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 neither we nor our independent registered public accounting firm, as applicable, will be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. We may discover significant deficiencies or material weaknesses in our internal control over financial reporting, which we may not successfully remediate on a timely basis or at all. Any failure to remediate any significant deficiencies or material weaknesses identified by us or to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we fail to maintain effective internal control over financial reporting and effective disclosure controls and procedures, we may not be able to accurately report our financial results in a timely manner or prevent fraud, which may adversely affect investor confidence in our company.

We are required to comply with the SEC's rules implementing Sections 302 and 404 of the Sarbanes-Oxley Act of 2002, which require management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of our internal control over financial reporting. As an emerging growth company and a low-revenue smaller reporting company, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an emerging growth company or a low-revenue smaller reporting company. At such time, our independent registered public accounting firm may issue a report that is adverse in the event material weaknesses have been identified in our internal control over financial reporting.

To comply with the requirements of being a public company, we have undertaken and will need to undertake additional actions, such as implementing new internal controls and procedures and hiring additional accounting or internal audit staff. Testing and maintaining internal control can divert our management's attention from other matters that are important to the operation of our business. In addition, when evaluating our internal control over financial reporting, we may identify material weaknesses that we may not be able to remediate in time to meet the applicable deadline imposed upon us for compliance with the requirements of Section 404. If we identify any material weaknesses in our internal controls over financial reporting or we are unable to comply with the requirements of Section 404 in a timely manner or

assert that our internal control over financial reporting is effective, or if our independent registered public accounting firm is unable to express an opinion as to the effectiveness of our internal control over financial reporting once we are no longer an emerging growth company, investors may lose confidence in the accuracy and completeness of our financial reports. As a result, the market price of our common stock could be materially adversely affected.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We are continuing to refine our disclosure controls and procedures to provide reasonable assurance that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized, and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline, even if our business is doing well.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We currently have limited research coverage by securities and industry analysts. If any of the analysts who cover us downgrades our common stock or issues an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target preclinical studies or clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Provisions in our amended and restated certificate of incorporation and restated bylaws and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may discourage, delay, or prevent a merger, acquisition, or other change in control of our company 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 market 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 include those establishing:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death, or removal of a director, which prevents stockholders from filling vacancies on our board of directors;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;
- the required approval of the holders of at least two-thirds of the shares entitled to vote at an election of directors to adopt, amend, or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;

- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president, or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

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 a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our amended and restated certificate of incorporation designates specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us.

Our amended and restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders, other than suits brought to enforce any liability or duty created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction and any action that the Court of Chancery of the State of Delaware has dismissed for lack of subject matter jurisdiction, which may be brought in another state or federal court sitting in the State of Delaware. Our amended and restated certificate of incorporation also specifies that unless we consent in writing to the selection of an alternate forum, the federal district courts of the United States shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, or the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above.

We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes or federal judges experienced in resolving Securities Act disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees, and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees, or agents and result in increased costs for stockholders to bring a claim. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our amended and restated 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 adversely affect our business, financial condition, or results of operations.

Our ability to use our net operating loss carryforwards and other tax attributes to offset future taxable income may be subject to certain limitations.

As of December 31, 2023, we had U.S. federal and state net operating loss carryforwards, or NOLs, of $187.4 million and $180.4 million, respectively, which may be available to offset future taxable income, if any. As of December 31, 2023, we also had federal and state research and development credit carryforwards of $12.4 million and $4.9 million, respectively. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change by value in its equity ownership over a rolling three-year period, is subject to limitations on its ability to utilize its pre-change NOLs and its research and development credit carryforwards to offset future taxable income. Our existing NOLs and research and development credit carryforwards may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change, our ability to utilize NOLs and research and development credit carryforwards could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, some of which might be beyond our control, could result in an ownership change under Sections 382 and 383 of the Code. For

these reasons, we may not be able to utilize a material portion of the NOLs or research and development credit carryforwards even if we attain profitability.

General Risks

Our business and operations may suffer in the event of information technology system failures, deficiencies, or intrusions which could materially affect our results.

Our information technology systems, as well as those of our CROs and other contractors and consultants, are vulnerable to failure or damage from computer viruses and other malware (e.g., ransomware), unauthorized access or other cybersecurity attacks, natural disasters (including hurricanes), terrorism, war, fire, and telecommunication or electrical failures. In the ordinary course of our business, we directly or indirectly collect, store, and transmit sensitive information, including intellectual property, confidential information, preclinical and clinical trial information, proprietary business information, personal information, and health-related information of our clinical trial subjects 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 human error (e.g., social engineering, phishing), a technical vulnerability, malfeasance, or other disruptions. The risk of a security breach or disruption, particularly through cyber-attacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. We may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. We may not be able to anticipate all types of security threats, nor may we be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations, or hostile foreign governments or agencies. Even if we identify security incidents, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. We cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, or breaches in our systems or those of our CDMOs, CROs and other contractors and consultants.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or our critical third parties' operations, it could result in a material disruption of our product candidate development programs, our operations and ultimately, our financial results. For example, the loss of preclinical studies or clinical trial data from completed, ongoing, or planned studies or trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that 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 incur liability and the further development of our product candidates could be delayed. Any such material security breach could compromise our information technology systems 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. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

We or the third parties upon whom we depend may be adversely affected by natural disasters or pandemics and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters or pandemics could severely disrupt our operations and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage, pandemic or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities on which we rely, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price.

The global economy, including credit and financial markets, has recently experienced extreme volatility and disruptions, including, for example, severely diminished liquidity and credit availability, rising interest and inflation rates, crises involving banking and financial institutions, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets continue to deteriorate, or the United States enters a recession, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. In addition, there is a risk that one or more of our CROs, suppliers, CDMOs, or other third-party providers may not survive an economic downturn or recession. As a result, our business, results of operations and price of our common stock may be adversely affected.

The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.

There has been increasing public focus by investors, patients, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, even if we are effective at addressing such concerns, we may experience increased costs as a result of executing upon our sustainability goals that may not be offset by any benefit to our reputation, which could have an adverse impact on our business and financial condition.

In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, would be your sole source of gain.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain all available funds and future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies 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 resources, which could harm our business.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.

None.

Item 3. Defaults Upon Senior Securities.

Not Applicable.

Item 4. Mine Safety Disclosures.

Not Applicable.

Item 5. Other Information.

a) Disclosure in lieu of reporting on a Current Report on Form 8-K.

None.

b) Material changes to the procedures by which security holders may recommend nominees to the board of directors.

None.

c) Insider Trading Arrangements and Policies.

During the third quarter of 2024, no director of officer, as defined in Rule 16a-1(f) of the Exchange Act, adopted or terminated a Rule 10b5-1 trading arrangement intended to satisfy the affirmative defense of Rule 10b5-1(c) or a “non-Rule 10b5-1 trading arrangement,” as defined in Item 408 of Regulation S-K.

Item 6. Exhibits.

Exhibit Number	Description	Incorporated by Reference			Filing Date	Filed/ Furnished Herewith
		Form	File No.	Exhibit		
3.1	Restated Certificate of Incorporation of Omega Therapeutics, Inc., dated August 3, 2021 and Certificate of Amendment to the Restated Certificate of Incorporation of Omega Therapeutics, Inc., dated June 20, 2024.	8-K	001-40657	3.1	06/24/2024	
3.2	Amended and Restated Bylaws.	8-K	001-40657	3.1	12/11/2023	
4.1	Specimen Certificate of Common Stock.	S-1/A	333-257794	4.2	07/26/2021	
4.2	Amended and Restated Investor Rights' Agreement, dated March 4, 2021.	S-1/A	333-257794	4.1	07/26/2021	
4.3	Amended and Restated Warrant to Purchase Stock issued to PacWest Bankcorp, dated September 30, 2019, to purchase Series A preferred stock.	S-1/A	333-257794	4.3	07/26/2021	
10.1	Amended and Restated Shared Space Arrangement by and between Omega Therapeutics, Inc. and Apriori Bio, Inc., effective September 1, 2024.	8-K	001-40657	10.1	08/30/2024	
10.2	Amended and Restated Shared Space Arrangement by and between Omega Therapeutics, Inc. and Metaphore Biotechnologies, Inc., effective September 1, 2024.	8-K	001-40657	10.2	08/30/2024	
10.3	Amended and Restated Shared Space Arrangement by and between Omega Therapeutics, Inc. and Prologue Medicines, Inc. (formerly Flagship Labs 89, Inc.), effective September 1, 2024.	8-K	001-40657	10.3	08/30/2024	
10.4	Shared Space Arrangement by and between Omega Therapeutics, Inc. and Flagship Labs 101, Inc., effective September 1, 2024.	8-K	001-40657	10.4	08/30/2024	
10.5	Shared Space Arrangement by and between Omega Therapeutics, Inc. and Flagship Labs 104, Inc., effective September 1, 2024.	8-K	001-40657	10.5	08/30/2024	
10.6	Third Amendment to Lease Agreement, dated July 31, 2024 between Omega Therapeutics, Inc. and ARE-MA Region No. 94, LLC.	10-Q	001-40657	10.10	08/06/2024	
10.7	Shared Space Agreement, dated August 1, 2024 by and between Omega Therapeutics, Inc. and Flagship Labs 97, Inc.	10-Q	001-40657	10.8	08/06/2024	
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a)/15d-14(a).					*
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a)/15d-14(a).					*
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350.					**
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350.					**
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because 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 (embedded within the Inline XBRL document)	*

* Filed herewith.
** 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.

Omega Therapeutics, Inc.

Date: November 14, 2024

By: /s/ Mahesh Karande

Mahesh Karande
President and Chief Executive Officer
(Principal executive officer)

Date: November 14, 2024

By: /s/ Barbara Chan

Barbara Chan
Chief Accounting Officer and Senior Vice President, Finance
(Principal financial and accounting officer)

Exhibit 31.1

CERTIFICATIONS

I, Mahesh Karande, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Omega 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 14, 2024

By: /s/ Mahesh Karande

Mahesh Karande
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATIONS

I, Barbara Chan, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Omega 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 14, 2024

By: /s/ Barbara Chan

Barbara Chan
Chief Accounting Officer and Senior Vice President, Finance
(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 of Omega Therapeutics, Inc. (the "Company") on Form 10-Q for the period ended September 30, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Mahesh Karande, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(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 14, 2024

By: /s/ Mahesh Karande
Mahesh Karande
President and Chief 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 of Omega Therapeutics, Inc. (the "Company") on Form 10-Q for the period ended September 30, 2024, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Barbara Chan, Chief Accounting Officer and Senior Vice President, Finance of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(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 14, 2024

By: /s/ Barbara Chan

Barbara Chan
Chief Accounting Officer and Senior Vice President, Finance
(principal financial officer)